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The Founding Fathers' Self-Reflections and Creations: How the Union was Saved By
Shaoqing Ni

In the period of time following the American Revolution, the new union of the United States faced a tumultuous period of time known as the Critical Period (roughly 1780-1789). During the Critical Period, the very basis of the union started to crumble due to a variety of seemingly unrelated problems and flaws such as the inability to collect taxes, lack of unity between states, and lack of power in the federal government (*The Vices of the Political System of the United States*). The symptoms of the problems showed themselves as an unsatisfied farmer and war veteran population, lack of foreign relation power, and difficulty in inter-state trading (in-class discussion). Finally, Shays' Rebellion was the final straw for the Founding Fathers, since they finally felt the need to write a brand new constitution and create a new government (in class discussion). The governing body, as well as the constitution devised by the founding fathers, solved the issues of misrepresentation and tyranny of the majority by providing checks and balances, creating a senate that equally represents all societal classes, and relying on the stakeholder theory as a basis of the government.

Madison suggested that the problems such as debt, inability to collect tax, lack of power in the federal government and lack of unity between states should be resolved from its roots. Towards the ending of *The Vices of the Political System of the United States*, Madison suggests that what seemed like a list of unrelated problems could be boiled down to 2 causes. The first of which lies in the Representative bodies of the government during the Critical Period. He describes that the representative bodies of the Articles of Confederation are not perfect since their members are "sought by ambition, personal interest and public good"(*The Vices of the Political System of the United States*). Although "public good" is a good way to choose these representatives, the first two are much more prevalent in the election of representatives. This would mean that those who have a common interest in the confederation Congress would gather together and "join in a perfidious sacrifice of [the public good] to [the ambition and personal interest]" instead of focusing on making the needs of the people satisfied. The focus on the personal ambition instead of public good makes the government an inaccurate representation of both the social classes of the US and the people's interests (*The Vices of the Political System of the United States*). Another more fatal and widespread cause lies among the people of the United States, according to Madison. He demonstrates that there are simply too many factions of people within the United States, such as the rich, the poor, the merchants, and the manufacturers, to name a few. Therefore, a congregation of several of the more powerful factions could lead to the leaving out of the interests of the minorities, which would lead to the tyranny of the majority and no proper way of representing the common interest of the minority (*The Vices of the Political System of the United States*). Furthermore, in a Calvinistic and Realist way, he points out that human selfishness will stop societal values such as respect, communal good, and religion from restraining the tyranny of the majority from happening (Hofstadter). Thus, Madison explained that the root of the problems during the Critical Period stems from the representatives being

selected for their own ambitions instead of for the public interest, and the majority's ability to always preside over the opinions of the minority.

Thus, after understanding the points made by Madison, the founding fathers of the United States of America solved the problem from the basics. The first cause of the problems in the Critical Period that they addressed was the problem with representation of all social classes. The founding fathers realized that opting for a true democracy would not be optimal since there are unstable opinions that could be made into laws, while a representative democracy would have wiser people chosen by the masses to make educated decisions on behalf of the people for the good of the country. However, Representative Democracy also needs to be deliberately set up in a way or else it will not be able to fully represent certain social classes and their interests. Therefore, the Constitution set up a new Congress made up of the house of representatives and the senate. The house of representatives was designed to represent the people's interests, and their members are elected by the people every 2 years. On the other hand, the senate was originally designed to be representative of the state's and the elites' interests, and the senators are elected originally by state legislatures every 6 years, surpassing the president's term because only then will the senate not be affected by the president's interests (based on in class discussion and Constitution of the United States). The careful balancing of the power of the Senate and the power of the house of representatives allows for equal representation of the classes and allows the opinions of the majority of the population to be heard and acted upon.

Another minor cause of the problems that was fully resolved was the possibility of representatives serving for their own ambitions rather than for the benefit of the nation. The solution provided was to base the government on Stakeholder theory. The Stakeholder theory explains that as long as the government officials have a "stake" in the rise and fall of the nation, or will gain or lose based on how well they manage it, they will do their jobs well. The founding fathers argued that the possession of moderate plots of property gave them sufficient stake in society, and by reason, the elites who own large plots of property have even greater stakes, essentially making their own gain or loss aligned with those of the country.

The most fatal cause of problems during the Critical Period that the Constitution and the modern government removed was the possibility of tyranny of the majority and tyranny in general. Madison stated during *The Vices of the Political System of the United States* that the human's vice and selfishness cannot be restrained by the societal ideas of protecting collective ideals and respect of character(*The Vices of the Political System of the United States*). Thus, in a realist manner, they decided that if no one has the virtue to counter the vices, then the vices shall be used to counter the vices. They set up a "balanced government", an idea as old as Aristotle and the ancient greeks. Not only is the Congress able to represent the interests of the state, the elites, and the lower classes equally, but a the founding fathers also set up 3 branches of government to counteract each other's power and prevent tyranny by majority by providing several safety nets by following Montesquieu's Theory of Separation of Power (Hofstadter). For example, the Legislative branch has the power to make laws, but they are checked by the president, who could immediately veto each law, preventing them from being enacted unless

Congress passes it with ⅔ votes. In addition, the Supreme Court later gained the ability to judge the rightfulness of laws based on the constitution. Another example is that when the legislative branch declares war, the executive branch will manage the army and participate in the war. Therefore, by installing safety nets and giving veto powers to different branches, the threat of tyranny of majority is contained as the decision of one of the branches has a chance of not being the final one (Constitution of the United States).

In conclusion, the variety of problems brought up during the Critical Period was organized into two causal flaws in the system: the representatives not addressing the public's needs and instead focusing on personal ambitions, and the majority's opinion drowning out those of the minority. The founding fathers tackled these problems by creating a Constitution and a government based on the Stakeholder theory that not only included a Congress that equally represented the needs of the lower classes, elites, and the state, but also included checks and balances to prevent the occurrence of tyranny or tyranny by majority. This would prove to be a successful government that brought the nation out of the critical period and eventually shaped the nation into one of the most powerful in the world.

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Possible Causes and Treatments for Alzheimer's Disease By Kyra Wang

Author Biography

Kyra Wang lives in New York and is currently enrolled as a junior at Brooklyn Technical High School. Her academic pursuits are driven by an interest in pursuing a career in medicine, which has influenced her decision to publish this research paper. Beyond her academics, Kyra also enjoys engaging in a variety of interests, including ice skating, artistic expression through drawing or painting, and listening to music.

Abstract

As the cases of Alzheimer's Disease (AD) increase worldwide, it is important to spread awareness about the possible causes and understand the early signs of AD development. AD is a pressing public health concern, affecting millions worldwide. Tracking AD includes the use of biomarkers such as amyloid beta and tau proteins for early diagnosis and monitoring. Advanced modeling techniques and tools like the AD Course Map are improving our understanding of AD progression and clinical assessment. Through these markers, we can outline the various factors that may impact the development of AD such as air pollution, lifestyle choices, and genetic factors. Many treatment strategies are evolving, by experimenting with disease-modifying therapies and innovative therapies like recollection-based occupational therapy programs. Other designs, such as the Global Deterioration Scale for People with Down Syndrome (GDS-DS), are designed to monitor AD in specific at-risk populations. There are continuous efforts to combat AD and offer hope for more effective strategies for the future.

Introduction

Alzheimer's Disease (AD) is the most common dementia type, affecting around 10% of the elderly population in the United States. According to WHO (World Health Organization), over 55 million people suffer from dementia and 60%-70% of these cases are AD. This disorder can affect patients' cognitive abilities, which can negatively impact their livelihood. Therefore, it's crucial to advance our methodology to distinguish AD and find potential treatments. AD is generally associated with memory loss and cognitive impairment, but it can also impact other cognitive functions, behavior, and emotions. The exact cause of AD is not fully understood, but age, genetics, and certain environmental factors are believed to play a crucial role (Swanson et al., 2021). Currently, there is no cure for AD, but treatments and interventions can help manage symptoms and improve the quality of life for affected individuals.

Common findings in patients with AD

There are new treatments that require different approaches to identify and treat patients early. AD progresses from pathophysiological changes which are affected by patients' independent experiences. Some examples of AD characteristics are the build-up of tau protein, amyloid B proteins, which is a plaque in the brain that causes cells to die, and tau proteins

forming tangles that harm brain cells. Undiagnosed patients may not have prior symptoms or have different/mild levels of cognitive disorders. AD may progress and additional symptoms may occur such as confusion, disorientation, mood changes, aggression, and even delusions in later stages (Chen et al., 2023). However, because normal aging also has cognitive deterioration, it's hard to distinguish between AD and normal aging. This will challenge experts' abilities to diagnose and often may lead to underdiagnosis. In fact, over half of the individuals who have AD are never formally diagnosed.

Some studies even suggest that environmental factors can increase AD's progression. In a study that observed over 400,000 participants over 12 years and provided evidence that higher levels of air pollution, more specifically PM2.5 (particulate matter with diameters ≤ 2.5 nm) and NOx (nitrogen oxides), were associated with an increased risk of various types of dementia, including AD. Additionally, they found that those with a high genetic risk for AD who were exposed to higher levels of NOx had an increased risk of developing AD (Yuan et al., 2023). This study demonstrates the importance of reducing air pollution, which may be a potential factor in lowering the risk of dementia.

Another study showed the involvement of oxidative stress, neuroinflammation, and protein aggregation due to pollution, which could make the general public more vulnerable to AD. However, it's been suggested that more research should be done to understand the relationship between pollutants and AD. Impaired insulin signaling may also contribute to the development and progression of AD. Insulin is not only involved in glucose regulation but also plays an important role in brain function, including memory and cognitive processes. Insulin resistance, which is usually associated with type 2 diabetes, reduces the effectiveness of insulin signaling in cells, leading to increased blood glucose levels (Nguyen et al., 2020). The impact of insulin resistance on brain health can lead to various harmful effects. One of the key mechanisms is the disruption of the brain's insulin-regulated pathways, which are essential for neuronal growth, plasticity, and synaptic function. Insulin resistance also promotes neuroinflammation, oxidative stress, and the accumulation of toxic proteins such as amyloid-beta and tau, hallmark features of AD.

Usage of Biomarkers and Possible Treatments

Many studies have stated that amyloid B proteins are a cause of AD. Scientists gave doses of lecanemab, an anti-Aβ protofibril antibody targeting amyloid B proteins, to show the effectiveness of subjects. A study used a Bayesian adaptive design to analyze the effects of lecanemab on the subjects and had 12-month marks as well as 18-month marks to show the effectiveness of this design (Swanson et al., 2021). The participants were divided into two groups: people with mild cognitive impairment due to AD and those with mild AD dementia. They showed memory problems, which are measured by an MMSE score, which measures a patient's cognitive status, of 22 or higher at screening and baseline. The end goal was to see how things changed after 12 months using a measure called ADCOMS, which tracks cognitive changes. They also looked at brain amyloid levels after 18 months using a special scan in some

participants. They checked other factors like memory and biomarkers to compare the effects of the drug with placebo after 18 months for different groups of people (Swanson et al., 2021). Although there were a lot of limitations within this study, lecanemab reduced cognitive decline compared to a placebo and reduced brain amyloid levels, showing positive effects on biomarkers in cerebrospinal fluid. These results show the effectiveness of this drug.

Another paper looked at the correlation between DNA methylation levels in blood and the progression of AD (Li et al., 2021). DNA methylation is an epigenetic modification that can influence gene expression and play a role in various biological processes, including AD. The study involves collecting peripheral blood samples from individuals at different stages of AD progression. DNA methylation profiles within these samples are then analyzed to identify any alterations that may be linked to disease progression. The objective of the research is to determine whether specific DNA methylation changes in peripheral blood are indicative of the severity or advancement of AD. If significant associations are found, these changes could potentially serve as biomarkers for tracking disease progression, aiding in early diagnosis and monitoring. They found areas in genes that were different in people who had more memory problems and correlated these changes to AD genes (Li et al., 2021). The findings of the study could help with future understanding of the epigenetic factors involved in AD and for developing non-invasive methods to assess disease progression. However, there were some challenges during the process.

Another method of biomarkers to help trace AD is using serum tau proteins as indicators for tracking the progression of AD (Nam et al., 2020). The study looks at whether changes in tau protein levels within the bloodstream could function as reliable biomarkers, reflecting the advancement of the disease. Tau proteins are closely linked to the development of neurofibrillary tangles, a hallmark feature of AD. The accumulation of tau in the brain is associated with neuronal degeneration and cognitive decline. This investigation centers on quantifying tau protein concentrations in blood serum, which could potentially mirror analogous changes occurring in the brain. The study collects serum samples from individuals at varying stages of AD progression. These samples are analyzed by concentrations of tau proteins. By comparing the levels of serum tau proteins with the progression of the disease, the study establishes whether these proteins can accurately signify the severity and evolution of AD. The scientists discovered that tau proteins in tiny particles, which are called exosomes, in the blood were better at showing AD progression. The exosome tau levels could predict disease status more accurately. They suggested that these could carry harmful proteins from the brain to the blood. However, there are variations in tau protein levels, and serum tau proteins as biomarkers for AD progression could show significant implications for relatively early diagnosis, disease tracking, and evaluating treatment outcomes.

Changes in the connectedness of the brain as AD progresses. The research focuses on understanding how the dynamic interactions between brain regions are affected during the progression to AD. The connectome, which shows the networks of the brain, is a time-varying functional pattern between different brain regions. It provides insights into how different brain

areas communicate and collaborate to support cognitive functions. This study investigates how these connections change as AD develops. They analyze neuroimaging data, such as fMRI, from individuals at different stages of AD progression. They track alterations in the dynamic interactions and connectivity patterns of the brain's chronnectome over time. The study's goal is to identify specific changes in the connectedness of the brain's chronnectome that are associated with the progression to AD. By analyzing these alterations, researchers aim to understand how the disruption of functional connectivity contributes to cognitive decline and the development of AD-related symptoms (Ghanbari et al., 2022). The findings of the study could help our understanding of the neural mechanisms underlying AD progression. If significant changes in the brain's connectome are identified, it could offer insights into potential biomarkers and therapeutic targets for early diagnosis and intervention.

Another recent study shows the changes in gray matter volume within the cerebellum as AD progresses and helps identify specific patterns in the cerebellum throughout different stages of AD. The study uses neuroimaging techniques like MRI to visualize and measure the volume of gray matter in the cerebellum. Gray matter is a common feature in AD and it is associated with cognitive decline. The research aims to uncover how the cerebellum is affected by AD progression, the cerebellum is associated with motor coordination but also plays a role in cognition (Toniolo et al., 2018). By examining patterns of gray matter loss in this brain region, the study seeks to determine whether the cerebellum's degeneration is consistent or varies across different stages of AD. The findings of the study could give insight into the relationship between the cerebellum and cognitive decline in AD.

Neuroinflammatory markers, chitinase, and pentraxin are used in the frontal cortex as AD progresses. Chitinase and pentraxin are proteins found to be associated with neuroinflammatory processes in the brain, leading to AD pathogenesis. Neuroinflammation is a key feature of AD and plays a role in the progression of the condition. A study analyzes tissue samples from the frontal cortex of individuals at different stages of AD. These samples are collected and the goal is to measure the levels of chitinase and pentraxin in the brain tissue and determine how these levels change as the disease progresses. The research aims to identify specific alterations in chitinase and pentraxin levels that correlate with the stages of AD progression. By studying these neuroinflammatory markers, the researchers can better understand how neuroinflammation occurs in the development and progression of AD (Moreno-Rodriguez et al., 2020). The findings can provide beneficial information into the role of chitinase and pentraxin in neuroinflammation during AD progression. If there are changes in these markers observed, it could contribute to our understanding of the disease and even lead to the development of targeted therapies or diagnostic tools.

Tracking AD

A recent study has shown an approach to model the progression of AD by using multiple data sources. The method combines recurrent neural networks, variational autoencoders, and multiple data channels to enhance the accuracy of disease progression modeling. This focuses on

multimodal data, which includes various types of information like imaging, clinical, and demographic data, to better understand and predict AD progression. They propose a Multi-channel Recurrent Variational Autoencoder (MC-RVAE), a sophisticated neural network architecture, to help track the progression of AD. The MC-RVAE combines two key components: recurrent neural networks (RNNs) and variational autoencoders (VAEs). RNNs capture temporal patterns and dependencies within data sequences, which is important for modeling disease progression over time. VAEs provide a rough framework that allows for capturing structures within the data, helping in feature extraction and generation. The paper also talks about how MC-RVAE is designed to use multiple data sources at the same time, providing different types of information. This enables the model to see complex relationships and interactions across various modalities, leading to improved disease progression predictions. The research was effective on the MC-RVAE approach by applying it to AD progression modeling using multimodal data (Tahami et al., 2022). The results show enhanced predictive capabilities compared to other methods, emphasizing the potential of integrating diverse data sources for a more comprehensive understanding of disease evolution.

In a different study, researchers were able to chart the progression of AD over time. This map provides a comprehensive and visual representation of the stages and key milestones of AD as the condition advances. The AD Course Map is designed to help clinicians, researchers, and caregivers understand the typical trajectory of the disease. It may include various stages, such as preclinical, MCI, and different stages of dementia. The map gives cognitive, functional, and behavioral changes that occur as the disease progresses (Koval et al., 2021). With this tool, people can gain insights into the typical patterns of decline in memory, reasoning, language, and other cognitive functions. It also shows how these cognitive changes impact a person's daily activities and behavior.

Potential Therapies and Treatment

Referring to an earlier study, because of the founded information, researchers were able to test by studies disease-modifying treatment, which can help treat the disease before it causes irreversible damage to the brain, but for this to be accurate, the patient needs to be diagnosed, which can be quite challenging as previously mentioned. It is also commonly known that AD is a brain condition causing memory problems and is caused by abnormal proteins and cell damage. Another study looked at compounds from a coral fungus to see if it can help with inflammation in AD. There may be potential between benzaldehyde compounds derived from *Aspergillus terreus* C23-3 to decline neuroinflammation and neuronal damage to slow down the progression of AD. The researchers aimed to understand the mechanisms behind the compounds' effects on AD-related processes. The paper showed that these benzaldehydes exhibit beneficial effects in reducing neuroinflammation and protecting neurons. Neuroinflammation and neuronal damage are key factors in the development and progression of AD. The compounds' mechanisms of action involve making immune responses and preventing cellular damage in brain cells.

In a therapy program on people with AD, the research has a randomized controlled trial design to investigate the effects of this therapy program on various aspects of AD patients. This program involves engaging participants in activities that encourage recollection and memory recall, which are areas affected by AD. The therapy's goals are to increase the cognitive functioning, emotional well-being, and functional abilities of people with AD. They randomly assigned participants to two groups: one that receives the recollection-based occupational therapy program and another that serves as a control group, receiving standard care or an alternative intervention. By comparing the outcomes of both groups, the researchers aim to determine whether recollection-based therapy has a significant impact on AD patients. The results included cognitive improvements, emotional well-being, functional abilities, and potentially the overall quality of life for participants (Kim et al., 2020). This means that there is potential for a recollection-based occupational therapy program for people with AD. If the therapy is effective, it could offer an important approach to addressing cognitive challenges linked with AD.

Another study has discovered an AD tracker, specifically designed for people with Down syndrome. It's called the GDS-DS (Global Deterioration Scale for People with Down Syndrome) and it is composed of different stages that correlate to different stages of cognitive decline and functional impairment, mirroring the progression of AD. This will help clinicians and researchers track the deterioration of cognitive abilities, memory, language, and everyday activities over time in individuals with Down syndrome who are also affected by AD. This is an important study because people with Down syndrome are at a higher risk of developing AD. The GDS-DS helps in early detection, accurate monitoring, and understanding of the unique course of AD in this specific population.

Conclusion

AD is the most common form of dementia affecting the elderly and is a significant public health concern around the globe. With over 55 million individuals affected by dementia, 60%-70% of which is attributed to AD, according to WHO, it is important to enhance our understanding and management of this condition. AD primarily manifests as memory loss and cognitive decline, eventually impacting various cognitive functions, behavior, and emotions. While the exact cause remains unclear, age, genetics, and environmental factors are implicated. However, distinguishing AD from normal aging proves challenging due to overlapping cognitive deterioration.

Several studies are advancing novel approaches for early detection and treatment of AD. Promising biomarkers such as amyloid B proteins and tau proteins, DNA methylation, and serum tau levels are being explored to aid in diagnosis and progression monitoring. Neuroinflammation, oxidative stress, protein aggregation, and impaired insulin signaling have been associated with AD development. Notably, environmental factors like air pollution, particularly PM2.5 and NOx, are linked to increased AD risk, emphasizing the importance of reducing pollution. New approaches are emerging for AD progression modeling. MC-RVAE uses different data sources,

offering a more comprehensive understanding of disease evolution. Another research effort involves charting AD progression using an AD Course Map, which depicts cognitive, functional, and behavioral changes at various stages. Additionally, treatments are being explored, including disease-modifying therapies (DMTs) that target the underlying mechanisms of AD, and recollection-based occupational therapy programs that enhance cognitive function and emotional well-being. Tailoring methods to specific populations, a study introduced the GDS-DS tracker to monitor AD in individuals with Down syndrome, who are at an elevated risk. This tracker helps in the early detection and monitoring of AD's unique course in this population. These research initiatives help aim to improve our knowledge of AD, refine early detection methods, and develop effective interventions for both the general population and specific subgroups like those with Down syndrome. Cases of AD are bound to increase in the coming years and it's essential for the general public to not only remain aware of the potential risks and causes of AD but also understand that some potential treatments and therapies have effective results.

Acknowledgments
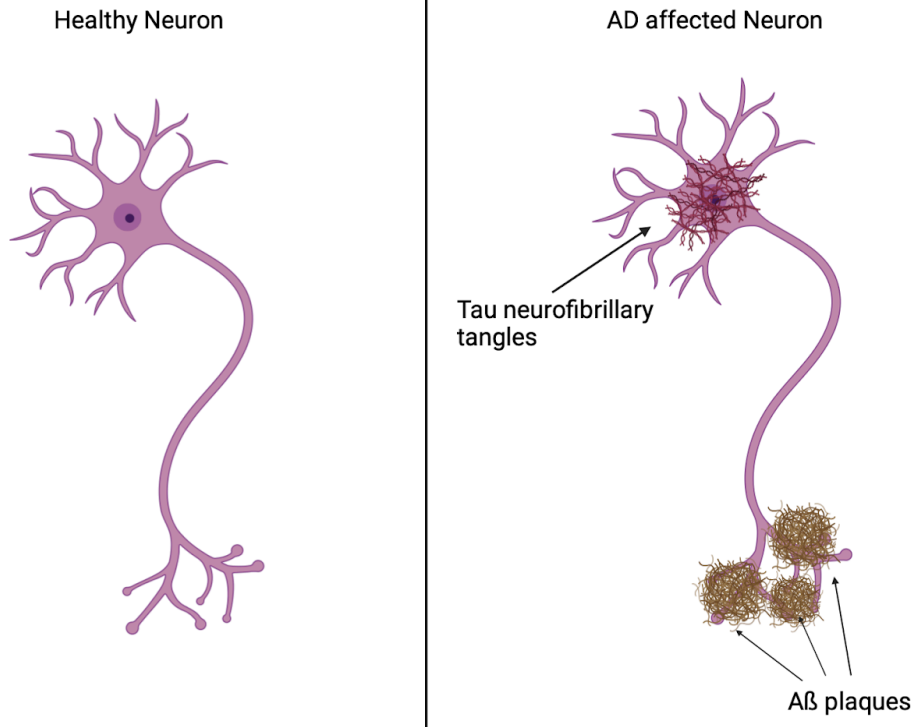
Figure 1. Tau neurofibrillary tangles and amyloid plaques compared to a healthy neuron.

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How can the CRISPR-Cas9 gene editing system be implemented to alleviate and treat major depressive disorder? By Jiaxin Gu

Abstract

Rates of major depressive disorder have continuously risen over the years and depression has become one of the leading causes of disability worldwide. Numerous studies and experiments have been done recently reviewing the biological mechanisms that underlie cognitive aspects of depression. With the continuous advancements and refinement of the genome-editing tool CRISPR-Cas9, we propose how the genetic associations of major depressive disorder and discoveries of risk SNPs can be leveraged as a practical therapeutic method to alleviate depression. Gene therapy for such psychiatric disorders is presented as a prospective goal for researchers in this review and several potential approaches are demonstrated; however, there are still a substantial amount of clinical and regulatory issues to be addressed and overcome before such therapies can be implemented.

Key words:
CRISPR, depression, major depressive disorder, genetics of depression, GWAS, gut-brain axis, SNPs, Cas9 nuclease

1.0: Introduction to MDD

Now a third leading cause of years lived with disability worldwide (Mullins, 2017), Major Depressive Disorder (MDD) is a complex disease thought to arise from multiple factors, including changes in physiologies, genetics, protein regulation, and environmental causes (Drevets, 1998)**.** A loss of interest characterizes a low mood, diminished cognitive performance, stress and anxiety, and sleep disturbances. Due to its high prevalence with around 6% of adults worldwide affected (Curtin & Ahmad, 2022), depression is recognized as contributing significantly to the global disease burden. This incapacitating disorder, resulting from emotional, memory, and cognitive impairment, also accounts for a significant share of absences from work, a diminished quality of life, poor physical health, and suicide deaths. With MDD projected to become the number one health concern by 2030, (Herselman et al., 2022) the rate of diagnosis for MDD has subsequently increased, making it imperative for extensive research into the underlying causes and potential treatments to meet the increasing pervasiveness.

The Global Burden of Disease (GBD) statistics for 2020 show that subsequent lockdowns and COVID-19 resulted in a 27.6% rise in MDD cases compared to the previous year (L. Liu et al., 2022). By improving our knowledge of the causes of depression, the general public can yield a more thorough and nuanced understanding of this multidimensional and debilitating disorder (Disner et al., 2011). Moreover, it is now a top objective for scientific study into multiple aspects of this disorder, such as the genetic associations of depression using techniques such as the Genome-wide association studies (GWAS) (Mullins, 2017) and alterations or disruption of neurotransmitters and proteins involved in signaling between neurons (Han et al., 2017). A twin

study performed by Sullivan et al. (2000), helped scientists better understand the genetic basis of this disease, obtaining a result of an estimated heritability of 37%, implying that there is a genetic variable to depression. The genetic cause of this disease was investigated by implementing GWAS and documenting a list of common single nucleotide polymorphisms (SNPs) associated with an increased risk for depression. Single nucleotide polymorphisms in a gene are variants in the DNA code where one nucleotide base is replaced with another one, and these genetic changes sometimes alter the expression of a protein, acting as a biological marker and often lowering the efficiency of transcription, affecting its function, and abating the expression of a gene (Gunter, 2023). On other occasions, a SNP within a gene's coding region may change the protein's amino acid composition, leaving the expression unchanged, but the function of the protein may be compromised. In a pathological context, the meaningfulness of these changes by SNPs can be challenging to elucidate. The effect could vary from a minor scale to essentially salient consequences induced. Researchers indicated that the genetic links of depression might have contributed to its development and predisposition (Hasin et al., 2005). Similarly, given GWAS studies had already identified a list of potential SNPs and genes affiliated with depression, researchers were able to develop an improved comprehension of the molecular mechanisms of major depressive disorders. This enables gene editing or CRISPR strategy to eradicate some of these genetic anomalies and aberrations that contribute to depression. In short, there has been recent evidence for genetic links to depression. We will provide an overview of the cognitive model of depression in the following sections and dive further into genes associated with this debilitating disorder.

In this paper, through evaluation of recent trends of depression rates and prospective studies in this field, I explain of the psychological and genetic determinants of major depressive disorder, examine the applications of the genome editing tool CRISPR-Cas9, and provide suggestions for the application of CRISPR to edit the microbiome. Lastly, I will also address potential hindrances and obstacles to pursuing experimental trials using CRISPR and propose apt resolutions.

1.1: Cognitive model of depression

According to Mayberg (2003), depression is a multidimensional, systems-level disorder that stems from limbic cortical dysregulation. The pathophysiology of this neuropsychiatric disorder is yet to be fully understood, as interactions between environmental factors, genetic associations, and the underlying neurobiology intertwine to bring about the dysfunctions (Herselman et al., 2022). Clinical patients with MDD have a divergent cognitive model with biased attention to emotional stimuli (Disner et al., 2011). Individuals show a distorted attentional bias for sad stimuli and cannot disengage from negative stimuli. This perpetuates a positive feedback loop of depressive symptoms as patients tend to exacerbate symptoms of dysphoria.

Biased processing due to schema activation of depression patients alters emotion and memory processing and elevates self-referential processing while reducing top-down inhibition of the process stimulating ruminative thoughts (Disner et al., 2011). Moreover, Aaron Beck's proposed cognitive model of depression presents a third element—biased thoughts and rumination. Depression symptoms are suggested to be brought by internalizing negative emotional stimuli and allowing unfavorable life experiences to negatively impact one's self-esteem and self-image (Beck 1964). Further ruminative patterns of thought reinforce depressive symptoms; these mechanisms are facilitated by variances in several parts of the brain. A comparison between the behaviors exhibited in healthy individuals versus MDD patients is displayed in *Table 1*. Some of these disparities includes the sustained amygdala, hippocampal activation (prolonging emotional experience), increase in Medial Prefrontal Cortex (MPFC) activity, and alteration in rostral ACC function (anterior cingulate cortex), causing failed inhibition of negative emotional stimuli. Numerous lines of research point to evidence suggesting the presence of altered mechanisms in the brain of MDD patients, consequently increasing the salience of negative stimuli compared to positive ones. These changes, in turn, trigger biased attention, biased processing, biased thoughts and rumination, and biased memory, leading to more frequent and severe depressive episodes (Gunter, 2023).

Healthy individuals	MDD Patients	Category of Behavior
Normal activity in right VLPFC, right DLPFC, right superior parietal cortex, leading to sufficient attentional disengagement	Right superior parietal, right DLPFC, and right VLPFC showed reduced activity, which prevents emotional disengagement from unpleasant stimuli. As a result, there is insufficient attentional disengagement, and attention is focused on stimuli with a *negative* valence.	Biased attention
Greater activity in the rostral anterior cingulate cortex (ACC) when successfully inhibiting attention-*positive* stimuli. More cognitive effort is required to divert attention away from positive stimuli.	Greater activity in the rostral ACC when successfully diverting attention to *negative* stimuli. Thus, it requires more cognitive effort to divert attention from unfavorable and negative stimuli.	Biased attention

Normal amygdala reactivity that increases during the processing of emotional information but has an inverse relationship with left DLPFC activation, which is suggested to represent a system of higher-order cognitive intervention.	Up to 70% more intense and up to three times as long-lasting amygdala reactivity than in healthy controls. Faster and increased amygdala response is associated with quicker processing of *negative* stimuli and decreased levels pf psychological well-being. Because of this, MDD patients not taking antidepressants, which have displayed a diminished extent of amygdala reactivity to *negative* stimuli, are more likely to attend to negative stimuli but also experience a stronger and longer-lasting neural response to these stimuli. Increased amygdala reactivity generates bottom-up signals that skew higher cortical areas' processing of emotional stimuli. This maladaptively changes how people view their environment and social interactions.	Biased attention

Functional and normal cognitive control over the amygdala is associated with bilateral DLPFC. Which, for example, includes grey matter volume, resting state activity, and reactivity to both *positive* and *negative* stimuli.	Reduced cognitive control over the amygdala in conjunction with abnormal activation in the bilateral DLPFC may contribute to the persistence of perception of *negative* information. Issues like decreased grey matter volume, lower resting-state activity, and decreased sensitivity to both *positive* and *negative* stimuli are brought on by anatomical and functional abnormalities in the DLPFC. The detachment of left DLPFC and amygdala activation results from these anomalies.	Biased processing
Normal functioning of both *right DLPFC and left DLPFC* which results from sufficient cognitive control and adequate levels of amygdala reactivity.	The right DLPFC's hyperactivity, frequently observed alongside left DLPFC hypoactivity, is linked to the anticipation of negative stimuli and may bias attentional resources towards emotional stimuli. Reduced cognitive control is associated with altered function bilaterally in the DLPFC, which makes the amygdala reactivity more reactive and eventually leading to dysfunctional emotional processing.	Biased attention, biased processing

Nucleus accumbens are associated with the hedonic coding of incoming stimuli by the caudate nucleus to prompt appropriate reinforcement mechanisms. Nucleus accumbens activity is influenced by PFC activity in healthy individuals. Levels of the nucleus accumbens are not hyperactive, and the response is active, unlike that in depression patients, whereas the nucleus accumbens response is blunted.	After presenting *positive* stimuli, MDD patients show drastically decreased nucleus and PFC activity. As a result, it will reduce *positive* affect in response to reward. Substantial decreases in the nucleus accumbens and PFC activity are, in turn, caused by the impaired capacity to maintain positive affect through top-down control lead. Reduced or blunted nucleus accumbens responses to rewards are linked to decreased volume and activity in the caudate nucleus, indicating that the rewarding characteristics of a stimulus may not be correctly labeled.	Biased thoughts
Un-present memory bias in healthy individuals, normal amygdala function during encoding, and adequate levels of hippocampal, caudate, and putamen activity during recall of negative information	Elevated hippocampus, caudate, and putamen activity during the recall of *negative* information all contribute to the enhanced amygdala function during encoding. Depressive recollection is enabled without the involvement of top-down prefrontal regions due to bottom-up regulation of the hippocampus, caudate, and putamen triggered by amygdala hyperactivity.	Biased memory

Require less cognitive effort (e.g., by the MPFC) to recall happy personal memories, whereas recall of negative memories requires more top-down influence.	In depression patients, the ventral MPFC is hyperactive during recall of self-relevant happy events. In contrast, it is hypoactive when recalling self-relevant sad events. Recalling positive personal memories requires more top-down influence (e.g., by the MPFC), whereas recalling negative memories requires less top-down influence. This is partially due to the increased automatic bottom-up processing of sad stimuli.	Biased memory, biased thoughts
MPFC with standard baseline activation.	MPFC is the most active and has the highest baseline activation when a participant is not actively engaged in a task. This implies that MPFC may respond to self-focused stimuli in MDD patients.	Biased thoughts and rumination
Serotonin transporter (5-HTT) binding is a key moderator of pessimism (a specific self-referential schema). Normal levels of 5-HTT facilitate serotonin uptake.	Elevated 5-HTT binding is hypothesized to increase the risk of depression, as it promotes serotonin reuptake in the PFC, ACC, putamen, and thalamus. This diminishes the amount of available extracellular serotonin that is accessible. Thus, it is thought to contribute to a heightened risk of depression.	Biased thoughts and rumination

Table 1: Differentiations in the biological pathways and cognitive models of MDD patients compared to healthy individuals. The following acronyms represent regions of the brain, DLPFC: dorsolateral prefrontal cortex, VLPFC: ventrolateral prefrontal cortex, MPFC: medial prefrontal cortex. Information obtained from (Mullins, 2017).

1.2: Genetic basis of depression

In addition to the psychological basis of depression, the genetic basis of major depressive disorder has been recognized by several molecular genetic studies and genome-wide association studies (GWAS). The GWAS study aims to test a sizeable sample of hundreds of thousands of genetic variants across many individual genomes to discover SNPs statistically associated with a disease or trait (Uffelmann et al., 2021). Its results have a range of applications, including establishing a phenotype's underlying biology, estimating its heritability, calculating the genetic correlations, and much more. Any variants overrepresented in the specific disease population examined could disclose the etiology of the disease. The genetic dissection of MDD utilizes GWAS to identify 178 genetic risk loci and propose more than 200 candidate genes (Hyde et al., 2016). As a complex disorder with a heritability of 37% (Mullins, 2017), valid identification of genetic factors had to be acquired through a large sample size or empirically driven efforts to reduce heterogeneity. However, several studies successfully overcame these hindrances and adopted strategies that helped scientists better comprehend the genetic underpinnings of depression. Data was collected by these studies, evaluating the putative genes and SNPs associated with depression. As shown in the first column of Figure 1, seven independent SNPs stood out from the meta-analysis, which captured the polygenic architecture of MDD, including the *SIRT1 gene*, *LHPP*, and *DCC gene*. Multiple SNPs with modest effect sizes contribute to and are involved in processes prospectively associated with depression, such as the development of neurons and mitochondria biogenesis. Thus, novel approaches to therapeutic treatments for depression could be leveraged from the identified SNPs and GWAS studies. Allowing treatment by the gene-editing tool CRISPR to rectify mutations and alterations underpinning biological pathways of depression, scientists can potentially translate these new biomarkers into therapeutic targets and clinical tools.

Single Nucleotide Polymorphism (SNP) loci	Definition	Function	Depression phenotype
SIRT1 gene, intron of LHPP (CONVERGE consortium, 2015)	Sirtuin (silent mating type information regulation 2 homologs), Pholsolysine Phosphohistidine Inorganic Pyrophosphate Phosphatase	*SIRT1* is involved in the biogenesis of mitochondria, which is the power-supplying organelle for cells. LHPP suppresses tumor and cell proliferation.	Recurrent MDD in women

KSR2, DCC gene (Okbay et al., 2016)	Kinase suppressor of Ras 2, deleted in colorectal cancer gene	*KSR2 gene* encodes a transmembrane receptor involved in axon guidance. *DCC gene* also encodes the netrin-1 receptor DCC, a transmembrane protein required for the guidance of axons.	Depressive symptoms in the past 2 weeks were assessed by 2 questions; lifetime MDD
THEM161B-MEF2C (Hyde et al., 2016)	Transmembrane protein 161B-myocyte enhancer factor 2C	MEF2C plays a significant role in synaptic learning and memory; variants in this gene have been implicated in epilepsy, schizophrenia, and mental retardation (Direk et al. 2016).	Self-report of diagnosis or treatment for MDD
NEGR1 gene (Hyde et al., 2016)	Neuronal growth regulator 1	Involved in neurite outgrowth (Sanz et al. 2015) and is associated with several human pathologies, such as obesity, depression, and autism (Yoo et al. 2022).	Self-report of diagnosis or treatment for MDD
FHIT (Direk et al., 2017)	Fragile histidine triad diadenosine triphosphatase	Encoding a tumor suppressor protein and regulating cellular DNA repair. Furthermore, involved in oxidative stress and the circadian clock.	Depressive symptoms in past weeks assessed by questionnaires; lifetime MDD

Figure 1: Table of Single Nucleotide Polymorphisms (SNPs) loci and putative genes, the relation of major depressive disorder and their function. Note that this is not an exhaustive list, and ongoing research is likely to identify additional genes associated with depression.

1.3: The Discovery of CRISPR

The term Clustered regularly interspaced short palindromic repeats came to be known as CRISPR when Francisco Mojica discovered a strange repeated sequence in the genome of a

microbe isolated in the port of Santa Pola; he did not expect it to become the premise of a new era with worldwide genome editing (Lander, 2016). With this technology, CRISPR has a broad range of applications that may be used, from developing sophisticated animal models of malignancies and inherited diseases to running genome-wide screens in eukaryotic cells to identifying the gene responsible for specific biological processes. Its discovery has been based on the foundation and works of several renowned scientists, with the discovery made by Mojica in the natural setting of CRISPR, in vitro experiments, and initial trials carried out by the labs of Doudna and Charpentier, and publications of its protocols, as well as in vivo experiments further contributed to by Zhang's lab. The unprecedented innovations they have created using CRISPR have proven the efficiency and applicability of the Cas9 endonuclease in cleaving any target DNA sequence of interest. This proficient, programmable, and versatile system surpasses any obstacles met with previous gene-editing techniques, such as designer zinc-finger nucleases (ZFs), transcription activator-like effectors (TALEs), and utilization of restriction enzymes (Rasul et al., 2022). Doudna and Charpentier have proposed that the RNA-programmed Cas9 could offer the once unimaginable potential for gene-targeting and genome-editing applications (Jinek et al., 2012), winning the Nobel Prize in Chemistry in 2020.
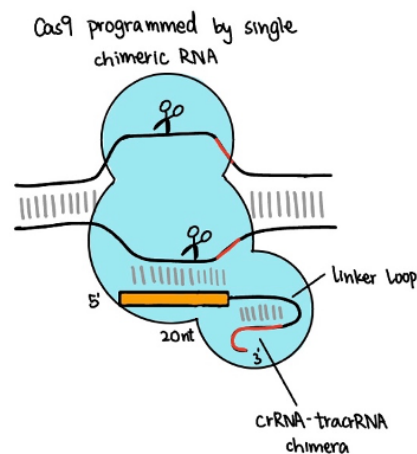
Figure 2 -The mechanism and process of the Cas9 enzyme programmed by single chimeric RNA, sgRNA, to induce cleavage at specific target sites. Adapted from Jinek et al., 2012.

Known as the sharpest tool for gene editing, the CRISPR-Cas 9 genetic scissors can provide precise homology-directed repair, enabling simultaneous edits within the genome at several sites (Cong et al., 2013). Its prevalent applicability, and programmability can be acclaimed to the short RNAs (sgRNAs) that direct Cas9 nucleases to create breaks within the target DNA—with minimal mutagenic activity (Cong et al., 2013). This mechanism initializes from the defense mechanism of prokaryotes to protect themselves from viruses. In nature, CRISPR-Cas9 exhibits a prokaryotic adaptive immune system that incorporates small fragments of invasive viral genomes, known as spacers, into the CRISPR locus to memorize prior virus invasions. When an infection recurs, the spacers between repetitions are produced as short guide

CRISPR RNAs (crRNAs), which Cas9 proteins utilize to target invading viruses based on their specific DNA sequence. To sum up, as the Cas9 enzyme recognizes the virus DNA and cuts it, the viral genome is subsequently dismantled. Bacteria consequently survive infection from viral invasions (Jinek et al., 2012; Lander, 2016).

In the experimental process, scientists adapted this bacterial defense system into a gene editing tool by facilitating and constructing guide RNAs to target a gene of interest and using a more streamlined version of the bacterial defense system with only one RNA molecule (sgRNA), and the Cas9 enzyme to induce a site-specific cleavage anywhere in the human genome, as demonstrated in Figure 3. To dispatch the applicability of Cas9 nucleases, the guide sequences are encoded into a single CRISPR array (illustrated in Figure 3) enabling edits of specific sites within the genome. The system also allows for multiplexing, where multiple edits are done simultaneously. The Non-homologous end joining (NHEJ) and Homology-directed repair (HDR) pathways in edited cells, such as edited human cells, are mechanisms for the repair of the double-stranded break (DSB) caused by Cas9 when it cuts the target DNA sequence. The repair produced by the NHEJ pathway is error-prone and randomized on occasions introducing an insertion or deletion in a gene, inducing a mutation, and removing the function of a gene (gene knockout or deletion) (Xue & Greene, 2021). In contrast, Homology Directed Repair in cells employs an endogenous or exogenous fragment of homologous DNA as a template to repair a patch of DNA (Papadopoulos et al., 2016). The consequence is a directed gene edit or the addition of new genetic information to be presented. This exogenous fragment of DNA, employed by the HDR pathway, is supplied during the CRISPR-Cas9 edit by the individual performing the edit. As a result, there is substantial flexibility for scientists to design this DNA fragment to contain any specific sequence desired. The sequence will be inserted subsequently into the genome, carrying a correction for a mutation or potentially new genetic information (Hille & Charpentier, 2016). The complex and versatile mechanism of CRISPR enabled its function to perform edits in the genome with a streamlined version of the bacterial defense system, with only a single RNA molecule manipulated by the researcher to guide Cas9 virtually anywhere within the genome. CRISPR-Cas9 can be employed to correct genetic aberrations, thus successfully presenting depression. The following section considers recent trends in this area of research.

2.0: Trends in this topic

Numerous disorders have been researched to determine their underlying genetic basis since the widespread availability of gene sequencing technologies. The primary analysis conducted in this paper explored the specific number of studies present in a destined year for the following key terms of CRISPR, depression, and genetics to analyze trends in the literature about the study of depression's genetic component and CRISPR-Cas9. A hypothesized outcome of this analysis is an increasing trend, as depression becomes endemic in our society nowadays and technological advances in genome editing take a huge leap. The resulting graph in Figure 3 details the positive relationship between the number of results obtained and the years ranging

from 2012 to 2022. As shown in Figure 3, the number of years we considered began eleven years back in 2012 and continued till 2022 (as data for 2023 is ongoing and incomplete). The increasing trend suggests a larger number of studies conducted over the years, demonstrating a clear interest in these topics, a substantial number of scientists investigating this field of interest, and consequently, a proliferating need for treatment of this disorder (in Figure 3).

A perceptible increase in the number of results from 2020 to 2022 corresponded to the climax of the COVID-19 pandemic. Several eligible studies constitute evidence by reporting similar trends in the high prevalence of depression during this period (Santomauro et al., 2021) due to factors such as isolation, limited human mobility, and bereavement. An alternative explanation for the increase is the consumption of social media and widespread digital use amongst the general population. Research has shown that the use of social media platforms, such as Facebook, correlated with an elevated frequency of depressed mood (Eggermont & Frison, 2015), while Woods and Scott (2016) portrayed a proportional relationship between the frequency of social media consumption and poorer sleep quality, decreased levels of self-esteem, and higher levels of depression and anxiety**.** In the following years, the prevalence of this debilitating disorder is expected to increase, as illustrated by the trend in *Figure 4*, due to numerous factors, such as demanding societal standards, increased competition in multiple industries, and elevated financial pressure. The number of studies published in the ongoing period of COVID-19 corresponded to the data from *Figure 4* displaying an increase in the rate of depression in years ranging from 2020 to 2022.

Finally, the trendlines depicted in Figures 3 and 4 suggested the estimated growth of the number of novel studies published per year, as well as a gauged increase rate of clinically diagnosed depression in the US. Figure 3 displays an equation to provide an approximate estimation in the number of studies in a specific number of years after 2012. According to equation 1 from *Figure 3 y*=518.8x-496.36, there are approximately 519 innovative studies every year inspecting research on CRISPR, genetics, and depression. The accumulating number insinuates a growing interest in this field of study, thus the advent of rapid development and discoveries for therapeutic methods. Based on my formula, by 2033, there would be an estimated 9879.64 studies published. This accentuates the increased interest and attention brought to this topic yet again. Moreover, an approximate 1% increase in rates of depression every year is calculated by the equation in *Figure 4,* y= 0.9109x-1825.2, which demonstrates a continued growth of this debilitating disorder, divulging the necessity to develop new treatments urgently. Data has shown that elevating numbers of studies are being published in this field to support the treatment of MDD, while a growth in rate of depression has increased simultaneously. Researchers have worked diligently to yield new innovative therapeutic measures using new technology, CRISPR-Cas9 being one of them. The following section explores several recent advances in the understanding of depression's genetic basis, as well as specific applications of CRISPR-Cas9 gene therapy in this field of study.
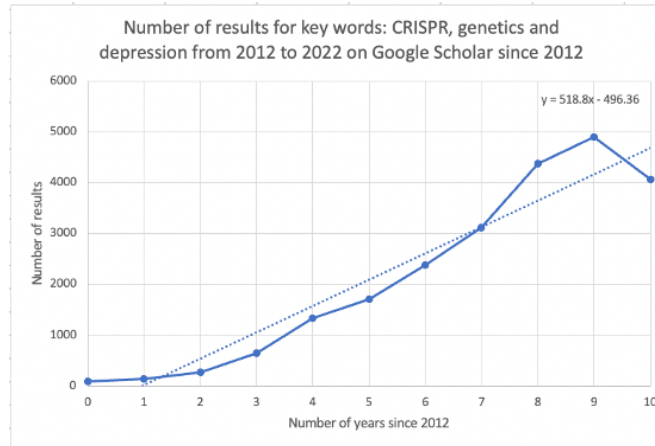
Figure 3: Analysis of the number of search results yielded on Google Scholar in years since 2012. (Dotted line indicates linear trendline determined by automatic linear regression performed by Microsoft excel.)
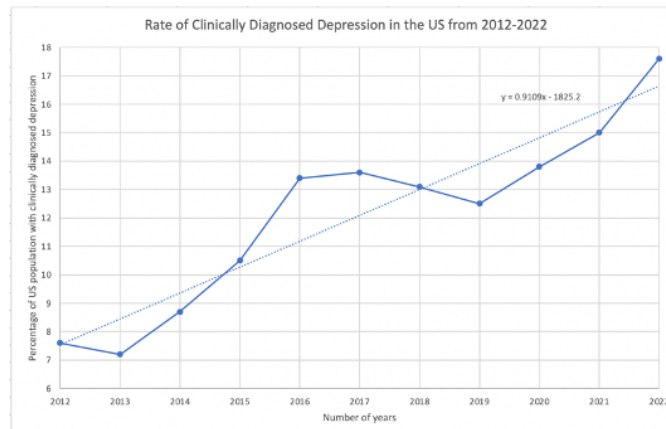
Figure 4: Rate of clinically diagnosed depression in the US from 2012-2022. Adapted from sources NIH.gov, Cambridge.org, samhsa.gov. (Dotted line indicates linear trendline determined by automatic linear regression performed by Microsoft excel.)

2.1: Animal Models of Depression and Obstacles to be Addressed

Since mouse models exhibit a generally comparable symptomatology and similar etiology to humans, their models are often used by scientists in the exploration of underlying biological processes (Vanhooren & Libert, 2013). Genetically modified models offer an ideal platform to demonstrate the idea of a gene's functional gain or loss using approaches like a mutation or knockout. To study neurological diseases in a model organism using CRISPR, a genetic link has to be established to the particular disease. Furthermore, CRISPR-Cas9 can be utilized to introduce the appropriate genetic mutations into model species such as mice (Mou et al., 2015). Scientists are able to gain a more thorough understanding of the impacts, causes, and consequences of a disease by analyzing the differences between the mice with the genetic mutation and without it (Lam et al., 2021). Prospective medications or treatments will then be administered to the mice to mitigate their symptoms or occasionally aid in the cure of the

disease. Proper utilization and engineering with the CRISPR-Cas9 system can make gene therapy an appealing option, which gives some benefits for the treatment of certain disorders and offers unique chances to eliminate the aberrant genetic components in individuals with these illnesses, this general strategy is outlined in *Figure 6.*
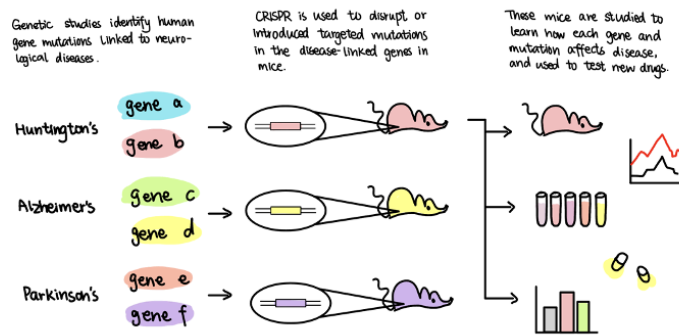
Figure 6: Scientists using CRISPR-Cas9 to evaluate and investigate neurological disease in organisms. Adapted from (Lam et al., 2021).

Henceforth, as described above in *Table 2*, depression is underlined by multiple genes and labeled as a multifactorial disease, demonstrating a certain amount of uncertainty in its predictive validity (Becker et al., 2021). Single gene deletion or overexpression will generally not overlap with core symptoms of depression. Conventional genetic deletion in mouse models of certain genes causes function attenuation to extend throughout the body's system and results in metabolic and system impairments that are often not as severe in human depression (Becker et al., 2021). Moreover, the etiology of major depression is still to be understood; epigenetic, genetics, and environmental factors contribute to this disease. Recent studies have shown that disrupting the function of genes utilizing CRISPR-Cas9 has led to depression-like symptoms in mice. This indicates the molecular associations of depression and genetics, as well as a potential approach to improve therapeutic interventions through gene therapy in these disorders (G. Liu et al., 2019).

In addition, a major dilemma in developing a therapeutic for the brain is getting it past the blood-brain barrier (BBB), as it serves the main purpose to isolate and safeguard the neural tissue while restricting molecular access and, thus, hindering delivery. Only 5% of the approximately 7,000 drugs evaluated in the Comprehensive Medical Chemistry database could pass through the BBB and enter the central nervous system (Pardridge, 2005). These factors also inhibit the ability of CRISPR-Cas9 to reach the brain tissue, which will be discussed in depth in the subsequent section.

2.2 Potential treatment of depression with CRISPR -Cas9

Despite an incomplete understanding of all the molecular details of MDD, a number of pharmaceutical drugs and medical prescriptions have been developed and shown to be effective

for treatment. Characterized by monoamine synaptic imbalance (Mullins, 2017), antidepressants and pharmacological medicine implement various drugs to raise synaptic concentrations of serotonin or norepinephrine. The presence of current antidepressants decreases the propensity of individuals with MDD to attend to negative, schema-consistent stimuli. Certain neurotransmitters are present in the brains, such as serotonin; these neurotransmitters serve to regulate the mood of an individual. As the amount of serotonin is increased, extraneous serotonin in the prefrontal cortex (PFC) may improve excessive 5-HTT binding and reinforce cognitive control. In this case, 5-HTT is a serotonin receptor that plays a prominent role in facilitating the amounts of serotonin uptake in an individual (Otte et al., 2007). In other less invasive tactics for cognitive intervention, such as attention training, patients can learn to divert their attention from negative instances or material instinctively. The effectiveness of pharmaceutical interventions cannot be guaranteed for every patient; even though they can treat certain individuals, alternative approaches to devising novel depression treatments, such as gene therapy using CRISPR-Cas9, should be considered.

The CRISPR system and its variants offer a wide range of previously unimagined opportunities for genome analysis and speculation, the discovery of potential early expression markers, and the creation of tailored treatments with effects on neurodegenerative diseases (Hu et al., 2018) –which depression is suggested by increasing evidence to be categorized by (Higgins, 2004). Although scientists still do not fully understand all the constituents to depression, recent identifications of numerous genes and pathways that may be associated with MDD has been summarized in *Table 2,* plausible methodologies for assuaging symptoms of this debilitating disorder with CRISPR-Cas9 can be done through targeting a few pathways. The first possible pathway is the serotonin receptor (5-HTT), which moderates a particular self-referential schema known as pessimism. Scientists hypothesize elevated 5-HTT binding to increase the risk of depression due to the enhancement of serotonin reuptake in regions of the brain such as the PFC, ACC, putamen, and thalamus (Disner et al., 2011). The binding of these proteins reduces the amount of extracellular serotonin accessible to MDD patients. Serotonin is essential for body functions such as mood, sleep, and digestion. It also creates a long-lasting feeling of positive mood and well-being.

In the study by Owens et al. (2012), the effects of early childhood adversities and the serotonin transporter gene (5-HTTLPR) on adolescent cognitive and emotional processing have been investigated in depth. Researchers used a sample of 238 adolescents from a community study characterized by the presence of the short allele of 5-HTTLPR and the past experience of childhood adversities or trauma. There are two alleles for the 5-HTTLPR gene, the short (S) and long (L) alleles. Owen et al.'s (2012) study discovered that for adolescents with experience of CA, inheritance of the S allele raises an individual's risk of developing depression. The presence of the S allele is linked to decreased expression of this serotonin transporter, which results in an elevated risk and susceptibility. Teenagers exposed to childhood adversities (CA) and homozygous for the S allele of the 5-HTTLPR were found to perform poorer at differentiating between negative and neutral stimuli, responding to ambiguous negative schema with more

errors (Owens et al., 2012). Additionally, diagnoses of depression were linked to abnormalities in cognitive and emotional processing, as mentioned in section 1.1 of the paper. The application of CRISPR-Cas9 could potentially be efficacious for reducing risk of susceptible individuals with the S allele and experience of CA in developing depression. Scientists can perform an edit on the genome of neurons, replacing present S alleles with L alleles. Diminishing predispositions and precariousness of the development of MDD in future situations. To perform this hypothetical edit, researchers could potentially design a gRNA that targets the sequence of the short allele, then introduce CRISPR-Cas9 into neurons and cut the DNA at the specific location. Researchers could then supplement the cells with a template DNA for the long allele, and the cells could perform an HDR (Homology-directed repair) to replace the short allele with the long allele. This may prove to be a viable strategy for reducing the risk of developing depression following childhood adversities. Only one of the two alleles require an edit, as heterozygotes are the same as LL individuals—making the CRISPR-Cas9 edit easier to complete.

By utilizing modified versions of Cas9 to activate the gene expression of DNAs like the 5-HTT (Serotonin Transporter) and HTR2A (Serotonin Receptor 2A), researchers are able to perform further in-depth study of the gene. This approach is apt for patients with depression that, unfortunately, do not find relief with antidepressants. An estimated 14 million Americans diagnosed with MDD, including one-third of that 14 million, are not susceptible to the influence of SSRIs and antidepressants (Dryden, 2018). The novel approach targets another receptor type, utilizing CRISPR-Cas9 to perform a genetic edit. Instead of conventionally boosting serotonin levels to regulate mood and social behavior, scientists target to alter the delta-type GABA receptors. Neurosteroids are naturally occurring chemicals in the brain, involved in motivational and emotional brain networks. These substances are used to target GABA receptors (Dryden, 2018), done by implementing a derivative form of CRISPR known as CRISPRa. Such methodology utilizes a mutant Cas9 which does not cut DNA, rather activating expression of the gene that it binds to (Higgins, 2004). This could be employed to elevate the expression of 5-HTT, leading to normal levels of expression of the gene. Levels of serotonin transporter or receptor in the brains of depressed individuals could be augmented, as Cas9 binds to the designated location by the gRNA, and instead of cutting the DNA, recruits transcription factors to boost gene expression. This increases the level of HTT protein in the neurons, simultaneously increasing their signaling and counteracting depression symptoms. This approach is considered safer than the editing version of Cas9, as there is decreased risk of off-target mutations being introduced. However, it is important to note that the proposed edits are at the moment hypothetical, and there are no current clinical trials being conducted using CRISPR in vivo to treat depression. Technical challenges, safety concerns, and the feasibility of this approach is an active area of research, and while it has not been manifested yet, it is a exciting prospect in the years to come.

2.3 CRISPR-Cas9 to modulate the gut microbiome

Genetically modifying genes and applying CRISPR-Cas9 in the human brain is yet to be pioneered, as the blood brain barrier (BBB) present in the central nervous system (CNS) acts as a functional and structural roadblock to microorganisms; it similarly impedes the CRISPR-Cas9 complex from successfully yielding a site-specific DNA cleavage in the brain. The genetic scissors would have to be encapsulated or changed in form to pass through. However, genetically modifying the gut microbiome is plausible yet efficacious for treating depression. Anxiety, stress, or depression can be a byproduct of intestinal distress and affliction in the gastrointestinal (GI) system (Liu et al., 2023). Prevailing experiments examining the role of gut microbiota and its metabolites in depression were published by scientists in 2023 (L. Liu et al., 2023).

Additionally, multiple recent studies corroborate the relationship between the gut-brain axis (Herselman et al., 2022; Raes, 2023), as well as postulating the prominent role of gut microbiota in the pathogenesis of depression. The involvement of the multifaceted, bidirectional communication axis between the gut and central nervous system mediates the state of mood, which in turn regulates intestinal motility (Herselman et al., 2022). Association between the gut microbiome and biogenesis of major depressive disorder promotes the development of microbiota-targeted interventions, such as CRISPR-Cas9 gene editing in the gut. With obstructions from the BBB, direct-genetic modification in the brain proves problematic (Daneman & Prat, 2015). However, viruses like filamentous bacteriophages can be harnessed as agents for gene delivery to the gastrointestinal tract (Lam et al., 2021). Utilizing a bacteriophage called M13, CRISPR-Cas9 is delivered to conduct species-specific genomic eliminations in the gut. This experiment was carried out in mouse models, demonstrating the prospect of using phage-delivered CRISPR-Cas9 for strain-specific deletion in the mouse gut, inducing chromosomal deletions both in vitro and in vivo (Lam et al., 2021). The gRNA is intended to specifically target and eradicate harmful species of gut bacteria, while keeping the helpful and unrecognized bacteria species alive. At a molecular level, the gRNA would be specific to a singular or multiple species, induce breaks in the DNA, and result in the impairment of only harmful bacteria contributing to the depression. (Depletion of Coprococcus and Dialister bacteria have been found to be depleted in patients with depression)

Consistent propositions have been presented regarding the differing microbial diversity and relative amount of specific bacterial taxa of MDD patients and healthy individuals. Specifically, it has been divulged that an enriched amount of pro-inflammatory bacteria and a depletion of anti-inflammatory bacteria will play a pivotal role in the inflammatory hypothesis of depression (Liu et al., 2023). Microbial dysbiosis-an imbalance between different organisms present in an individual's gut - precedes MDD onset, as proven by transplantation of fecal microbiota from MDD patients to mouse models (Kelly et al., 2016). Depressive symptoms were induced in the mouse models, and evidence also supported a microbiome shift early in depression, further stimulating pathological changes and contributing to dysbiosis by changing the gut environment (Liu et al., 2023).

To briefly sum up the content mentioned above, the utilization of CRISPR-Cas9 to target the imbalance in microbial compositions, such as a disproportioned Bacteroidetes: Firmicutes

ratio (Liu, Wang & Zhang 2022), provides novel prospects for future research and clinical transformation for microbial-targeted therapeutics for depression. Compelling evidence of the relationship between the gut-brain axis is further provided by a review by Taylor and Holscher (2018), proposing the contribution of gastrointestinal microbiota to mood and behavior disorders, such as depression. Dietary interventions in MDD patients were able to ameliorate moods, suppress biological markers of stress, and reduce depression scores (Taylor & Holscher, 2018).

By implementing a similar strategy to the one used in Lam (2021), the "unhealthy" commensal human bacteria could be removed. As we understand more about the intricate nature of the gut-brain axis, thus allowing researchers to make subtle modifications to these gut bacteria, in vivo, to elevate levels of serotonin signaling and treat depression using CRISPR-Cas9. The surplus advantage to this line of treatment is the alleviated risk of genome editing directly in the brain. As one of the most complex entities in our body, a single mutation in the brain may lead to irreversible damage. Therefore, this strategy is less invasive and addresses the hindrance of passing the BBB.

2.4 Surpassing the BBB with CRISPR Editing

Despite the challenges associated with the BBB, one recent study has overcome this by directly accessing the brains of the mice, becoming a potential treatment to consider. This treatment is underlined by a study performed by Han (2017), where the researchers inputted a shunt/tube into the brain of mice and mutated the brain of these experimental mice. According to the paper, blockage and disruption of the proteins TRIP8b and HCN channel produced antidepressant-like behavioral effects, presenting the potentiality of using genetic ablation targeting protein-protein interactions to alleviate depression symptoms. Thus, a trial utilizing CRISPR-Cas9 would be to reference this viable technique and potentially make genetic edits to the brain tissues of patients with depression by inserting encapsulated tubes through the BBB. Suppose the obstacles of the BBB permeability inside the CNS and, as well as successfully preventing the possibility of off-target edits—as they could provoke undesirable mutations within the patient's brains—could be addressed and overcome. In that case, this experiment presents an eventual direction for potential treatment and could be attended to through further research. The viability of this therapeutic approach to alleviate MDD is not inspected in depth or ensured to be efficacious yet. It should be implemented first in mouse models before being experimented on in humans. An important aim of these mouse models in initial trials would be to ensure the safety of the edit, minimizing chances of off-target edits, and focus the change on the gene of interest only instead of removing or disrupting other important genes in the brain. This type of intervention is extremely invasive for patients and would likely be solely considered in acute cases. An individual would likely have experienced previous attempts through less invasive approaches such as antidepressants and clinical therapy before embarking on this strategy.

Large rearrangements of DNA are likely to be stimulated during CRISPR-Cas9 edits; this theoretically triggers cancer and autoimmune diseases—especially with the lack of proper

delivery techniques (Rasul et al., 2022). Whereas genome editing bacteria in the gut microbiome has the advantage of a safety backup plan—killing off bacteria if unsuccessful edit occurs. Scientists are able to use a high dose of antibiotic drugs, like penicillin, to kill off bacteria, avoiding any long-term damage for the patients. Aiming to modify bacteria in the digestive system has been an approach to treat microbiome-related health issues led by Peter Turnbaugh, Ph.D., a professor of Microbiology and Immunology, who has successfully altered the DNA of microbes in the gut. They have done this by focusing on *E. coli,* as certain strains of this bacterium are known to induce food poisoning. Scientists utilized the virus M13 to inject a CRISPR-Cas9 system to cut harmful strains of *E. coli* while leaving others undisturbed. As expected, the results showed a targeted strain in the gut of mouse models rapidly disappearing. While two weeks into the experiment, targeted strains of *E. coli* represented only one percent of the monitored cell population (Lam et al., 2021). By using a similar approach, we envision this stratagem could someday be employed to promote the growth of "good" gut bacteria in humans. Suppose scientists altered the genes in specific bacterial strains to enable the bacteria to feed on rare nutrients. In that case, an individual with depression may acquire some influence over the assortment of microorganisms in their gut by introducing considerable amounts of these nutrients to their diet (Lam et al., 2021). Thus, implications for the correlation between the gut-brain status suggest another target for CRISPR-Cas9 edits. Genome editing could potentially rectify microbial dysbiosis of the gut microbiome and recuperate the gut environment of depression patients, theoretically alleviating depression scores and accelerating remedial processes.

3.0 Conclusion

The leading role of major depressive disorder in worldwide disability emphasizes the necessity for competent and effective therapeutic options. A rising trend, however, escalates the concerns of global health organizations and the general public. Fortunately, with research amassing the necessary sample size to be effective, the first steps toward identifying genetic variations in MDD have been established. The discovery of genome-wide associations of MDD leads to new biomarkers for establishing molecular mechanisms and gene editing techniques, such as CRISPR-Cas9. Scientists now obtain a comprehensive and evolving understanding of stratagems like CRISPR-Cas9, owing to the extensive and innovative work of previous scientists and researchers. This precise and effective gene editing tool can leverage this debilitating disorder's pre-established genetic associations. This review provided a fundamental introduction to CRISPR-Cas9 while expanding into the preliminary framework for identifying multiple neurobiological underpinnings of depression. Consequently, assisting and providing potential therapeutic targets to facilitate development of somatic and psychological treatments for MDD, through employing approaches of genome editing. Use of CRISPR-Cas9 to directly boost the expression of neurotransmitter-associated genes like 5-HTT or editing of the microbiome with CRISPR may prove to be effective applications of gene therapy to treat major depressive disorder. The implementation of CRISPR technology to treat MDD has not been fully optimized yet, but future research in this area may provide viable treatments for millions of people affected.

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Enhancing Learning: California High School Educator's AI Integration Views By Meghna Chellapilla

Abstract

   This paper discusses the topic of artificial intelligence, and whether its implementation in US public high schools increases average academic outcomes. This includes state test scores, GPA, graduation rates, etc. We define artificial intelligence in the form of software and educational cobots, and how the use of both can benefit learning in the classroom. When we discuss US public high schools, we are disregarding magnet, charter, and religious schools, and focusing on the average US high school. AI has been a growing topic of concern regarding its use in education and whether it can be detrimental to student learning by allowing them to cheat. However, this paper mainly discusses the merits of using AI in public high schools. The paper argues that schools can use AI to help teachers target specific learning scenarios for each individual student to improve their learning experience. This paper explores the AI implementation best practices through an online questionnaire sent out to California public high school educators, intended to gain an idea of teachers' opinions on future implementation of AI.

Introduction

   Artificial intelligence (AI) has been a growing area of interest this past year. The rise of ChatpGPT, Bard, and other AI software has raised an essential question for all parents and teachers: how does this impact child education? With an artificial intelligence engine readily available for free use, many people predicted an increase in laziness and unmotivated students. However, many people have been asking whether it can improve the education field. Access to an AI engine is almost like having a personal tutor; students can ask questions and receive answers in much more logical ways and are readily available for student use.

   Within the past two decades, technology usage in US public school classrooms has significantly increased. From chalkboards to smartboards, to having laptops and tablets available in various places on school campuses, to using computer games and resources to quiz students on material, technology is part of so many teachers' lesson plans and curriculums. Many students have found sites to help them study for tests, to communicate with peers and teachers, and to help them with their school assignments. But why stop there? The potential benefits of artificial intelligence assistants in education should be considered alongside potential challenges and limitations. Striking a nuanced balance between leveraging AI for specific tasks and preserving the unique qualities of human-led instruction is key. As we navigate this evolving landscape, understanding how to interact with AI becomes a valuable skill, but it is equally important to remain mindful of the complexities and ethical considerations surrounding its use in education.

Background Literature

   The use of artificial intelligence (AI) for educational purposes has increased in the past decade or so. The incorporation of AI at the high school level encourages creative thinking and

adaptation regarding new technological advancements. Past research focuses on the ability to utilize AI in a classroom, from creating lesson plans to supporting administrative work. Despite the benefits, past research also acknowledges concerns, including the potential limitation of social and emotional engagement, policy debates, and the risk of AI replacing teachers. In general, it emphasizes the need for a balanced approach that recognizes AI as a supportive tool rather than an adversary, particularly in preparing high school students for a future where AI plays a significant role in various fields.

In 2017, Georgia State University used AI to help students who committed to their university in the transition from high school to college. The failure of high school students to matriculate affects 10-20% of high school graduates every year (Page, Gehlbach, 2017). In this instance, an AI virtual assistant provided personal assistance to support these students and outreach to remind them to matriculate, and did so in a completely personalized way, increasing the number of students who matriculated by 3.3 percentage points (Page, Gehlbach, 2017). This is one way AI has been utilized at the high school level in the past, but with the growing advancements in the field, there is potential for a more hands-on implementation in high school classrooms.

AI has the potential to be used in education for two main purposes. The first is for student interaction. As explained in Timms (2016), one future vision for the direction of AI in the education field is in the form of educational cobots. These are essentially robots that can reside in classrooms along with students, interact with them, and help answer any questions they have. One of the benefits of an educational cobot is that it stimulates the social aspect of learning which has been a concern in regards to AI in classrooms (Timms, 2016). However, large scientific advances in both robotics and artificial intelligence fields would have to occur before educational cobots are even a possibility. But whether as a physical robot or not, students can interact with artificial intelligence in the classroom and ask any questions about topics they are struggling with, and the AI will be able to help them along the way. In addition to this, AI can identify areas of weakness for specific students to the teacher, and suggest lesson plans tailored to each student to help them master the concepts. Overall, AI can help teachers target specific learning scenarios for each individual student to improve their learning experience (Luan, Geczy, Lai, Gobert, Yang, Ogata, Tsai, 2020).

The second purpose AI can be utilized for is as a teacher's assistant, aiding educators in administrative tasks. Essentially, this could consist of developing lesson plans for the teacher in order to target specific concepts that students find particularly challenging, or working with the teacher to create engaging material for the students to use both in and out of class. One other side to this purpose is for administrative roles; AI software can handle attendance keeping and scheduling, which frees up time for the teachers to give instructions. Additionally, it can handle grading homework and trivial assignments given in class, so the teacher is able to focus their attention on the more important weighted assignments in their class. Overall, AI should work with teachers to make teaching more about facilitating student learning, by handling some of the workload and by helping create lesson plans. It is important to note, however, that AI

implemented in schools should complement teachers rather than replace them. Human interaction is a key process during a learning period, and teachers help foster growth, creativity, and engagement in students on a level that AI cannot achieve.

While there are benefits of utilizing AI in the education sphere, there are also negative effects that we simply cannot ignore. Some of the clear benefits have been discussed in the previous sections of the paper: teachers have the possibility of having their own assistant to help them manage the curriculum and teaching, and also the fact that teachers can be free of more rote tasks and truly focus on teaching the students. However, there are finite risks that cannot be ignored. First off, the use of AI could lead to the limitation of social and emotional engagement within learning environments. Human interaction is critical during developmental learning stages for adolescents, and teaching is not a job that could be replaced with AI; we live in a world where social interaction is required no matter what, and integrating AI further always runs the risk of having it replace teachers permanently. We have to strike a balance so teachers are the primary resource for school learning, while AI is more of a support tool. Another concern is about policies regarding AI; many high schools have already banned the use of AI software such as ChatGPT, and it has become a topic of political debate. With potential pending restrictions on the use of AI, implementing it in the future might not be feasible. However, if we keep on treating artificial intelligence as the enemy, it will become just that. We need to recognize the assets of using AI in schools and in our daily lives, and by doing so we can make great growth in many different fields.

In this paper, I define the use of artificial intelligence as software; the main use of AI that we are currently seeing is in the form of generative AI, such as ChatGPT, Bard, etc, so working with this form of AI for students is the most feasible. This would also be beneficial to work with software that will be readily accessible to youth in the future, to prepare them for after their education where they will interact with AI constantly. I also focus on AI in the form of an education cobot, as a physical AI tool to turn to in the classroom. The reason we are focusing on AI implementation at the high school level is that high school is one of the most critical periods of a person's education when they are preparing to make the transition to adulthood. High schoolers are preparing to go to college or join the workforce after they graduate, and both of these pathways need high schoolers to be familiar with AI and the various topics covered in their education.

Research Questions

I decided to explore two essential questions about the use of AI in education:
- What is the relationship between the implementation of AI in US public high schools and student academic outcomes in low SES neighborhoods?
- What are the perceptions of public high school teachers on the implementation of AI?

In order to truly gauge the impact that AI can have in the field of education, analyzing the perceptions and opinions of public high school teachers can help determine areas of AI implementation in schools that will need more fine-tuning and revision. Overall, we can

determine the best way to go about administering interaction between students and AI by gathering the thoughts of US high school teachers.

Methods: Sample Demographics and Study Site

This paper discusses whether the implementation of AI will improve student academic outcomes. I chose to approach teachers at Evergreen High School (pseudonym) and send them a questionnaire about their opinions and knowledge about the implementation of AI in public schools in order to gauge the possible impact AI can make on the education sphere.

I reached out to eight teachers at Evergreen High School, who taught various core subjects including math, science, social science, English, and technology. They expressed interest in participating in this study and participated in an online survey. Out of these eight, five chose to complete the online questionnaire.

Teachers were all employed by Evergreen High School. Evergreen High School has a student population between 1,500 and 1,700. Of these students, 41.8% of them are socioeconomically disadvantaged, and 50% are current English Language learners (CA School Dashboard, 2023, https://www.caschooldashboard.org/reports). The city in which Evergreen High School resides has a total population of 764,442 people (2020 Decennial Census). The population is primarily made up of Latine individuals. In the last year, the median household income of $145K was significantly above the statewide median household income of $85K (US Census Bureau).

Data Collection and Recruitment

I approached my school psychologist, vice principal, and one of our biology teachers to be my IRB committee, and once they signed the IRB form and provided any feedback that they had about the questionnaire, I started preparing to send it out to the teachers. I created a separate email for this questionnaire, so the participants could email me about any questions they had, and created an informational flier that had all of the information about the questionnaire. I contacted the teachers in my school from the English, Math, Social Science, and Science departments, and sent them an email with the link to the questionnaire. All information about what was required of participants, the risks and benefits, the window to complete the questionnaire, and the goals of this research study were shared with the teachers, and they were invited as collaborators to fill out the questionnaire to aid me in collecting data.

Analytic Strategy: Survey and Variables

The questionnaire sent out was intended to gauge the teachers' experience with technology, such as laptops, tablets, computer games, and more, in their classroom as learning devices, and whether they use it on a daily basis. It was also to see what their perceptions were on AI, and their thoughts on whether it could be a useful teaching/learning tool. The variables identified include career trajectory variables, AI integration variables, perception variables, and demographic variables (see the specific survey questions in the appendix).

The quantitative data I collected from this survey includes race, age, and years of teaching. There is a range of qualitative data from the survey, including teachers' opinions, thoughts, and experiences with technology and AI. I used this data to determine multiple trends/themes I found throughout the data set. Then, I used those to conclude whether the implementation of AI would be beneficial, as well as future steps in this field. I used these variables in order to identify patterns in the teachers' responses, determine the common trends, and analyze their answers.

Quantitative and Qualitative Survey Analysis

To analyze the sample quantitative data, I conducted a descriptive analysis where I measured the min, max, and range of all the variables we were looking at. I measured the number of people that are a certain race and used that to go into more specifics about the racial distribution of the sample size. I limited the potential for response bias, trying to identify certain areas where the responses might hold inherent bias based on demographics such as race, age, sex, and so forth (Creswell, 2014).

To analyze the qualitative data in this survey, such as the ranging opinions of teachers and varying degrees of experience, I took on a thematic analysis approach. While reading through the responses, I separated the process into two phases. Phase one consisted of reviewing each participant's responses individually, and taking notes about anything that stuck out to me; whether they used casual language or more technical jargon to see how familiar they were with the topic of AI, any extreme opinions they had on any given question, and overall takeaways. Phase two involved making connections between different participant's responses. Any common trends in responses or similar expressed concerns on the topics I noted down and started to form themes in the responses. After I developed my themes, I started working on a loose theoretical plan to best implement AI in US public high schools.

Findings

Out of the eight teachers who were invited to collaborate through the sent-out questionnaire, five responded and filled the questionnaire out. It is important to note that the sample I analyzed data from is a convenience sample; as a California public high school student, these teachers provided necessary input to determine the best course of action to implement AI in classrooms in the future. Nearly 80% of the participants identified as being White, while 20% reported being Italian. They ranged between 10-25 years of experience in teaching high schoolers, with 60% of them having taught high schoolers for over 20 years. 100% of participants had a Masters in Education, and 60% had a Bachelor's Degree (see *Table 1*). All teachers were implementing technology in their classrooms, from the usage of AP Classroom, Kahoot, and Quizlet, to the use of devices such as Google Chromebooks.

Theme 1: Limited to generative AI

All teachers indicated being familiar with generative AI such as ChatGPT, Bard, and this bias was clear in their responses. As they responded to various questions about the

implementation of AI, they only seemed to keep generative AI in mind, expressing concerns/applications of such AI engines in their classrooms. When prompted to contemplate where AI could be useful in their curriculum, one participant responded they could "use a generative text AI" and ask it questions about their subject and "see what it has correct and what, if anything, it has incorrect or unclear." There is no mention of any other types of AI possibly being utilized.

Theme 2: Are we teaching skills or concepts?

The question of whether AI is applicable in a classroom setting, teachers explained, depended on the applicability of it to their subject; if they are teaching skills such as critical thinking and analysis, these are skills that cannot be aided by an AI engine of any kind. But if they are teaching concepts, more applicable to STEM subjects, the learning scope of students is more open to such subjects.

One difference I noticed in responses was how STEM teachers viewed AI implementation compared to different subject teachers, such as English or social science. STEM teachers were more open to working with AI, whether it be used to show students what ways it does not produce accurate responses to prompts, or to help create exercises to work on in class. However, as the non-STEM teachers pointed out, their subjects are more nuanced; unlike STEM subjects, there is not one definitive answer to a problem, and the topics require more multifaceted approaches. When asked whether they would implement AI into their subject curriculum if it were made free of charge, 60% of participants responded "no," all of them being English or social science teachers. One participant expressed, they "see writing as an important skill - it is a way to express one's feelings, thoughts, understanding. As [they] work with young adults who are still learning the skill, [they] see [AI usage] as a short cut from actual learning." Such skills, as seen by most non-STEM teachers, are irreplaceable and an integral need for our society today. Thus, they view AI as unnecessary aid in their respective subjects, one that they do not foresee being useful to teach these nuanced ways of thinking. This sentiment was not reciprocated with STEM teachers, who foresaw using AI to "Creat[e] exercises, writ[e] solutions to exercises, [and] creat[e] mathematical diagrams," and help students "learn/review [a] skill and then be able to successfully implement it in class."

Theme 3: Supplementing vs. replacing student work

Another common trend in responses was a concern regarding the misuse of AI; whether it would be used by students to supplement their understanding of a given subject, or whether it would be abused. Out of all participants, 60% conducted demonstrations, independent of this paper, in their classroom about how AI fails to produce responses up to par with what they are expecting of their students to obtain higher than a passing grade. They expressed that an excessive reliance on AI for tasks like grading and problem-solving could lead to a decline in students' development of critical thinking and creative problem-solving skills, overall limiting the scope and quality of education students will receive in the future. One teacher identified the biggest challenge of AI implementation to be its misuse; "There will have to be some way to identify its misuse. AI models can constantly be improved, and therefore the

monitoring/identification/misuse of AI will constantly be changing since AI could be trained to evade the tools that would be used to identify its misuse."

Many teachers highlighted the flaws of generative AI, and how the responses it produced should not be taken at face value. But, with the growing misuse of such AI engines, the teachers expressed concerns about students not recognizing the correct/incorrect aspects of responses, and thus failing to apply critical thinking or any skills learned in class.

Discussion

This study did a virtual questionnaire that dug into California public high school educators' perceptions of AI. I found educators are wary of AI, as only its potential for misuse has been demonstrated thus far, but some are hopeful about the positive impact it can bring to the education sphere. STEM teachers generally exhibit more openness to integrating AI into their teaching methodologies compared to non-STEM teachers, who emphasize the meticulous nature of their subjects, particularly in English and social science. The reluctance among non-STEM teachers to adopt AI, even if made available for free, stems from the belief that certain skills, especially in writing, are best learned through traditional methods without shortcuts. Additionally, a recurring concern across responses is the potential misuse of AI by students. There is a consensus that an overreliance on AI for tasks like grading could hinder students' development of critical thinking and creative problem-solving skills, emphasizing the limitations of generative AI in fostering critical thinking skills, as teachers worry about students accepting AI-generated responses without adequately discerning their correctness or engaging in thoughtful analysis. This study highlights the complex interplay between teachers' perceptions, subject-specific considerations, and concerns/opinions about AI's impact on student learning and development.

The future of AI in education has many possibilities. As education witnesses a surge in technological advancements, the conclusion drawn is that a thoughtful and balanced approach is crucial in implementing AI in public high schools. While AI has the potential to address educational disparities and enhance learning experiences, caution must be exercised to prevent its misuse and ensure that it complements, rather than replaces, the vital role of teachers in fostering critical thinking, creativity, and social and emotional engagement in students. Striking this balance is essential for realizing the positive impact of AI on education and preparing the upcoming generation for a future where interaction with AI is inevitable.

Future Research and Practical Implications

Future research endeavors should delve into the possibilities of integrating AI within the classroom setting through practical trials conducted in collaboration with public high school teachers. These trials should involve the utilization of generative AI, specifically addressing concerns related to academic honesty. Additionally, exploring the implementation of AI as an educational cobot within the classroom environment presents an avenue for enhancing social interactions and supporting student learning. However, it is crucial for such research to remain

cognizant of the ethical considerations associated with AI implementation. The focus should be on establishing frameworks that not only harness the potential of AI to assist teachers but also ensure that these technologies complement rather than replace the invaluable role of educators in the learning process.

Based on the responses to the questionnaire, most non-STEM teachers were not open to implementing AI in their classrooms, on the basis that it would not be nuanced enough to beneficially teach students the skills needed for their respective subjects. So, in the future, we should put efforts into enhancing STEM subjects with the use of different forms of AI.

One form of AI that should be explored is generative AI, like the novel AI engines publicly available. This can be used to clarify trivial questions students have on a respective concept or subject, but would not be directly integrated into the curriculum. Rather, it could be a tool available to the students during school hours, in order to regulate its usage and make sure it would not be abused for academically dishonest reasons.

The other form of AI is one similar to an educational cobot, where it would act as a physical support for students and teachers in the classroom. It would aid the teacher in answering more complex questions about the subject material by identifying the student's areas of weakness and come up with different ways of explaining the solution in ways that the students will understand. Focusing students' weaknesses on given subject material and adapting to their learning styles, allowing for genuine comprehension. But furthermore, it would ultimately support the teacher in the classroom as an assistant, which would leave the teachers to prioritize the educational progress and well-being of the students, and ultimately leave the teachers in charge of the curriculum.

The persistent presence and undeniable influence of artificial intelligence in the realm of education signal a transformative era that is here to stay. As we navigate the evolving landscape of learning technologies, it becomes imperative for educators, institutions, and society at large to acknowledge the multifaceted nature of AI's impact. While its effects may elicit both positive and negative outcomes, the key lies in proactive engagement rather than passive observation. By embracing the potential of AI in education, we can harness its capabilities to enhance learning experiences, tailor education to individual needs, and prepare students for a future shaped by technological advancements. As we move forward, a collaborative and informed approach is essential, ensuring that AI becomes a tool for empowerment, inclusivity, and innovation within the education sphere.

Tables

Characteristic	Average	Range	Percentage
Age	40.25	32-48	N/A
Sex	N/A	N/A	
Male			60%
Female			40%

Nonbinary			0%
Teaching qualifications	N/A	N/A	
Masters			80%
Bachelors			40%
Grade levels taught	N/A	N/A	
9			60%
10			80%
11			100%
12			100%
Are they utilizing technology in their classroom	N/A	N/A	
Yes			100%
No			0%
Sometimes			0%
Familiarity with AI **('not at all familiar' to 'very familiar')**	3.2	1-5	N/A
Perception of AI **('very negative' to 'very positive')**	4.2	1-10	N/A
Have/are they implementing AI	N/A	N/A	
Yes			0%
No			60%
Sometimes			0%
Once			40%
Does AI affect learning/academic outcomes for students ('not at all' to 'very much')	3.2	1-5	N/A
Willing to implement AI in their classroom	N/A	N/A	
Yes			20%
No			60%
Maybe			20%

Table 1. Demographic Characteristics
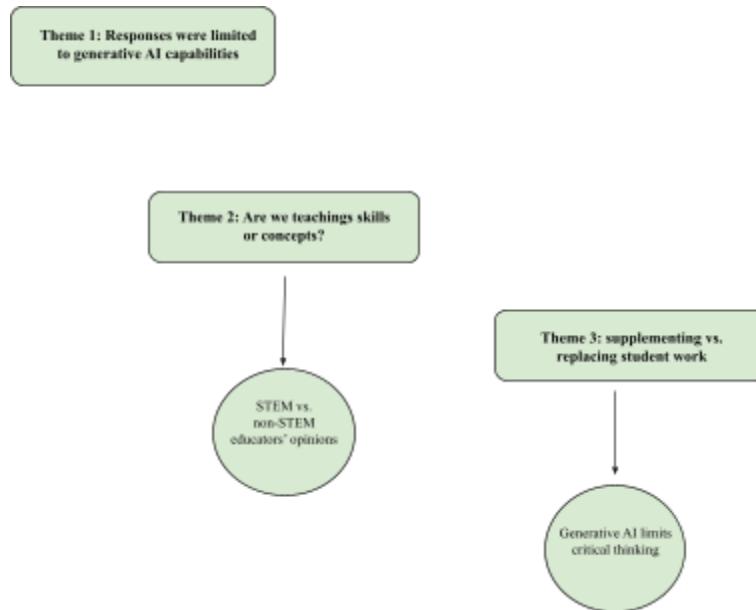
Figures

Figure 1. Themes based on educators' responses to the questionnaire

Theme and Subtheme	Representative Quotes
Theme 1: responses were limited to generative AI capabilities	
"I know there was a nation-wide panic when ChatGPT started becoming popular " "People can use it write based on prompts" "I know it makes connections, searches the web, generates words" "My understanding of AI is fairly limited, but I genuinely don't see how it'll be useful in my classroom beyond checking for grammar — but again, it has significant limitations."	
Theme 2: Are we teaching skills or concepts?	
STEM vs. non-STEM educators' opinions	"While it may boost GPAs for some and provide graduation options for students who would otherwise not complete the work, it is not teaching students the skills." "I have a feeling like there are a few classes such as art and courses with lots of writing/papers that will be impacted the most. I don't

	think it will impact math and science as much." "Cheating, lack of creative thought. It's just a tool" "If a kid has trouble in AP Physics with algebra I could tell them to pull up ChatGPT (or similar) and ask it, "how to solve for a variable in the denominator of a fraction" and see the instructions it returns. So they can learn/review that skill and then be able to successfully implement it in class."
Theme 3: Supplementing vs. replacing student work	
Generative AI limits critical thinking	"Again, I think the most (rightfully) controversial issue has been with art AI because of plagiarism, intellectual property, etc." "Also, if students (or anyone) just blindly accept results from ChatGPT as truth that's problematic, as such tools are using predictive text based on the internet, not necessarily using CORRECT information."

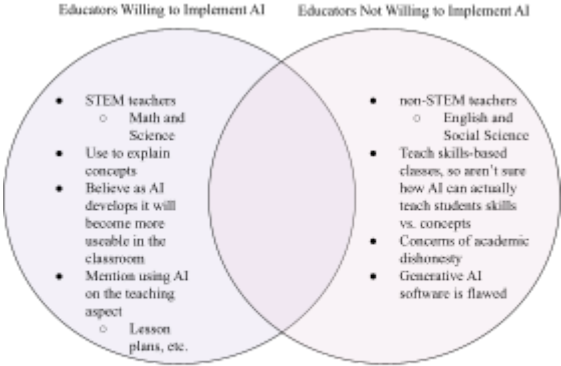*Figure 2*. Quotes representative of qualitative analysis

Figure 3. Venn Diagram showing the trends in responses of educators willing to implement AI vs. educators who aren't
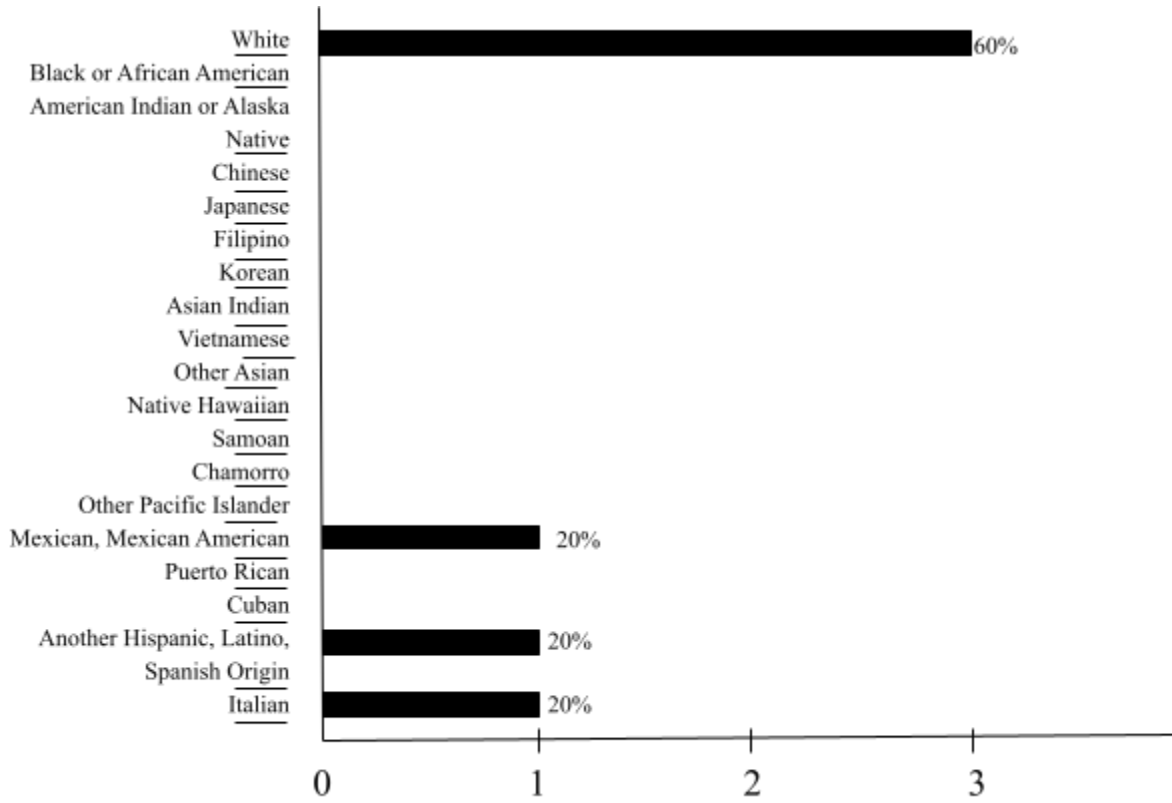
Figure 4. Race/ethnicity distribution of participants

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Exploring the relationship between emotions and music-evoked autobiographical memories
By Chengting Xie

Abstract

This study investigates the relationship between music, memory, music-evoked autobiographical memories (MEAMs), and emotions. This paper synthesizes recent research on these topics to consider how the different facets interact. I hypothesize that music's emotional valence and arousal play a vital role in evoking autobiographical memories by enhancing the memorability and vividness of recollections, with variations on individual cases such as personality, musical preference, or cultural background. This paper will add further nuance to our understanding of the role of emotion in cueing MEAMs by providing a comprehensive overview and explanation of MEAMs and the relationship between music, memory, and emotion.

Keywords: MEAMs, Memory, Music, Emotions, Review

Introduction

Renowned author Hans Christian Andersen once said, "Where words fail, music speaks" (Anderson). Music is essential to many people's lives and serves many functions, ranging from a tool for regulating emotions and reflections to a unique gateway to remembering one's past. This literature review explores these interactions in three key sections: 1. An overview of the relationship between music and memory. 2. An introduction to MEAMs as an example of the overlap between music and memory. 3. An exploration of the relationship between MEAMs and emotions and the implications, limitations, and extensions of these findings. This paper argues that music's emotional propensity plays a vital role in evoking autobiographical memories by enhancing the memorability and vividness of recollections, with variations on individual cases such as personality, musical preference, or cultural background.

Defining Concept

Music has the fascinating capability to evoke autobiographical memories, termed MEAMs (Music-Evoked Autobiographical Memories), casting us back to the past and immersing us in their associated emotions. These memories are deeply linked with episodic memory, which records our experiences regarding events, places, and emotions (Jäncke 1). Cross-modality highlights our ability to intertwine our senses, like recognizing someone by merging a visual image with a voice (Parr). Understanding these terms is essential to fully grasp the relationship between music, memory, and emotions and to appreciate how music is intricately intertwined with the human experience.

Music and Memory

The intricate bond between music and memory has piqued the interest of many researchers. Lutz Jancke's studies highlight how certain music-evoked autobiographical information. Neurologically, he emphasizes the role of the "inferior frontal and inferior temporal

brain areas" in identifying familiar songs. Instead of relying on our semantic systems that typically process meanings, music taps into our "perceptual memory system," concentrating on melodies and rhythms (Jäncke 1).

Bob Snyder delves into the structural aspects of music. He notes that music with a distinct hierarchical organization, especially with "multiple closure levels," imprints more effectively on our memory. In contrast, tunes missing such patterns make individual details harder to recall, shedding light on the therapeutic potential of music in memory retrieval (Snyder 66).

However, the nexus of music, learning, and memory is not just about recollection. Lehmann and Seufert's research introduces a nuanced observation: the nuanced interplay between background music and an individual's working memory capacity. Interestingly, those with better working memory tend to benefit more in comprehension from background music (Lehmann and Seufert 8).

The phenomenon of "earworms," incessant tunes replaying in our heads, adds depth to this discussion. Some research, like Claire Arthur's, underscores the remarkable precision of musical memories. Unlike verbal memories, which often give an essence without exact duplication, our recollection of music is typically "verbatim" (Arthur 6). This hints at a sort of "photographic memory" fortune.

This foundational understanding paves the way for further examining Music-Evoked Autobiographical Memories (MEAMs), underscoring the rich tapestry of music's relationship with memory.

Music-Evoked Autobiographical Memories and Recall Mechanisms
Music is deeply connected to memory, particularly autobiographical memories, encompassing personal experiences and self-awareness, such as attending schools or past relationships (Conway; McAdams). MEAMs arise when hearing familiar tunes from the past, frequently accompanied by potent, often joyous, emotions (Salakka 2). These memories, prompted by music and associated feelings, constitute a unique category within autobiographical recollections.

The research underscores the spontaneous, almost involuntary nature of MEAMs. Such memories often surface without conscious effort (Jakubowski). Moreover, music's power to evoke memory differs from other sensory triggers. In particular, musical memories are more episodic than those invoked by alternative stimuli (Belfi).

MEAMs are distinct in several respects. They are frequently tied to positive emotions, social themes, perceptual details, and specific life periods (Jakubowski). Further research has delved into how musical elements, like emotional valence, arousal, and song familiarity, impact MEAMs. One study involving older participants emphasized the link between a song's emotional resonance and its autobiographical significance (Salakka). MEAMs tap into multiple memory retrieval pathways from a neurological vantage, especially within the medial prefrontal cortex

(Janata). This neural engagement suggests that MEAMs' recall process differs from standard memory retrieval, underscoring their inherent intricacy (Frankland et al.).

In summary, MEAMs distinguish themselves from conventional autobiographical memories due to their emotional depth, spontaneous recall, and profound ties to musical elements. Their unique nature invites further exploration into their intricate web of connections.

Nexus of Music, MEAMs, and Emotion

Music has a unique capability to elicit powerful, predominantly positive emotions intertwined with clear autobiographical memories (Jakubowski). Various musical components, such as musical pulse and harmonics, are central to this intertwining of MEAMs with emotions (Salakka).

Research emphasizes that distinct musical attributes, from tonality to rhythmic patterns, can simultaneously spark profound emotions and vivid memories (Salakka). A survey of 113 senior participants showcased a direct link between music-evoked emotional reactions and memories. This research highlighted the role of a song's emotional intensity in evoking MEAMs, sometimes even more so than other emotional characteristics (Salakka). Songs with strong emotional valence and arousal are particularly adept at capturing attention and reigniting associated memories with intense emotional depth (Juslin). A study by Eerola delved into how different musical genres impact emotional valence. Results indicated significant variations in emotional responses to positive music across genres, underscoring the intricate interplay of musical features and emotional outcomes (Eerola).

Further, Baumgartner's research explored personal memories triggered by specific songs. An overwhelming 84% of memories recalled were positive, corroborating that MEAMs typically evoke positive recollections (Baumgartner). Interestingly, many memories carried a nostalgic tone, with respondents favoring tracks from their early twenties, often associated with treasured moments like school dances. In conclusion, the relationship between music, MEAMs, and emotions is profound. These insights deepen our understanding of the complex mechanisms underpinning this triad.

Implications, Limitations, and Future Directions

The studies discussed here present the depth of music's influence on memory systems, highlighting music as a robust mnemonic tool. Understanding that the brain processes musical memories differently than semantic ones offers a gateway into therapeutic avenues, particularly for those with memory impairments. Music's varied closure levels further demonstrate how particular pieces may resonate more with specific individuals. Furthermore, the notion that background music can enhance comprehension for those with high working memory capacity is an exciting prospect, particularly in educational settings. The prevalence of earworms, brainwashing tunes that loop endlessly throughout daily thoughts, underscores the strength of musical memories, proving they are often more resilient than those triggered by other senses.

Exploring the realm of MEAMs, the emotional depths unveiled by music-linked memories are evident. MEAMs offer a rich tapestry of personal history infused with emotion,

from spontaneous involuntary evocations to the distinct neural pathways they follow. Notably, musical features such as tonality, loudness, and rhythm play pivotal roles in this emotional and mnemonic dance. The predilection for nostalgia, especially concerning tunes popular during formative years, suggests robust emotional ties that marketers or content creators might leverage. However, despite the strides made, some limitations persist. A common thread across many studies is a limited sample size or demographic specificity, which challenges the generalizability of the findings. The richly subjective nature of musical experience adds complexity, with personal preferences, moods, and past experiences potentially shaping each individual's response. Looking ahead, many uncharted territories remain ripe for exploration. Two areas, particularly, beckon for deeper investigation. Firstly, the nuanced variations within musical genres and their distinctive impacts on memory and emotion hold promise. For example, how might jazz, with its improvisational flair, differ from the structured crescendos of classical music in evoking memories? Secondly, the potential therapeutic applications of music, particularly in memory rehabilitation and emotional well-being, could revolutionize care methodologies. Leveraging the power of music in alleviating the burdens of conditions like PTSD or memory-related ailments might also lead to a new era in holistic healing and medical treatments.

The symbiotic relationship between music, memory, and emotion remains a vast, intricate tapestry. There is still much to uncover, explore, and understand. As the melodies of research continue to play, there will likely be a richer understanding of the resonant chords of humanity.

Conclusion

This research explored the deep connections between music, MEAMs, memory, and emotions. It revealed that music's impact goes beyond auditory experiences, acting as a bridge between memories and current emotions. The study examined musical elements, their interactions with memory via MEAMs, and their entwined relationship with emotions. A standout observation was music's unique ability to elicit clear autobiographical memories. The diverse responses to musical stimuli highlight the intricate nature of this relationship. These variations indicate the need for more comprehensive studies and detailed research into individual differences. The current limited participant scope suggests the requirement for larger research initiatives. Ultimately, these findings enhance understanding of the bond between humans and music and suggest potential therapeutic applications.

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Epimedium suppresses the proliferation of hormone receptor-positive breast cancer cells in vitro by Sude Kurdoglu, Sanem Naz Kafali, Buse Kurdoglu, Hazal Ceylan, Erkan Yurtcu

Abstract

We aimed to examine the antiproliferative effect of Epimedium on human estrogen receptor-positive breast cancer cells. Human estrogen-positive breast adenocarcinoma cancer MCF-7 cells were cultured. Cell viability was determined with a trypan blue exclusion test. The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay was performed to assess cell proliferation. The proliferative index at 1 mg concentration of Epimedium was 96,10%; however, at 2.5 mg and 5 mg of Epimedium, it was 95,68% and 86,83%, respectively. Epimedium reduced MCF7 cell proliferation in a dose-dependent manner. Epimedium's anti-neoplastic effects in hormone-receptor-positive breast cancer warrants preclinical and clinical evaluation.

Keywords: Epimedium, anti-neoplastic effect, hormone receptor-positive human breast adenocarcinoma cell line

Introduction

Globally, breast cancer accounts for one in eight of all cancer diagnoses, surpassing lung cancer as the world's most commonly diagnosed cancer (Sung, et al.). In total, 2.3 million cases of both sexes were diagnosed newly in 2020, and it represents one-fourth of all cancer cases by ranking first in female deaths (Siegel, et al.; Sung, et al.).

Breast cancer is a heterogeneous disorder with various subtypes that are based on genetic profiles, histological backgrounds, or molecular deviations. The clinical outcomes within a histologically identical tumor type and mostly in infiltrating ductal carcinoma (IDC) have shown considerable differences (Makki). Therefore, to improve the treatment strategies, several breast cancer molecular subtypes like triple-negative breast cancer (TNBC), HER-2 enriched, basal-like, luminal A, and B were defined by their gene expression profiles (Makki). Greater than 70% of all cancers of the breast are diagnosed as estrogen receptor-positive (ER+) by showing ER expression in 1% to 100% of the nuclei of the tumor, immunohistochemically. For prognosis, progesterone receptor (PR) testing is also performed by applying similar principles in ER+ breast cancers (Allison, et al.). In recent years, while the trend for triple-negative breast cancer has been gradually declining, the incidence of luminal A and B breast cancer has been increasing in particular ages and racial or ethnic groups (Acheampong, et al.).

In breast cancer with hormone-receptor-positivity, molecular interaction between ER and PR signaling may lead to an effect of modulation of PR on ER action for attenuating the growth of tumors in multiple ways. Additionally, the cellular metabolism of estrogen and progesterone hormones, which is receptor-independent, produces some metabolites with different effects on the cells related to cancer development (Russo, and Russo; Wiebe, et al.). Conventional endocrine therapy of clinical breast cancer with molecular subtypes of Luminal A and B, which are positive for hormone receptors, targets mainly the biosynthesis of estrogen, ER function, and the receptors for growth factors. Systemic toxicity, the emergence of drug-resistant cancer stem

cells, and acquired resistance to tumors are the most significant drawbacks of the therapies, which may lead to therapy-resistant disease progression eventually. Therefore, their nontoxic alternatives need to be tested to overcome the limitations of targeted endocrine treatment in breast cancer with hormone receptor positivity (Telang).

Recent modern pharmacological studies have reported that Icariin (ICA), which is extracted from the dried leaves and stems of Epimedium has broad biological functions in various cancer types including the cancer of breast (Liu, et al.). In light of the results indicating that it has no toxic effects on human normal mammary epithelium (Song, et al.), it can decrease breast cancer cell resistance to chemotherapy in various ways (Cheng, et al.), and it can improve the tumor cell sensitivity to chemotherapy and radiotherapy with icaritin (ICT) which is its hydrolytic form (Hong, et al.), ICA has a favorable applicative value for the therapy of breast cancer patients in the future.

MCF-7 cell line of human breast carcinoma, which is both ER and PR positive and may express nonamplified HER-2, is a representative model of clinical breast cancer with the molecular Luminal A subtype (Subik, et al.). This study aimed to explore Epimedium's antineoplastic effect on the MCF-7 cell line in vitro since it has a high incidence with a rising trend. Therefore, this investigation was conducted by high school students under the supervision of Prof. Dr. Erkan Yurtcu.

Materials and Methods

MCF-7 (HTB-22) cell line was purchased from the American Type Culture Collection (ATCC, Rockville, Maryland, United States) and cultivated in Roswell Park Memorial Institute (RPMI) 1640 Medium (Biochrom AG, Berlin, Germany). The media were supplied with streptomycin–penicillin (Biological Industries, Kibbutz Beit-Haemek, Israel), L-glutamine (Biochrom AG), and heat-inactivated 10% FBS (fetal bovine serum, Biochrom AG). Within a Heraeus incubator (Hanau, Germany), incubation conditions were provided at 37 ^{0}C in a humidified atmosphere, including 5% CO_2.

The assay of trypan blue exclusion was used to determine viable cell numbers included in a cell suspension. Cultures with 95% or more cell viability were included in the study, and cell numbers were determined using a Thoma cell counting chamber.

Epimedium extract (EE) was purchased from a local manufacturer (Epimedium Ekstrakt 50 gr, Nurbal Şifa Merkezi). EE was dissolved in Dimethyl sulfoxide (DMSO). The DMSO concentration in cell cultures did not exceed 1%.

Cell proliferation was assessed using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT, Sigma, St Louis, Missouri, USA). Briefly, EE was applied to cells at 1, 2.5, and 5 mg concentrations. To each Epimedium well, 1 X 10^4 cells were seeded, and the plates were incubated for 48 h at 37 ^{0}C. Afterward, 20 µL from MTT solution in 5 mg/ml concentration with a final volume of 0.59 mg/ml was added into each well, and the plates were further incubated for 4 hours at 37 ^{0}C. In the last step of incubation, 100 ml of 10% sodium dodecyl sulfate (SDS) solution was added to each well, and

then the plates were incubated overnight at 37 ^{0}C. The absorbance at 540 nm was measured with an enzyme-linked immunosorbent assay (ELISA) reader (ELx800 Absorbance Microplate Reader, Biotek Instrument, Winooski, Vermont, USA).

Cell viability of Epimedium treated cells was given as the percentage of inhibition compared to the controls, which was calculated using their optical densities. Viable cell percentages were calculated by subtracting OD (optical density) values of cell culture medium from treated and untreated cells.

Results

Epimedium suppressed MCF-7 cell proliferation concentration-dependently (Table 1, Fig 1). MCF7 cell viability at 1 mg concentration of Epimedium was 96,10%, but at 2.5 mg and 5 mg of Epimedium, the viability was 95,68% and 86,83%, respectively (Table 1). We discovered that the mean optic densities of medium and untreated cells were 0,02 and 0,69, respectively, but the mean optic densities of the Epimedium treated group at 1 mg, 2.5 mg, and 5 mg doses were 0,67, 0,66, and 0,60, respectively.

Table 1. Percentage viability of Epimedium-treated cells in various concentrations of Epimedium

Epimedium concentration (mg)	Percentage (%) viability (Mean ± Std Dev)
5	86.83 ± 0.04
2.5	95.68 ± 0.10
1	96.10 ± 0.04

Fig 1. Percentage (%) viability of Epimedium treated cells
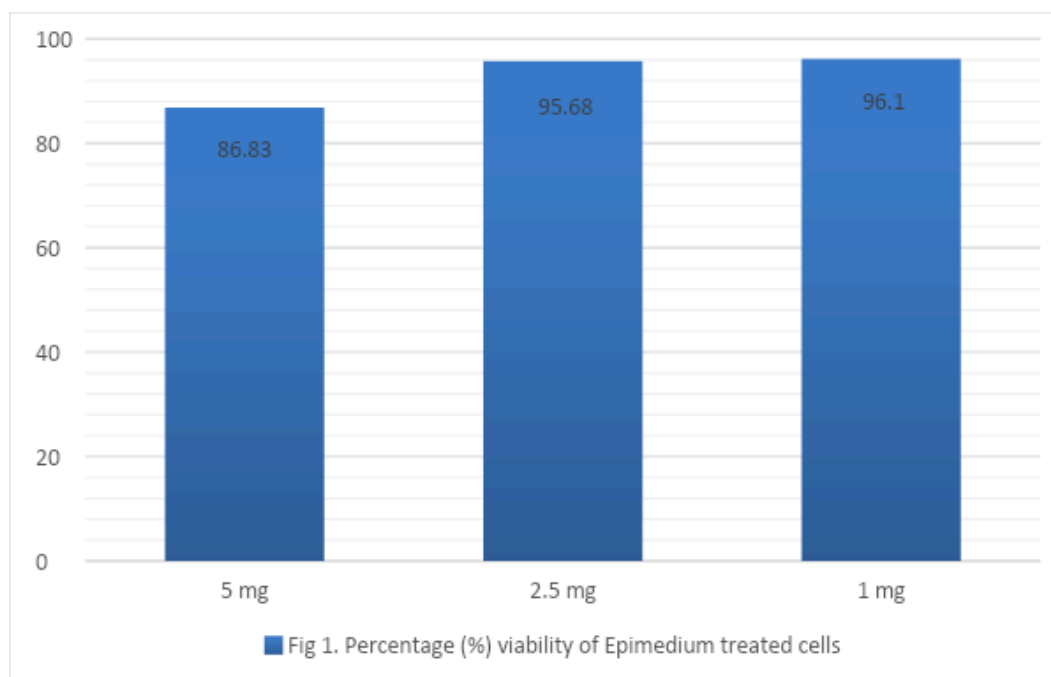
Discussion

Estrogens are highly involved in breast carcinoma pathogenesis, and the breast cancer subtypes expressing estrogen receptor-alpha (ERα) are suitable for hormonal therapy aiming to block estrogenic stimulation. For the past three decades or more, tamoxifen, with its anti-estrogenic effects, has been in the usage of hormonal treatment of breast cancers positive for ERα as an adjuvant after surgery or as a first-choice agent in an advanced disease (Lewis, and Jordan). However, the efficacy of tamoxifen is obliterated by acquired and de novo resistances, and the treatment is usually temporary with eventual relapses (Normanno, et al.). Therefore, new treatment modalities are necessary for the therapy of ER+ breast cancer.

ICT has been described to have estrogen-like growth stimulatory activities on ER+ MCF7 breast cancer cells in nanomolar (nM) concentrations (Wang, and Lou). However, Guo et al. reported that ICT showed potent anti-estrogenic growth inhibitory activity on the breast cancer cells in micromolar (μM) concentrations (Guo, et al.). Therefore, like tamoxifen, ICT may have ER modulatory activities in breast cancer cells depending on its concentration. Since we also used ER+ MCF7 breast cancer cells in our study, their results may be compared with ours, showing that Epimedium's inhibition of MCF7 cell proliferation is dose-dependent. Epimedium had no prominent cytotoxic effect on MCF7 cells at the dose of 1 mg (96,10% viability) and little better toxicity at 2.5 mg (95,68% viability), but its cytotoxicity markedly increased at a dose of 5 mg (86,83 % viability).

Guo et al. proposed that ICT could induce the death of cells and G2/M arrest in MCF7 cell cycles (Guo, et al.). Breast cancer stem cells and progenitors were preferential targets for ICT, which differed from tamoxifen's effects, inhibiting only the non-stem/progenitor cell growth. Since many therapies for cancer, including the hormonal ones, may kill only the bulky tumoral cells and may finally fail, ICT might be advantageous at this point by eradicating stem cells and progenitors that live to form new tumors. Furthermore, their investigation showed that the continuous MAPK/ERK pathway activation with ICT was another mechanism of its effects on these cells (Guo, et al.). These mechanisms may also be valid in the mechanism of cytotoxic effects of Epimedium observed in our study.

In consistent with our results, a recent report by Cheng et al. indicated that ICA exhibited a dose-dependent anti-proliferative activity and decreased cell viability in tamoxifen-sensitive and -resistant MCF-7 cell lines using MTT assay like in our study. They also found that ICA had the potential to overcome resistance to tamoxifen in MCF-7/TAM (a cell line of tamoxifen-resistant breast cancer) by inhibiting autophagy that allows cell survival (Chen, et al.; Cheng, et al.).

In conclusion, our findings showed that Epimedium could produce dose-dependent cytotoxicity towards MCF-7 cells and provide a powerful justification for its preclinical and clinical evaluation for breast cancer therapy with hormone receptor positivity.

This study was carried out by high school students who aspired to be doctors in the future, accompanied by a senior researcher.

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Factors Influencing Postcolonial States' UN Votes in Regards to Russia's Ukraine Invasion
By Anastasiya Chernitska

Abstract

The invasion of Ukraine has been unprecedented and devastating, yet some states have failed to speak out. These states that failed to speak out had similarities between them, the largest and most paradoxical being that they themselves had histories of postcolonial rule or foreign imposition. This research aims to understand why postcolonial states, despite their experiences with colonialism or intervention, did not criticize Russian violations of international norms and sovereignty by comparing votes from the United Nations General Assembly with information about economic and security ties to Russia as well as states' ratings of democracy. The data gathered reveals trends about what can influence states' foreign policy as it delves into the realist and liberal theories of international relations to ultimately better understand how states can side with perpetrators of norms violations.

Introduction

The ongoing conflict between Russia and Ukraine, sparked by Russia's invasion of Crimea in 2014 and subsequent invasion in 2022, led 96 states in the United Nations General Assembly to introduce a new resolution, UNGA Res. ES-11/1, to condemn the Russian violation of international law. Most states supported the resolution, given that 141 voted in favor of it (United Nations, 2022). Yet, others stood with Russia in solidarity by voting against the resolution, while still others chose to abstain or were absent from the vote altogether.

Not all states' choices about how to vote on Resolution ES-11/1 align with their traditional foreign policy stances. Some of these decisions to support Russia - either explicitly, with a vote against the resolution, or implicitly, through abstention - are perplexing. For instance, states like Pakistan and El Salvador, who are far from Russia's traditional foreign policy allies, chose to align themselves more with Moscow. Other supporters, like Belarus, voted against the resolution with far less surprise. What is more, taking many of these countries' national histories into account reveals that many of the states who failed to clearly side with the resolution, like India and Burundi, have been victims of colonialism or foreign invasion themselves.

This raises the question: What explains why states with colonial pasts failed to criticize or oppose Russia's egregious violation of international norms—like those of non-aggression and respect for national sovereignty? To address this puzzle, this paper sheds light on a range of factors which may contribute to postcolonial nations' foreign-policy stances towards Russia in multilateral settings such as the United Nations.

The first section of this paper reviews theoretical frameworks from existing political science literature to identify which factors might explain states' behaviors within current international relations and, more generally, shed light on the reasons behind their voting in forums such as the United Nations General Assembly. The second section describes data gathered on a number of indicators of states' security dependencies, economies, governments,

and histories to test a number of hypotheses that emerge from these existing frameworks. The third section analyzes the results of a quantitative analysis of voting outcomes and a range of covariates to see if they can support the hypotheses.

I find support for hypotheses that emerge from both realist and liberal theories of international relations; through the data analysis, which takes over 500 data points into account, states voting correlates with other factors including historical legacy, regime type, economic ties and security interests to varying extents. More specifically, I find that postcolonial democracies have the highest tendency to vocalize their non-support of Russia through votes for Res. ES-11/1 while both postcolonial and non-postcolonial autocracies are least likely, revealing differences in foreign policy behaviors across democratic and non-democratic states. Next, states with greater security reliance on Russia have higher rates of voting against or abstaining from Res. ES-11/1, implying that there is an association between arms trade and foreign policy support in this instance. Ultimately, this paper adds to the existing discussion of what influences behavior in international forums, with a focus on the invasion of Ukraine as it sparked the largest European war since the Second World War.

Literature Review and Theory

This research aims to identify what factors can predict postcolonial states' support of non-support for Russia. This is an important question as it explores the paradox in which some postcolonial states exhibited support, whether vocal or vague, towards Russian neocolonialist actions. According to Stanard, neocolonialism is defined as the control, whether indirect or direct, a state attempts to continue or to reimpose over another independent state following the end of formal imperial and colonial rule in the mid-20th century (Stanard, 2018, pg. 5). The definition of neocolonialism is broadly considered to include economic imperialism, cultural imperialism, and in the case of Ukraine, invasions to claim their sovereign land (Eymond-Laritaz). In the context of how states responded to Russian aggression against Ukraine through their voting behavior with respect to Resolution ES-11/1, the answer to this question can shed light on why states' reactions to violations of international norms and law vary more generally.

The existing literature, however, is inconclusive in its assessment of which factors are most likely to influence states' behaviors in such instances the most. According to Dreher, Nunnenkamp, and Thiele, aid, economic ties, and alliances can influence votes in the United Nations, the most important multilateral forum where states can issue clear, unambiguous responses to international events like armed conflict and other types of violations of international law (Dreher, et al., pg. 23). There are two contrasting theories for why certain reactions to violations of law or conflict might occur: the theory of neorealism and liberalism in international relations.

Neorealist theory expects nations to act in their own best interest. States, simply a larger conglomerate of people, are self-serving and egoistic by nature as they can only rely on themselves for security and support, unless they are willing to form alliances to merge

asymmetrical power (Riley, 2008). This suggests a strategy within international relations where states internationally vote, vocalize support, and ally themselves with other states to help themselves secure their own interests on a global sphere, with no central authority, where gathering power is the ultimate strategy states must pursue to survive (Weisiger, 2016).

Economic and security interests are the most compelling interests as states must pursue them to survive, given that they are essential to assuring safety and prosperity for citizens. For instance, to pursue prosperity, states rely on trade with allies, superpowers, and other nearby states to obtain necessary goods and products. When trade relations fail, a state might lose an important import. In the case of Russia–a major oil, lumber, and arms exporter–loss of Russian cooperation in trade could damage a state's security or economic interests. For the arms trade in particular, arms acquired from Russia may be important components of how a state seeks to fortify itself from enemy states, protect its citizens from terrorist groups, or more generally, gain power in the international sphere.

Since the 2010s, Russia has pledged assistance and foreign aid to African nations, signing numerous economic and development agreements. Most notably, Russia has accounted for 41% of arms sales to the continent (Gopaldas, 2023, pg. 12). The largest buyers of arms included Algeria, Angola, and Uganda–all of whom abstained in voting for or against resolutions against Russia in 2022 (Gopaldas, 2023, pg. 13). These examples suggest that, consistent with neorealist theory, cooperation with Russia on important security and economic matters may be an important predictor of which states will be most likely to vote in support of Russia, or to hold a more morally gray and neutral position through abstentions in the case of a forum like the United Nations (Hypothesis 1).

On the other hand, the liberal theory expects that some types of states, by virtue of their domestic institutions, are more likely to place greater emphasis on upholding principles of freedom, cooperation, and mutual development–despite security and economic interests. Putnam's theory characterizes international behavior as a product of a two-level game that leaders play between international and domestic audiences (Putnam, 1988). In this framework, a state's regime type can influence which domestic interests are likely to be included in the political decision-making process and, thus, be reflected in foreign policy behaviors. In democracies, the mass public is more able to influence whether their leaders join in an international outpour of support for (or, alternatively, do not support) countries targeted by norm violators like Russia. Other domestic interest groups include the political and foreign affairs elite as well as corporations, oligarchs, and other powerful economic or business leaders. If these individuals and organizations hold economic or security ties to Russia in a given state, Putnam's framework leads to the prediction that such states are more likely to voice support. In autocracies, where citizens may have fewer opportunities to express opposition to violators of international law, these other groups may be more likely to have an uncontested influence over leaders' foreign policy decisions.

The major upshot of this theory is that domestic institutions, like states' regime type, should condition how states see their interests. One set of interests derived from states'

institutions that might be reflected in states' foreign policy decisions is generally higher support for other states who uphold democratic norms, like the rule of law, including at international level. If states' foreign policies reflect their domestic institutional structures, we would expect to see more democratic states with stronger democracies show less support for Russia and see more autocratic states show more support for Russia (Hypothesis 2).

One set of particularly salient interests in cases of violations of norms of non-aggression and sovereignty could derive from historical legacies and discourses that persist among the populations of countries. For many postcolonial states, their historical legacies of colonialism have become prominent features of their states' foreign policy as a result of institutional membership in international organizations, their democratic public demanding redistributive policies after colonial rule, or autocratic governments seeking to compensate their states' less than ideal economics as described in dependency theory. These characteristics of postcolonial states in contemporary politics may, in principle, have the power to influence states' responses to conflict and norms violations in the context of international affairs.

In Putnam's framework, populations who experience colonial rule or descend from such populations may be more personally aware of the negatives of colonialism. They may therefore be more outspoken against neocolonialism and seek to persuade their leaders to uphold values of democracy, support other states' compliance with norms, and value sovereignty. Combined with liberal theory, this generates the prediction that *democratic* postcolonial nations, in which the mass public has greater influence over state voting behaviors in the United Nations or other international forums, ought to most consistently voice opposition to norm violators. By contrast, for *autocratic* postcolonial nations, the effect of popular opposition to colonialism may be muddled, as non-democratic institutions prioritize elites' interests compared to those of the mass public. The same is likely to occur in autocratic nations without colonial pasts as well, though here, the chances that the mass public are sensitive to neocolonialism are less, making non-postcolonial autocracies even less likely than postcolonial autocracies to oppose Russia. On the other hand, nations without colonialism and with democracy, typically Western nations, would act to uphold norms and international law, conforming to the liberal ideas.

In addition, postcolonial nations that have achieved independence and established democracies tended to have less social fragmentation and greater development (Bernhard, et al., 2004, pg. 245). In turn, these postcolonial states with democracy and development may be less likely to be swayed by aid or economic trade. Therefore, the combination of a state being both postcolonial and democratic should influence international votes in the United Nations to show non-support based on past principles and also ideas of mutual cooperation as seen in the liberal theory of international relations (Voeten, 2013). Altogether, as Table 1 summarizes, liberal theory that accounts for states' postcolonial histories expects opposition to Russia to be highest among postcolonial democracies, second highest among non-postcolonial democracies, third highest among postcolonial autocracies, and lowest among non-postcolonial autocracies (Hypothesis 3).

Table 1. Predictions of state support for UNGA Res. ES-11/1 based on interaction of colonial history and regime type.

Democratic	Moderate-high support (3)	High support (4)
Non-democratic	Low support (1)	Moderate-low support (2)
	Non-postcolonial	**Postcolonial**

This set of contrasting theories illuminates why states may voice their opposition to violations of norms and international law, either on the basis of interest dependency as neorealism predicts or as an externalization of democratic norms. Regime type indicators and security or economic ties are therefore potentially influential predictors of the likelihood that a state may show support or non-support for Russia's neocolonialist actions in the context of the Russia-Ukraine war.

Methods & Data

Dependent Variable: Support for Russia

This paper works to explain factors associated with support or non-support of Russia in the context of the Russian invasion of Ukraine in 2022. In this research design, the dependent variable is whether a nation will vote against or abstain during resolutions signaling support for Russia, or if it will vote for those resolutions.

In the context of this paper, support for Russia is considered to be ES-11/1 votes that are abstentions or are against the resolution. Non-support is considered a vote in favor of the resolution. The ES-11/1 resolution, voted on shortly after the invasion began, was a means to show support for Ukraine given the blatant violation of international law and territorial sovereignty, which is why it is considered the basis for support or non-support. This paper does not analyze states who were not present for the vote, as they could not have shown formal support or non-support by voting, nor is it possible to reliably interpret absenteeism, either as intentional or not, or as a protest in support of or against Russia. I draw the voting record data from the United Nations Digital Library.

Independent Variables: Interests, Regime Type, and Postcolonial Status

The independent variables in this study are foreign policy interests with Russia (specifically, arms trade with Russia and economic dependence on Russia), regime type, and colonial history. These factors are what the theories discussed suggest may predict United Nations votes and, more generally, what may lead nations to show their support or non-support for Russia, either subtly or vocally.

First, to measure the strength of states' security interests and dependencies on Russia, I draw data on country-by-country arms imports from Russia from the Stockholm International

Peace Research Institute. The number of arms, counted as equipment units, from Russia are counted within the five year period between 2017 to 2021. Continuous arms imports and large arms trades establish that security interests are larger for certain nations relative to states who may import arms from Russia only infrequently. As such, I categorize states as having *high security interests* if a state received weapons for two years out of the five, or had acquired over fifty equipment units in total. Of the remaining set of states, I categorize any state that has received arms from Russia at least once during this period as having *low security interests*. Other states I categorize as having *no security interests*.

Second, to measure economic ties, I examine the percentage of states' imports from and exports to Russia based on the World Integrated Trade Solution website available from the World Bank. I use the most recent data that is available on this source, which spans from 2009 to 2020, with smaller nations typically having older data. The data denotes if Russia was in the top five of either exports or imports, or both. It also denotes if either imports or exports, or both, were less than five percent or less than ten percent. I categorize states as having *high economic interests* when Russia counts among a state's top five import or export partners. *Moderate economic interests* include states whose exports or imports were between 5% and 10%, or were above 10% and not in the top five. *Low economic interests* had both imports and exports under 5%.

Third, I examine states' regime type using the Polity IV data set's scoring of the quality of democracy in each country. The regime type of each nation is a score ranging from 10 to -10 to describe regimes from full democracies to full autocracies, respectively. The scores from 2018 are used as they are most recent, though it is worth noting that some regime types may have become more autocratic or even more democratized within the four-year period leading up to the Ukraine invasion. Still, this is a reasonable baseline from which to assess the liberal hypotheses.

Last, I consider states' colonial histories. There are differing definitions of postcolonial states, though, for the sake of consistency with prior work, postcolonial states will be defined as those that have previously had dependency relationships with other states. To be postcolonial, states must have been ruled by a foreign power prior to achieving their own independence. This definition mirrors that in the Issue Correlates of War (ICOW) Project Supplementary Data Set, which is the source of the data used to categorize states into *postcolonial* and *non-postcolonial* groups.

To analyze this data, I cross-tabulate the frequencies of votes for, against, or abstaining across each of the categories for each variable.

Results

What are the best predictors of how states voted in response to UN General Assembly Res. ES-11/1 on March 2nd, 2022? To begin with a baseline point of reference, Table 2 summarizes the outcome variable. The table shows the outcome of the vote, listing both the names of all states that voted for, against, or abstained from the vote, or otherwise did not attend the emergency session. As noted in the introduction, certain opponents of or abstainers from the Resolution vote are unsurprising, such as the several states of the former Soviet Union who at

least implicitly side with Russia (e.g. Kazakhstan, Belarus) or its clear military allies (e.g. Syria). Yet, what explains the motives of the others?

Table 2.   UNGA Res. ES-11/1 votes taken on March 2nd, 2022 following the Russian invasion into Ukraine.

In Favor	141	Afghanistan, Albania, Andorra, Antigua and Barbuda, Argentina, Australia, Austria, Bahamas, Bahrain, Barbados, Belgium, Belize, Benin, Bhutan, Bosnia and Herzegovina, Botswana, Brazil, Brunei, Bulgaria, Cambodia, Canada, Cape Verde, Chad, Chile, Colombia, Comoros, Costa Rica, Côte d'Ivoire, Croatia, Cyprus, Czech Republic, Democratic Republic of the Congo, Denmark, Djibouti, Dominica, Dominican Republic, Ecuador, Egypt, Estonia, Fiji, Finland, France, Gabon, Gambia, Georgia, Germany, Ghana, Greece, Grenada, Guatemala, Guyana, Haiti, Honduras, Hungary, Iceland, Indonesia, Ireland, Israel, Italy, Jamaica, Japan, Jordan, Kenya, Kiribati, Kuwait, Latvia, Lebanon, Lesotho, Liberia, Libya, Liechtenstein, Lithuania, Luxembourg, Malawi, Malaysia, Maldives, Malta, Marshall Islands, Mauritania, Mauritius, Mexico, Micronesia, Moldova, Monaco, Montenegro, Myanmar, Nauru, Nepal, Netherlands, New Zealand, Niger, Nigeria, North Macedonia, Norway, Oman, Palau, Panama, Papua New Guinea, Paraguay, Peru, Philippines, Poland, Portugal, Qatar, Romania, Rwanda, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Samoa, San Marino, São Tomé and Príncipe, Saudi Arabia, Serbia, Seychelles, Sierra Leone, Singapore, Slovakia, Slovenia, Solomon Islands, Somalia, South Korea, Spain, Suriname, Sweden, Switzerland, Thailand, Timor-Leste, Tonga, Trinidad and Tobago, Tunisia, Turkey, Tuvalu, Ukraine, United Arab Emirates, United Kingdom, United States, Uruguay, Vanuatu, Yemen, Zambia
Against	5	Belarus, Eritrea, North Korea, Russia, Syria
Abstained	35	Algeria, Angola, Armenia, Bangladesh, Bolivia, Burundi, Central African Republic, China, Congo, Cuba, El Salvador, Equatorial Guinea, India, Iran, Iraq, Kazakhstan, Kyrgyzstan, Laos, Madagascar, Mali, Mongolia, Mozambique, Namibia, Nicaragua, Pakistan, Senegal, South Africa, South Sudan, Sri Lanka, Sudan, Tajikistan, Tanzania, Uganda, Vietnam, Zimbabwe
Absent	12	Azerbaijan, Burkina Faso, Cameroon, Ethiopia, Eswatini, Guinea, Guinea-Bissau, Morocco, Togo, Turkmenistan, Uzbekistan, Venezuela

Hypothesis 1, derived from neorealist theory, predicts that lower levels of arms trade and economic dependence on Russia predict lower levels of support for Russia (i.e. higher levels of support for Resolution ES-11/1). This hypothesis finds rather strong support in the data. Based on the SIPRI data, I categorize 27 states as having *high security interests* (i.e. if a state purchased weapons equipment units for two years out of the five, or had purchased over fifty equipment units in total) and 19 states as having *low security interests* (i.e. states who acquired arms from Russia at least once between 2017 and 2021).

Table 3. Results of Security interests test of Hypothesis 1.

	No security interests	Low security interests	High security interests
Rate of support for Russia (i.e. vote against or abstention)	11.4% (16 of 140)	43.8% (7 of 19)	63.0% (17 of 27)

Table 3. summarizes the results of the analysis of security interests. Of the 181 states that voted in the United Nations, about 25.41% engaged in arms trade with Russia. These 46 states with security interests show a correlation to implicitly or explicitly signal complicity or support for Russia. As the table indicates, the percentage of states in each category of security dependency on Russia who failed to support the Resolution grows as the level of security interest increases.

Next, I examine Hypothesis 1 from the economic interests perspective. Of the 197 nations included in the UN voting tally, 13 had no data on their economics while 12 were absent for voting. The analysis of economic interests thus considers the voting patterns of 172 nations. Of these nations, 24 had high economic interests (i.e. Russia was in the top 5 of imports or export partners), 94 had median economic interests (i.e. exports or imports were between 5% and 10% of a state's total exports or imports, or they above 10% but not in the top 5), and 50 had low economic interests with Russia.

Table 4. Results of economic interests test of Hypothesis 1.

	Low economic interests	Moderate economic interests	High economic interests
Rate of support for Russia (i.e. vote against or abstention)	35.7% (10/28)	18.2% (18/99)	17.0% (9/53)

Table 4 summarizes the results of the analysis of economic data compared with the UNGA voting record for ES-11/1. Based on this measure, economic interests do not appear to be a predictor of states' support or non-support for Russia in the United Nations General Assembly.

This stands at odds with the proposition of Hypothesis 1. In fact, contrary to the predicted relationship between interests and support for Russia, states with *low* economic interests had the *highest* rate of support for Russia at 35.7%, while those with *high* economic interests had the *lowest* rate at 17.0%.

This might be explained by the way that states' imports from Russia are typically items like natural gas, metal and ore, chemical products, and lumber. Mainly nearby states have formed economic dependencies with Russia for agricultural and animal products; this is similarly true for other states who voted against or abstained in the resolution for their nearby agricultural and animal product producers. An example may be India and China supplying agriculture to Asian states, or Latin American states being major trade partners with the United States. Economics still plays a key role, but mainly for non-renewables, items like coal and natural gas. Another suggestion for why this might be is the lack of integration into the international trade order that some of the states with less economic interests experience. They may still be opposed to the U.S. and Western foreign policy, yet trade with those states out of necessity or proximity.

Table 5. Summary of state support for UNGA Resolution ES-11/1 (Results for tests of Hypothesis 2 and 3)

	Rate of support for ES-11/1 UNGA Resolution (i.e. vote in favor)	
Democratic	80.4% 41/51 H3 Prediction: Moderate-high support	88.6% 39/44 H3 Prediction: High support
Non-democratic	38.9% 7/18 H3 Prediction: Low support	64.1% 25/39 H3 Prediction: Moderate-low support
	Non-postcolonial	**Postcolonial**

Turning to the analysis of the remaining hypotheses derived from liberal theory, Hypothesis 2 predicts non-democracies will support Russia more than democracies, and Hypothesis 3 predicts that a postcolonial historical legacy will make non-support for Russia more likely within each regime-type category.

The results generate strong support in favor of both hypotheses. As summarized in Table 5, of the states analyzed, postcolonial democracies were least likely to support Russia (39 of 44 voting in favor of Res. ES-11/1, 88.6%), with non-postcolonial and non-democratic states being most likely to support Russia (7 of 18 voting in favor of Res. ES-11/1, 38.9%). Non-postcolonial democracies voted for the Resolution at a slightly lower rate (80.4%) than postcolonial democracies, and postcolonial non-democracies did so at a substantially higher rate (64.1%) than

their non-postcolonial non-democracy counterparts. Note that for 29 states, data on regime type, historical legacy, or both were not available and thus were excluded from the analysis; the totals in this discussion and the table thus reflect the population states who were not absent from the vote, and who had data on both regime type and historical legacy.

These results are consistent with the predictions of both Hypotheses 2 and 3. First, as Hypothesis 2 predicts, democratic states are substantially more likely to have voted for the resolution to signal opposition. Likewise, both among democracies and autocracies, postcolonial states are more likely to have supported the resolution critical of Russian behavior than are states without a colonial history. This is consistent with the general prediction of Hypothesis 3, that postcolonial societies are more likely to exhibit a greater sensitivity to norm violations. There is thus a strong correlation that democratic nations will vote in favor of the resolution condemning international rights violation. This also holds true for postcolonial nations, regardless of their regime types.

Discussion

The greatest limitation of this research is that some nations lack information about their economic exports and imports or their regime type in the chosen databases. Island nations mainly faced this issue and therefore had less presence in the paper. Another issue was the absence of certain states from voting; they could not count as showing either support or non-support towards Russia. With economic data, the database only provided the top five nations that other nations would import and export to. It was unclear what the exports or imports were and the vague nature of the data made it hard to determine if high percentages were indicative of a genuine reliance or a trade ongoing due to proximity. Therefore, there were the least number of states with low economic interests and such an opposite result, where states with higher economic interests were shown to be more in support of Russia than those with the low interests.

Another limitation is the scope of economic dependency indicators. For instance, humanitarian aid and developmental investment from Russia are important for many countries' economic interests but were not taken into consideration (Gopaldas, 2023). This is because data on Russian financing of infrastructure—and its less visible involvement in security relations—are readily available. These variables would require a lengthier qualitative approach that would require more vetting and would be of greater use in future case-based research. Further study of this might better explain African states' support for Russia, given that many of these countries did not have Russia as a leading trade partner. This could signal that the findings may instead characterize how proximity to Russia is an indicator of economic dependence or that the supporting postcolonial states are less connected with Russia in terms of trade.

As this paper analyzes states' relations to Russia through factors like trade and security and how those can affect outcomes in the United Nations, it is worth looking into how Western states can also have influences on these outcomes. The economic and humanitarian aid of Western states and their relationship with postcolonial states can be further investigated. This paper can add to the larger discussion in what factors shape a state's response to violations of

international law and norms. The research conducted indicates that inquiry into the factors that shape states' responses to violations of international law and norms is a useful way of understanding the political dynamics at play in important, individual cases of violation—like that of the Russian war against Ukraine.

Conclusion

This analysis of historical legacy, regime type, economic ties, and arms trade as variables that influence voting behavior in the United Nations General Assembly in response to violations of international norms and laws has several implications. The first is that arms trade and security ties hold great significance in determining whether postcolonial nations—or any state— choose to condemn perpetrators of neocolonialism, like Russia, in international forums like the United Nations (Hypothesis 1). This provides key evidence in favor of the neorealist theory. As for economic ties, the correlation uncovered in this analysis is blurred—in fact, reversed—between economic interests and UN voting (Hypothesis 1). This may reflect the presence of other factors not examined in this analysis or the need to consider other indicators of economic dependency in future research.

Yet, second, the liberal theory (Hypothesis 2 and 3) also stands its ground. Postcolonial and democratic states were the most likely to criticize Russia through their votes, followed by non-postcolonial democratic states. In addition, the hypothesis that postcolonial and non-democratic states would be least likely to vocalize support for Russia on an international forum finds support. Under liberal theory, mutual cooperation, respect of international laws and sovereignty are key values expected to inform states' foreign policy decisions.

Given support for both theories, how can one explain how states balance their interests against underlying political values, like those present in democracies and postcolonial nations, that they may want to represent in their foreign policies? For one, the two hypotheses can coexist with one another. Autocratic governments will likely not be at odds with their interests and values when supporting Russia, given that they could align through regime type and sometimes through arms trade, as in the case of Algeria. On the other hand, democratic postcolonial nations are more open to criticizing Russia through a vote in favor of Res. ES-11/1 despite possibly having existing security or economic interests. This may have to do with the fact that these nations align themselves with more Western policies, though it also opens an intriguing dialogue about the matter. The heavy correlation between arms trade and support or lack of criticism for Russia following a violation of sovereignty provided much support for the realist theory, yet economic ties were less conclusive and delivered the opposite of the predicted result.

This research builds upon previous work investigating what sways votes in the United Nations, though with a focus on examining postcolonial states through their votes shortly after the invasion of Ukraine. While niche, the results open up discussion on what other factors may be driving trends in the votes of postcolonial states. This can include foreign aid or even investment into infrastructure and development, which can be part of a growing form of neocolonialism and economic intervention.

These factors require further analysis and investigation as potential explanations. In a nod to the future, this paper suggests that historical experiences play a wider role in states' international response to these topics. It also highlights how memories of colonialism in the greater collective consciousness of postcolonial states impact diplomacy and international relations.

Acknowledgements

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Proposals for Improved Early Detection and Treatment of Glaucoma - Literature Review
By Anushka Praveen

Research Question: What are potential effective practices that can be taken to improve early detection, as well as methodical and efficient treatments for glaucoma?

Abstract

Glaucoma is a chronic neurodegenerative disease of the visual system. Over the course of the disease, pressure begins to build in the eye due to improper drainage of fluids, causing deterioration in the optic nerve, leading to eventual blindness if left untreated. Given that the visual cortex, situated in the occipital lobe, is also impacted by advancing glaucoma, the brain exhibits altered function as the disease progresses as well. Glaucoma is postulated to have multiple etiologies, including genetics, other diseases, and aging. Assessment of various aspects of eye and optic nerve health can be utilized to diagnose glaucoma; however, these tests alone have been shown to provide variable results, possibly due to a lack of uniformity in their deployment. There are a range of treatments available for glaucoma, although many come with harmful side effects and have varying efficacy. Given the lack of standardized diagnosis procedures and efficient treatments, there is a great need for improvement in these areas. In this paper, potential approaches to improving both early detection and treatment of glaucoma are discussed. The current literature on glaucoma diagnosis and treatment is summarized and reviewed. Next, additional brain changes seen in glaucoma patients are identified, analyzing behavioral tests which may be used to recognize symptoms of glaucoma. Lastly, technologies or methods that take advantage of the brain's inherent visual processing abilities are applied as a possible treatment for glaucoma.

Introduction

Glaucoma is a progressive, ophthalmological neurodegenerative disease characterized by loss of retinal ganglion cells in the retinal nerve fiber layer (rNFL), degeneration of the optic nerve, optic disc hollowing, and eventual tunnel vision or blindness if left untreated (Chan, et al. 2021). Prior research reveals that an increase in intraocular pressure (IOP) results in optic nerve atrophy, which may lead to darkened peripheral vision secondary to loss of ganglion cells. In 2020, there were a recorded 76 million cases of glaucoma, making it the second leading cause of blindness worldwide. A majority of cases occur in older individuals, as 38% of cases are diagnosed in those between the ages of 65-84, while 31% of cases are diagnosed in people older than 85 years old (Allison, et al. 2020). The frequency of glaucoma, however, fluctuates between certain race groups, as previous findings suggest 29.76% of glaucoma cases are diagnosed in black, non-hispanic persons (Allison, et al. 2020).

Glaucoma is characterized by optic nerve damage. Prior research demonstrates damage is secondary to ineffective drainage of aqueous humor from the anterior chamber of the eye through the trabecular meshwork. This may be from either the iris' improper angular position or

general insufficient drainage of humor by the meshwork (Dietze, et al. 2022). Glaucoma is most notably related to genetic factors that inhibit aqueous humor drainage, but the exact cause is often unknown and variable between patients (Dietze, et al. 2022). Additional risk factors include old age or frailty, hypertension and hypotension, obstructive sleep apnea syndrome, vasospasm, diabetes, smoking, an existing increase in IOP, and family history of glaucoma (Allison, et al. 2020). While the role of genetics is significant in the diagnosis of glaucoma, family history recordings may be unreliable due to the substantial number of undiagnosed cases (McMonnies, et al. 2017). In addition, many studies find abnormalities of the visual field and the optic nerve in accordance with the rate of progression of intraocular pressure (Rhee, et al. 2022). Prognosis can vary, but it is believed glaucoma intensifies the (asymmetric) loss of peripheral vision over time. (Gupta, et al. 2017). Progression and symptoms may only be detected at advanced stages where a significant number of ganglion cells have already been lost. .

Effects on Visual System

Glaucoma is thought to mainly cause visual impairment, including effects on binocular vision (resulting in ⅓ of patients being unable to drive), peripheral vision (resulting in inability to detect hazards in one's surrounding), the optic disc, rNFL thickness, loss of functionality in the visual cortex, and an overall change in multisensory integration and visuomotor areas of the brain (Trivedi, et al. 2019).

There are multiple types of glaucoma, with the two primary types being Primary Open-Angle Glaucoma (POAG) and Primary Angle Closure Glaucoma (PACG). In POAG, the iridocorneal angle is open but the drainage of aqueous humor is inefficient, causing a buildup of aqueous humor. In PACG, the peripheral iris closes in on the pupil, blocking the aqueous humor from traveling from the ciliary body to the trabecular meshwork (Gupta, 2016). Glaucoma entails mainly unilateral symptoms, such as an increase in IOP due to the build-up of aqueous humor. POAG includes symptoms consisting of progressive "tunnel vision," which is noticed once 40% of nerve fibers are lost. PACG is characterized by head pain, "halo" vision, and blurred vision. An influx in IOP is detectable in less than 50% of glaucoma patients, and glaucoma can be asymptomatic or undetectable until the advanced stages or when 30% of nerve cells are already lost (Gupta, et al. 2016) .

Diagnosis

Given the variability in the presentation of glaucoma, diagnosis often necessitates thorough examination of the color and shape of the optic nerve. Through perimetrical tests, finding a non-pink color, a cup/disc ratio of 0.9 compared to the normal ratio of 0.3, an atypical visual field, central scotoma, and an inferior altitudinal defect all serve as indicators of possible glaucoma diagnosis (Greco, et al. 2016). Other diagnostic methods include an rNFL evaluation, an accurate family history assessment, corneal thickness measurement, ocular coherence tomography, and tonometric measurement of intraocular pressure to detect a high amount of IOP above 21 mmHg. However, 50% of patients often have normal ranges of IOP until very

advanced stages (McMonnies, et al. 2017, Allison, et al. 2020, Gupta, et al. 2016). In addition, though IOP is a preferred tool for measurement, other studies highlight the difficulty of early detection through IOP measurements (Mendonza, et al. 2022). Many studies suggest medical intervention and treatment, or lack thereof, play a critical role in determining future progression of the disease. Therefore, early detection, which allows for early therapies, is vital for inhibiting harmful progression or blindness caused by glaucoma (Hu, et al. 2020). Overall, current diagnosis methods mainly focus on assessing changes to the eye and optic nerve, rather than broader visual system changes.

Treatments

Many common treatments include parasympathomimetic application solutions, such as β-adrenergic blockers and prostaglandin analogues. Carbonic anhydrase inhibitors may also help, as they too aim to minimize the production of aqueous humor (Joshi, et al. 2023). Other treatments involve operations such as implementation of a stent in the Schlemm canal (canal that collects aqueous humor), a trabeculectomy to adjust outflow pathways for the humor, laser therapy to minimize IOP, and a Cyclocryo-Coagulation to minimize production of aqueous humor (Joshi, et al. 2023).

Treatments may have accompanying injurious side effects, and not all treatments are equally efficacious. For example, stent or tube insertions have a 33% failure rate after 3 years (Jerkins, et al. 2020). Furthermore, parasympathomimetic solutions entail side effects ranging from pseudomyopia, minimized scotopic vision, and potential constriction of the visual field due to miosis (Cvenkel, et al. 2020). The failure rate of surgical approaches and possible visual-field harming side effects of drugs suggest better treatments may be necessary.

Gaps in Diagnostics and Treatments

Treatment plans for glaucoma, as well as diagnostic measures, face multiple complications. For example, neurological changes potentially correlated with glaucoma, such as changes in the supramarginal gyrus and overall postural control, indicate unrelated neurologic somatosensory implications of glaucoma. These behavioral changes which can be assessed through the use or development of noninvasive assays, may aid in earlier diagnosis by acting as symptomatic markers of glaucoma. Given the difficulties in producing early diagnoses, assessing behavioral changes may be a potential method to better diagnose glaucoma. Additional treatment modalities are necessary as well. Therefore, the goal of this paper is to further assess unrelated neurological and somatosensory changes in order to find potential feasible examinations to strengthen an accurate diagnosis, as well as to find additional possible treatments to stimulate the visual field even in the context of glaucoma. This will be done through a systematic literature review and summary of existing data regarding glaucoma diagnosis and treatment, as well as extrapolation of findings for the purpose of supporting proposals of new methodology in glaucoma diagnosis and treatment.

Proposals for Early Diagnosis of Glaucoma

Non-Visual Affected Brain Regions

There are previously noted changes in visual system brain regions such as the visual cortex, but other studies suggest other, non-visually related neurological changes are at play.

First, accompanying the loss in multisensory integration, postural control-related changes, such as impaired functionality between the visual network occipital (VO) and the supramarginal gyrus (SMG) (a region of the brain implicated in linguistics, but mainly balance, vestibular control, and posture) may indicate glaucoma (Black, et al. 2008). Minimized connectivity between the superior sensorimotor and occipital regions has also been detected. In normal brains, the left SMG and VO have increased functionality in comparison to glaucoma patients in visual-field mean deviation, as measured by tf-MRI (Trivedi, et al. 2019). Similar neurological changes in between the visual cortex and the SMG include white matter integrity damage (Ho, et al., 2015). With tract based spatial statistics and diffusion tensor MRI (MRI that measures axon connectivity), glaucomatous brains include compromised white matter integrity in regions such as the SMG and the superior longitudinal fasciculus (SLF) (Ho, et al., 2015). Such regions, in normal brains, perform motor functions, balance control, and language functioning (Black, et al. 2008, Trivedi, et al. 2019). The SLF white matter tracts have also been found to exhibit volume shrinkage, and provide spatial information and processing (Frezzotti, et al. 2014). However, with the SLF being jeopardized in glaucoma patients, potential language functionality and naming may also be impacted, but further research is needed.

Additionally, with the utilization of f-MRI detection (measuring blood flow), data reflecting blood-oxygenation-level-dependent (BOLD) signal changes may represent overall changes in blood oxygenation in certain brain regions. Glaucoma patients' SMG-BOLD signals deviated less than 400 seconds, whereas healthy patients' SMG-BOLD signals deviated by significantly more over a span of 400 seconds (Ho, et al., 2015, Trivedi, et al. 2019). This decreased BOLD signal change/deviation in glaucoma patients' brains compared to healthy brains suggest brain blood flow and oxygenation may be less productive for those with glaucoma, potentially indicating less nutrient delivery to neurons in the SMG. As such, fractional anisotropy, or axonal integrity, was found to be lower in some glaucoma patients as measured by diffusion tensor imaging (Trivedi, et al. 2019). The SLF, being part of the longitudinal fiber association, has functions including maintaining connections to the inferior parietal cortex, where parts of visual and ocular processing occurs (Wang, et al. 2016). This suggests the hindrance in vestibular control and balance accompanying many glaucoma patients may arise from the low fractional anisotropy.

Further, a recent study examined both white matter and non-white matter regions such as corticospinal tract, middle cerebellar peduncle, etc (Frezzotti, et al. 2014). When functioning properly, these regions perform tasks such as motor control from the neck to the spinal cord and relay signals from the cerebrum to the cerebellum regarding walking and speech (Wittenberghe, et al. 2023, Morales, et al. 2015). Fractional anisotropy lesions in the corticospinal tract have

been found to potentially cause impaired motor skills, while (general) lesions in the middle cerebellar peduncle have been found to cause motor deficits, ranging from deficits in walking to general movements (though, both results were found generally, not dependent upon a glaucoma diagnosis) (Doughty, et al. 2016, Morales, et al. 2015). The study further found affected gray matter areas, such as the hippocampi, cerebellar cortex, and the frontoparietal cortex (Frezzotti, et al. 2014). Neurologically, these regions control canonical memory, coordinated movements, memory and decision-making, respectively (Ardekani, et al., 2023, Manto, et al. 2015, Euston, et al. 2013). As such, lower fractional anisotropy in these areas may lead to hindrances in such functions, and it may be assumed that these could be a symptom of glaucomatous decreases in fractional anisotropy in respective regions.

Behavioral Changes Associated with Affected Regions

While behavioral effects related to these brain region changes have not been directly assessed in glaucoma patients, other patients with similar brain changes have been found to exhibit issues with balance. A significant neurological change in glaucoma patients is damaged white matter integrity along the SMG, optic radiations, and the central visual pathway (Trivedi, et al. 2019). White matter integrity damage in these regions and their pathways may result in an unsteady gait as a significant amount of people with white matter lesions had implications in their balance, as appearing in a Timed Up & Go test (fall-measuring test) (Shen, et al. 2016). Results included the increased probability of falls for those with white matter lesions. As such, in glaucoma patients, the neurological results of glaucoma such as lowered white matter integrity and shrinkage between the VO, SMG, SLF, and others may lead to increased falls (Freeman, et al. 2007, Shen, et al. 2016). Additionally, white matter integrity damage has been found to correlate with general mobility, balance, or memory impairments (Zhai, et al. 2020). In the case of glaucoma, increased falls may serve as a correlated symptom (Shen, et al. 2016). Additional related somatosensory and/or vestibular issues may include loss of postural control, as stated previously. As lower fractional anisotropy in the SMG and SLF may occur in glaucoma patients, specifically related to white matter fractional anisotropy, poor vestibular control may arise. For example, a recent study utilizing motor performance assessments, revealed that lower fractional anisotropy and lowered white matter integrity in regions such as the SMG result in alterations in balance, standing up, and avoiding falls (Trivedi, et al. 2019).

Further, a previously mentioned study examining the effects of certain non-white matter regions and gray matter regions with lower fractional anisotropy found patients with an affected corticospinal tract and middle cerebellar peduncle (Frezzotti, et al. 2014). Additionally, glaucoma patients were found to have changes in superior frontal gyrus and dorsal attention networks; impairment in such regions, as stated earlier, may cause impairments in memory-retention and motor skills. Thus, keeping in mind previously mentioned functions of these regions, along with the potential finding of these impairments associated with glaucoma, memory deficits and problems associated with motor skills such as walking may be exhibited with certain glaucoma patients. However, further study is needed to show such associations.

Associated Behavior Tests

There are many behavior tests to detect or study the potential glaucoma symptoms mentioned above. As the main symptom connected to many impaired brain regions with glaucoma entails motor impairments, especially in gait or balance, behavior tests to test a patient's motor ability could be employed. For example, white matter integrity can be assessed using a Timed-Up and Go test as well as a "9-item Berg Balance Scale" test (Shen, et al. 2016). Respectively, these tests entail walking at a regular pace from a chair to an area and a series of balance-testing performances including standing with eyes closed versus standing unsupported. (Herman, et al. 2011, Cantellops, et al. 2023). Other tests may include a Tinetti Performance Oriented Mobility Assessment (POMA). (Scura, et al. 2022).

Proposals on Vision-Stimulating Technology for Glaucoma Patients

Normal Visual Sensory Integration and Regular Functions of the Visual Cortex

A normal, non-glaucamatous brain has a multi-stage process for visual information relaying, processing and perception. Simply described, light hits and goes through the cornea and lens, which focus it onto the retina. The retina, at the back of the eye, containing photoreceptors called rods and cones process vision and focus to relay visual signals through the optic nerve. Ganglion cells travel to the lateral geniculate nucleus (LGN), which is a region of the thalamus, a region bridging the brain's sensory cortex (Gupta, et al. 2006). After that, the fibers convey visual signals to the visual cortex, a region in the occipital lobe that integrates and perceives visual information.

A regular visual cortex functions by utilizing neurons to process visual signals in their depth (depth perception), shape, motion, color, angle, and edge, in order to create an image that the brain processes (Perkins School for the Blind, Kate Votaw). Such processing is done through specialized neurons in the cortex called feature-detector neurons, neurons with different specialties that send signals to make an image. These neurons are specialized in certain categories, ranging from certain shapes or colors, and are activated when the visual signals detect their preferred feature. Oftentimes, the visual cortex forms images through its ability to create patterns and extrapolate those patterns; for example, the area of the eye where the optic nerve leaves is an area where no photoreceptor cells exist. As such, visual information in that area is not collected, making a blind spot (Urale, et al. 2022). However, people are not consciously aware of this blind spot, as the visual cortex uses the surrounding image and its patterns to fill in the area. The brain is able to do this by combining visual attributes from the left and right visual field and overlap them, thus utilizing surrounding information to fill in the blind spot with corresponding colors, depth, etc (Raman, et al. 2016). It is also found that this specific process is active in the early, primary visual cortex. Such processes are hypothesized by other studies to follow the Hierarchical Predictive Coding (HPC) system: a method in which layers of the visual cortex predict sensory information to help create visual perception, and then utilize forthcoming

information to correct any errors (Raman, et al. 2016, Clark, et al. 2018). The specific cellular systems that do this include neuronal ensembles, a range of neurons that are widely involved in computation of perception, motor skills, and more (Carrillo-Reid, 2021).

Process of Glaucomatous Visual Sensory Integration in the Visual Cortex

While a degenerative disease of the visual system, glaucoma may not cause degeneration of the visual cortex directly nor primarily. Instead, glaucoma affects the information being processed and the processing itself of lower-level visual input, altering vision. Many studies describe the perception of the visual field in a glaucomatous brain. For example, many patients, such as those with POAG, may report blurriness at early stages, while those who receive a diagnosis or begin feeling symptoms at an advanced stage report symptoms of tunnel vision, difficulty seeing objects, or depleted peripheral vision (Hu, et al. 2014). Their vision may include a small, potentially blurry center with colors and unclear objects, and visual field borders outside of a darkened center. However, it is found that the majority of patients noticed major symptoms reducing visual acuity and/or peripheral visions in advanced stages of glaucoma, exemplifying early stages' asymptomatic classification. As glaucoma is characterized by optic nerve degeneration, such symptoms may be caused by the neuron's inability to detect light, fine details, and colors, and send those signals to the visual cortex. Peripheral vision is primarily affected, as such photoreceptors and visual neurons carrying peripheral signals are the firsts to become damaged in glaucoma (Mount Sinai; The Grant Regional Health Center).

Often, other roots of glaucomatous hindrances lie in negative correlated brain metabolism and lower levels of choline (found with glaucomatous changes in visual perception, where deficiency leads to inability of visual cortex to be protected from ocular diseases) (Murphy, et al. 2016, Hwang, et al. 2021). Other issues include the visual cortex's lower functional activation and lower gray matter volume; as gray matter is associated with cognitive function, overall gray matter volume decrease in the visual cortex may lead to an inability to process and perceive visual information. Further, a recent study found that glaucoma-correlated RNFL (retinal nerve fiber layer, in front of the optic nerve) thinning leads to decreased BOLD signals in, especially, the primary visual cortex, indicating lower oxygenated blood flow and function in primary visual cortex neurons. This may be due to cell death in the RNFL, causing thinning and thus lower function. As such, the primary cortex is hindered and less able to produce a proper visual perception (Murphy, et al. 2016).

Past Visually-Stimulating Technologies

In the past, there have been some technologies used to stimulate vision. On a broader scale, many have utilized visual cortical prosthesis (VCP), such as an Orion CVP, to stimulate visual perception, especially in those who are blind. The technique allows neurons to be electrically stimulated by inserting such stimulators into the retina and the visual cortex (Liu, et al. 2022). The device, in the case of eye or optic nerve damage, is a camera that works by putting an electrical insert into different areas of the visual system, and sends phosphene: a shine of light

or color, to these parts (Beauchamp, et al. 2020). Thus, vision is stimulated inside the visual cortex, though one is already blind and cannot receive signals from the eye itself. Additionally, some tools have been created to activate neural ensembles, such as PatMap. PatMap uses computation to find neurons that activate neural ensembles to perform pattern-completion (O'Neal, et al. 2023, Wen, 2020).

Proposal for Vision Stimulation in Glaucoma Patients

Due to the history and increased interest in such technologies, a potentially effective proposal for glaucoma treatment would be a prosthetic machine or technology that potentially could stimulate vision in glaucoma patients. Such a technology would utilize the visual cortex's ability to fill in patterns. The proposal might be beneficial, firstly, due to the levels of diagnosis. As many patients aren't diagnosed early, and only during the advanced stages, many previously mentioned treatments may not prove to be sufficient to mitigate the harms of glaucoma. The forthcoming solution may be most effective for those in advanced stages in which peripheral vision has been significantly impacted. This solution uses pattern-filling because it allows for people to see the periphery, which doesn't have fine details, so it may be easier to fill in with potential, presumed visual information without accommodating for finer details. The brain, specifically the visual cortex, is already equipped with this technique and applies it when not only filling the blind spot, but additionally for other areas lacking proper visual input. For example, for perceptual filling-in during retinal scotoma, which is another medical condition leading to blind spots or darker regions of the brain. The brain can potentially be stimulated to utilize this pattern-filling skill to fill in peripheral vision that has been darkened/hindered by utilizing any remaining sensory input it can process.

If implemented, this may occur by using technological inserts in order to eventually stimulate HPC. According to past studies, in order for technologies, such as AI, to recreate the HPC model, it needs to allow the brain to both carry ability to form predictions about sensory input as well as carry ability to perform "precision-weighting" of errors, which is essentially the ability to consider predictive errors about sensory input (Mondragon, et al. 2018, Haarsma, et al. 2021). This could be done through, firstly, utilizing computational technology similar to PatMap, recognizing neurons that activate neuronal ensembles, specifically for the visual cortex (O'Neal, et al. 2023). PatMap, for example, does this task specifically by utilizing conditional random fields (CRF), complex statistical models utilized in pattern-recognition (O'Neal, et al. 2023, Sutton, et al. 2012). Utilizing that statistical model, the technology is able to find pattern-completing neurons to aid in stimulation of neuronal ensembles. If the same or similar methodologies are implemented, but engaging CRFs for only visual pattern stimulation and finding pattern-filling neurons only in the visual cortex, then pattern-stimulation for glaucoma patients' vision would be more easily attainable. Next, after the technology finds the neurons that stimulate perceptual neuronal ensembles, the neurons must be increasingly activated to more actively fill in patterns in glaucomatous vision. Brain stimulation therapies, such as electrodes, apply magnetic forces which neurons can react to, therefore becoming stimulated (National

Institute of Mental Health). This methodology is named "transcranial magnetic stimulation" (Ye, et al. 2022). The electrodes would entail specific magnetic nanodiscs, an emerging technique outlined by a recent study, in order to do this (Chandler, 2020).

As previously mentioned, glaucomatous peripheral RNFL deficits have been found to be correlated with lower BOLD signals in the primary visual cortex, hindering its ability and role as the major processor in creating visual perception (Murphy, et al. 2016). As such, it may prove beneficial to place electrodes near the primary visual cortex, due to the need for its functionality (which the electrodes may be able to aid in through its help in stimulating pattern-completion). Additionally, according to other studies, neurological processing of peripheral vision (not direct absorption of peripheral sensory input, which occurs through rod and cone cells in the retina) occurs specifically in the rostral (anterior) calcarine cortex, otherwise known as the frontal region of the primary visual cortex (Dragoi, 2020). As glaucoma impairs peripheral vision, causing darkness around that part of the visual field, the electrodes would be placed adjacent to the anterior calcarine cortex in order to stimulate pattern-completion of, specifically, peripheral vision. Thus, these may prove most effective to stimulate the visual cortex, where integration and making of visual perception occurs. For dendrite or axon (two functional parts of a neuron) stimulation, as well as location of pattern-stimulating neurons, two such electrodes may need to be inserted, mirroring previous studies' patterns of utilizing one for location, and one for the stimulation itself (Städele, et al. 2017). Such technological insertions would most likely be surgical. Majority of deep brain stimulation techniques utilize surgical implantation by inserting electrodes through holes in the skull, and inserting the electrodes in using a wire (Mayfield Clinic, 2022).

In summary, due to the technology's detection and activation of neurons and neural circuits that advance visual pattern-completion/HPC in glaucoma patients, peripheral vision may be filled in, thus, potentially forming a more complete visual perception to aid in preventing blindness (especially in advanced stages of glaucoma). It is important to note, however, that such an experiment has not yet been tested and requires testing before proceeding.

Discussion/Conclusion

In this study, we first reviewed glaucoma and its neurological effects. As a common visual neurodegenerative disease, glaucoma is one of the leading causes of blindness worldwide. We examined glaucomatous visual field symptoms, ranging from inability to notice fine details to, significantly, darkness and inability to see periphery. Despite the serious impact of glaucoma on visual perception, the disease often starts as asymptomatic, leading to difficulty in diagnosis until advanced stages, in which the visual field has already been significantly impacted. Accompanying its degeneration of the optic nerve, we investigate glaucoma's hindrances on other areas, not only the visual cortex and RNFL, but also possibly non-visual regions of the brain. As such, we proposed the opening possibility of examination of other symptoms potentially correlated with glaucoma, though they may include ones not conventionally tested for. Furthermore, we reviewed treatments for glaucoma that were previously established, but

noticed many side effects and similar approaches in many of them. All treatments established so far entail treatment to the eye directly, from pharmaceuticals to surgical adjustments. However, due to the high amount of diagnoses being in only advanced stages, ones in which significant damage to periphery/optic nerve occur, such existing treatments may not prove as efficient or successful in reversing the effects of glaucoma. As such, we proposed the idea of a different treatment, entailing treatment on the visual cortex rather than the eye itself; such a treatment may also work even in advanced stages, which may be beneficial in regards to the significant amount of advanced-stage diagnoses. Through further investigation, we suggested a technological insert into the visual cortex that would allow the brain to perform advanced pattern-completion, therefore potentially completing areas of the visual field which were hindered by glaucoma.

Through this study, we researched non-visual, but affected regions of the brain correlated with glaucoma. We found multiple regions that fit this specific category, including the supramarginal gyrus, superior longitudinal fasciculus, and others such as the corticospinal tract, etc. When such regions are affected by glaucoma, we discovered through research of recent studies that the functional connectivity, amount of oxygenated blood flow, and white matter in the region were unusually impacted. As such, through further examination of these regions, we maintained that the aforementioned effects on these regions may lead to difficulty in balance, increase in falls, and potentially other symptoms such as language impediments, though needing further testing to prove.

As we researched and compiled evidence of other regions glaucoma inhibits, along with observable impacts of the changes to such regions, it may prove to be a future method of diagnostics. Considering the current inability in diagnosing, as well as constrictions of diagnostic testing to visual testing of only the eye, testing of parts of the brain and for detection of other symptoms may increase the rate of early diagnostics. As such, many would be able to get effective treatments before significant damage to the eye and visual field occurs. In this study, we proposed multiple diagnostic tests accompanying the non-visual effects of glaucoma previously listed, including multiple balance tests.

Secondly, through this study, we investigated alternate treatment methods in order to aid in mitigating glaucoma's effects on one's visual field and perception. Primarily, we started with a proposal for a technology that would initiate the brain's functionality in pattern-completion in order to complete gaps in the visual field, thus forming a more-complete visual perception. Through thorough review and examination of previous studies, pattern-completion in the brain, and current, similar technology makings, we discovered first the brain's uses of pattern-completion in a healthy brain, such as filling in the blind spot. As such, we investigated the specific neurological processing that allows for pattern-completion in order to know what to recreate in the technology proposal. Additionally, we researched methods to stimulate neurons to start the pattern-completion process (HPC), and found that many technologies do so through magnetic field stimulation. Moreover, we evaluated the regions of the brain in terms of which regions are responsible for the specific visual sensory integration of the part of the visual field hindered by the glaucoma. As we discovered this specific region was the front part of the

primary visual cortex, we furthered our proposal to utilize the magnetic field-neuron stimulation on neurons in this region, as initiating pattern-completion in this region would make up for visual-field completion in glaucoma patients. Furthermore, we investigated which specific technologies would be used to stimulate pattern-completion and detect the neurons that do so in the front part of the visual cortex, and found that such stimulation would be done through electrodes. If two electrodes are inserted into the aforementioned region of the brain, one may be used for detection of HPC-stimulating neurons, while the other would use magnetic field forces to stimulate the pattern-completion process for the periphery of the visual field. However, it is important to note that such a technology has not been tested yet, and requires testing for confirmation of functionality. Though, such a method may prove to be efficient due to multiple reasons. It acts by activating pre existing functions of the brain, rather than altering the brain significantly. It may be a better method as it has the potential to work even in advanced stages of glaucoma, in which damage to the optic nerve is irreversible. This is relevant due to the high amounts of diagnoses in the advanced stages of glaucoma. Such a treatment may potentially stimulate and provide a basic, but complete visual perception, which serves as a reversal to the ultimate effect of glaucoma being hindrance to the visual field.

In the future, through further study of the non-visual, and more specifically, neurological rather than only ocular, changes occurring with glaucoma, the relationship between the disease and these changes may be elucidated further. Thus, in conclusion, through review and further analysis of this study, symptoms accompanying these brain changes may serve as potential, additional diagnostic measurements to improve rates of early detection and diagnosis. Further, due to the possibility of multisensory integration and overall perception potentially being compromised in glaucoma patients, as well as the uncertain rates of success and harmful side effects that current treatments encompass, aforementioned stimulating technologies could have potential to improve overall perception in the visual field if inserted into the visual cortex to aid it in glaucoma patients.

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On the Topic of Abortion: Consciousness and Potentiality by Alexander Gazdag

Abstract

      The abortion debate orbits the concept of personhood, with my perspective anchoring on the essence of conscious experience. I define personhood as an entity capable of manifesting conscious experiences. The preeminent experiences that we protect are conscious experiences. Determining life's end hinges on the cessation of consciousness. Once a person is dead, they no longer have a conscious experience. We don't try to save dead people; we bury them in the ground. The brain, the locus of conscious experience, defines our essence. In the abortion discourse, I temporally ground my stance, aligning with the emergence of conscious experience around 24 to 35 weeks. This boundary corresponds to criteria employed in ascertaining death, fostering symmetrical attitudes toward birth and death. The opposition to abortion often centers on potentiality, asserting that a fetus's ethical standing hinges on its potential for specific capacities, particularly consciousness. However, I find this problematic, attempting to assign value to something lacking current existence. When it comes to fetuses, lacking the requisite neurological development for conscious experiences, discussions surrounding the preservation of such experiences appear incongruous in the absence of their actualization. In addition to this stance, I further assert a distinction in the value attributed to human and animal consciousness. While human consciousness holds intrinsic value, I do not extend the same consideration to animal consciousness.

Introduction

      The abortion debate pivots fundamentally on the conceptualization of personhood. My foundational perspective revolves around the discernment of what constitutes a person and the essence of personhood itself. Rejecting the notion that personhood is merely an amalgamation of biological cells or a corporeal entity housing a brain, I contend that, in essence, a person is an entity endowed with the capability to manifest conscious experiences.

      Central to our discussions about life, death, and the need for protection is the conscious experience inherent in personhood. When we invoke the term "person," we are not referring to a mere physical form or the rhythm of a heartbeat; rather, we are addressing an entity capable of undergoing conscious experiences. The crux of the matter lies in identifying not a 'what' but a 'who' that is undergoing suffering or joy. Conversations surrounding pain, suffering, harm, happiness, and joy invariably pertain to an entity capable of experiential engagement with these emotions. In essence, personhood transcends the confines of mere bodily existence.

      When considering the parameters of ascertaining or terminating life, my thoughts converge on the significance of conscious experience. The determination of life's end appears to be the cessation of a conscious engagement, marking an individual as deceased. This idea gains prominence when pondering the replacement of body parts. While substituting organs like the heart preserves personhood, a distinct shift occurs when the brain is involved. Suppose one could sever my neck, offering the choice to sustain one element, the head, and affix it to another body, or maintain the entire remaining body and attach a different head. What criterion should be applied to determine the

continuity of my identity? If I were to transplant a human head onto a bionic body and simultaneously replace my body with a bionic head, the prevailing sentiment might not be one of perceiving two instances of "Alex." Rather, observers would likely characterize the entity with the bionic body as Alex, acknowledging that our essence resides in the brain, the locus of conscious experience. The replacement of the brain through a transplant fundamentally alters the person's identity. Some people who have an organ transplant might say "I feel a little bit different", but "I", the subject, the person, has not changed.

The essence of our being, comprising experiences, memories, and the subjective interpretation of the world, resides within the brain. Contemplating the nature of life and its termination, none of my reflections seem to orbit the parameters of a heartbeat or distinctive DNA. Rather, the crux of the matter appears to hinge on the conscious experience.

Turning to the concept of life's origin, discussions around artificial intelligence offer insight. In the realm of AI, the focus is not on creating physical entities, such as hearts or DNA, but on generating or mimicking conscious experiences within a machine. The core of our collective defense seems to revolve around preserving the sanctity of conscious experiences. This leads me to suggest that if life concludes and begins through conscious experience, that pivotal moment likely signifies the start of life itself.

Delving into the abortion discourse, my perspective hinges on the assessment of harm and its recipient. Although there is no complete scientific consensus, it is typically agreed upon that anywhere from around 24 to 35 weeks, marks the juncture at which the brain attains the requisite components for initiating conscious experiences (Falsaperla et al., 2022; Lagercrantz, 2014; Lagercrantz & Changeux, 2010; Kostović & Jovanov-Milosević, 2006; Padilla & Lagercrantz, 2020; Burgess & Tawia, 1996; Brusseau, 2008; Frohlic et al., 2023) Before this critical developmental stage, during the initial trimester, the conscious experience essential to personhood is not yet realized.

Consequently, my stance on abortion aligns with a temporal parameter. Prior to the formation of a conscious experience, up until approximately 24 to 35 weeks, I maintain a pro-abortion position. This temporal boundary is not arbitrary but corresponds to the emergence of the criteria we employ to ascertain death — the presence of a conscious experience. Our attitudes towards our birth and death should be symmetrical.

Upon the emergence of personhood, a natural preference tends to be asserted: to live and not be killed. My concern for conscious experiences stems from a simple reality: I, too, possess consciousness and wish for its safeguarding. However, recognizing the impossibility of persuading others to value the protection of my experience in the absence of a reciprocal commitment, we collectively establish a framework of rules, often manifested in what we commonly term as government.

This system of rules serves as a tool to instill in each of us a shared understanding—a commitment to respecting and protecting the asserted preferences of our fellow beings. This collaborative effort forms the foundation of a societal contract, a tacit agreement wherein humans, recognizing their inherent social nature, engage in a mutual exchange of values and preferences.

Potentiality

An oft-cited opposition to abortion centers on the concept of potentiality (Stone 1987; Buckle 1988; Hare 1988; Lockwood 1988; Manninen 2007; Morgan 2013). The abortion potentiality argument contends that the ethical standing of a fetus hinges upon its potential to evolve into a being endowed with specific capacities, particularly the faculty for conscious experiences. However, I find this line of reasoning problematic, as it implies a challenge inherent in any moral system attempting to assign value to something that presently lacks existence.

The notion of considering the preferences of an entity devoid of current or assertable preferences seems absurd. It appears more judicious and rational to posit that ethical and governmental frameworks should extend their regard and protection to entities once endowed with consciousness and capable of asserting preferences. Protection, after all, presupposes the existence of something to be safeguarded, rendering the notion of safeguarding non-existent entities seemingly incongruous.

To illustrate, the analogy of propelling a soccer ball through the air becomes pertinent. The acceptability of such an action is contingent upon the presence of a future window to receive the soccer ball, distinguishing between an act of pre-breaking and preventing a window from coming into existence. Engaging in the act of kicking a soccer ball through the air holds moral acceptability when anticipating the presence of a window in that location a year hence. The action does not equate to premeditated window breakage. Similarly, forestalling the emergence of a window does not morally equate to the deliberate act of shattering a window. Analogously, the contention that preventing the formation of conscious experience equates to terminating an existing one fails to resonate with me. I discern a meaningful distinction between these two scenarios, rejecting the equivalence drawn.

In grappling with the concept of respecting the potentiality of life, I find myself perplexed as to the inherent significance of this potential. My focus gravitates towards the discernible presence of a sentient being capable of asserting preferences. In essence, the core lies in the existence of preference-asserting entities, and the ethical considerations and protections that ensue are contingent upon this tangible reality.

Consider an individual undergoing general anesthesia as an illustrative case. While presently devoid of consciousness, the moral imperative dictates that it would be morally objectionable to terminate their existence. This moral objection arises from our speculative projection that, in a state of consciousness, this individual would assert a preference against their own demise. Implicit in this perspective is the acknowledgment that the subject undergoing anesthesia likely existed in a prior state of conscious vitality, wherein the preservation of life was a tacitly assumed preference. Consequently, ethically refraining from causing harm to this temporarily unconscious entity aligns with the stipulated definition of personhood as an entity possessing the capacity to manifest conscious experiences.

The salience of past sentience or consciousness lies in the absence of moral considerations preceding the emergence of a conscious experience. The ontological shift from non-consciousness to consciousness signifies the inception of preferences and rights. The past conscious experience, having asserted a desire to be treated as a living entity, becomes the ethical foundation upon which moral agents can recognize and uphold rights. While acknowledging potential exceptions, such as

cases involving suicidal tendencies, the normative human condition is characterized by a set of preferences—be it for sustenance, shelter, or other requisites—that necessitate fulfillment. It is only upon the advent of existence that these rights become recognizable; prior to such emergence, the moral terrain remains void of content and ethical obligations.

In the discourse surrounding preferences, a conventional linguistic practice involves attributing desires to entities, whether they be fetuses or trees. It seems incongruous to ascribe wants or desires to entities such as fetuses or trees. Rather, these entities undergo developmental processes devoid of conscious experience. These entities are typically perceived as existential entities that undergo existence rather than actively expressing volitional wants. The emergence of conscious experience marks the point at which preferences or desires materialize, warranting acknowledgment and reciprocal regard as sentient beings. It is only upon the emergence of conscious experience that preferences and desires manifest, attaining a status worthy of respect and reciprocal acknowledgment within the context of sentient living entities.

Generally, the assumption of a desire for continued existence is contingent upon a foundational level of brain functioning. This deviation becomes palpable in scenarios where an individual is declared brain dead, yet the remainder of the body maintains vitality. In such instances, the customary response refrains from presuming a desire for life, instead recognizing the cessation of brain function and the consequential absence of conscious experience.

My adherence lies not in the rationality but in the pursuit of a conscious experience akin to our own. The focal point of my consideration is directed towards any entity that has commenced a conscious experience similar to ours, deeming it worthy of value and, consequently, protection. While I acknowledge the potential for temporary lapses in consciousness, such as those encountered during periods of sleep or under anesthesia, these moments of dormancy do not nullify the antecedent affirmations of a desire for continued existence.

The heart of the matter becomes apparent when contemplating the status of a fetus. Unlike instances involving temporary lapses in consciousness, the fetus lacks prior assertions from which to draw reference. It has yet to embark on a conscious experience, with only a potential for such emergence in the future. Consequently, the valuation of a conscious experience that has not yet asserted itself becomes an untenable proposition—there is no foundation upon which to ground the imperative of protection.

Consideration is afforded to an individual under general anesthesia, who should not be subjected to harm due to the recognition of their prior conscious experiences. The precedence set by a preceding conscious experience is deemed valuable, necessitating the respect of asserted preferences, even in instances of temporary unconsciousness. If, for instance, an individual previously articulated a preference for the cessation of life, this desire would be honored, provided the appropriate procedures are followed. The United States employs the concept of "Do Not Resuscitate" (DNR) orders, emblematic of a commitment to respect the expressed wishes of individuals, allowing them to pass away in accordance with their asserted preferences.

There exists a contention that our lack of valuation for deceased individuals serves as evidence of our inherent esteem for potentiality. However, it is imperative to distinguish between two

fundamentally divergent categories of potential. The insinuation that I derive value from the future is a mischaracterization, as my focus is unequivocally rooted in the past—a temporal domain where an entity existed, asserted preferences, and subsequently ceased to be considered upon death.

There is a clear disparity between a conscious being that has asserted preferences, undergoes a temporary suspension of consciousness, and then resurfaces with an anticipated desire to uphold those preferences, and a prospective entity that has yet to come into existence. The term "potentiality" attempts to establish an equivocation between these distinct scenarios. However, the inherent dissimilarity persists—the potential for an entity to exist and articulate its inaugural preference differs markedly from an entity that has previously asserted a preference, experiences a temporary hiatus in consciousness, and is anticipated to maintain its established preferences upon reawakening.

In essence, these represent two different paradigms of potentiality. One encapsulates the potential for an entity to exist, an entity that has not yet realized its existence. The other, my perspective, revolves around an entity that has affirmed preferences, briefly departs from consciousness, and subsequently returns, likely desiring the perpetuation of its previously asserted preferences. The value, in this case, emanates from the already established preferences articulated during a state of consciousness.

The crucial distinction lies in the ontological difference between a thing and the potentiality inherent in a thing that is yet to manifest. These are not mere semantic nuances; they constitute fundamental disparities. Comparing a fetus in its pre-developmental state, lacking the requisite components for consciousness, to an individual presently unconscious due to anesthesia, reveals a pivotal dissimilarity. The fetus has never been conscious and lacks the essential parts to manifest a conscious experience, while in the latter case, there exists a continuum of a preceding conscious experience, with all the essential elements in place to rekindle consciousness once the temporary alleviation is lifted. The significance of continuation in this context resides in the emphasis placed on the foundational machinery—the ontological basis that is imbued with the inherent capacity to actualize a conscious experience. Within moral discourse, intuition assumes a paramount role, serving as the wellspring from which our ethical principles emanate. Ultimately, the crux of our valuation concerning other sentient beings appears to be rooted in the subjective experiences mutually shared in our interactions with one another.

If we were to bring a human into existence, there wouldn't be any prior experiences until that first moment of consciousness occurs. The fetus is on its way to developing the capacity for consciousness, but it hasn't reached that point yet. Unlike a person going to sleep at night, who has an ongoing subjective experience that resumes upon waking up, the fetus hasn't even begun to exist.

Within the realm of hypothetical scenarios designed to illustrate the valuation of potentiality, consider the following: a newborn possessing the developmental attributes of a first-trimester fetus, yet with the prospect of attaining the rationality or consciousness characteristic of a third-trimester infant after three months in an incubator. Within my philosophical framework, moral consideration is withheld until the entity in question has attained existence preceding its inaugural conscious experience.

One might raise a counterargument, contending that our moral intuitions would vehemently oppose my stance, particularly in scenarios akin to the hypothetical involving the potential dismemberment of that unconscious "newborn". I, however, assert that the term "brutal" carries with it connotations of experience, implying a form of suffering. Notably, for such suffering to transpire, there must be a concurrent conscious experience. Actions such as cutting hair or trimming fingernails are not labeled as brutal because they lack the experiential component. Hence, when discussing the brutal dismemberment of an entity devoid of conscious experience, I must point to the impossibility of inflicting brutality upon it, as the absence of consciousness precludes the existence of suffering.

Consider the distinction drawn between setting a living being on fire, constituting a brutal act due to the associated suffering, and the act of cremating a lifeless body, devoid of the experiential element. The crux of the matter lies in the presence or absence of suffering, inextricably tied to the state of consciousness.

The prohibition of abortion presents a moral quandary wherein a conscious agent, capable of articulating preferences, may express a desire to avoid hosting a living entity within its body—one that lacks preferences or a conscious experience. In advocating for the illegality of abortion, there arises a demand that individuals endure until the entity attains a developmental stage where relinquishing responsibility or pursuing an abortion becomes untenable. This effectively transforms women into live incubators, a moral stance I find problematic, particularly when the entity being incubated lacks any discernible conscious experience.

Moreover, my position maintains a reluctance to ascribe value to the mere potentiality of existence. The distinction is critical: potentiality does not equate to actual existence. This departure from other contexts is evident when considering bricks, where their mere presence does not warrant labeling them as a potential building, or a few drops of water, which we do not classify as a potential lake. The recognition of potentiality does not confer the status of the actualized thing.

Examining the trajectory of a zygote's development reveals a process that will culminate in consciousness. However, crucially, it has not yet attained a conscious experience. A distinction exists between the developmental trajectory of a thing and its actual instantiation, as opposed to its state of being en route to that instantiation.

Potentiality prompts a reflective inquiry—can this principle find parallel application elsewhere? Consider the analogy of the Starry Night painting by Vincent Van Gogh: if, hypothetically, I were to disperse all of Van Gogh's paints before the masterpiece was actualized, would such an act be tantamount to the destruction of the Starry Night? Despite possessing all the requisite components—the canvas, the paints, the brushes—the actualization of the artwork had not yet occurred. In this context, what I would have disrupted was not the Starry Night painting itself, but rather the incipient process leading to its emergence.

Drawing a parallel to abortion, a similar dynamic unfolds. The termination of a zygote or fetus, while constituting the cessation of an ongoing developmental process, does not signify the end of a human life in the same manner that spilling the paints before Van Gogh's artistic endeavor does not equate to the destruction of the Starry Night. The moment of consciousness is analogous to the

realization of the Starry Night, wherein possessing all the constituent elements does not confer the status of an actualized entity.

Consider a hypothetical scenario: encountering a sapling and extracting it from the ground. The question that emerges is whether this act can be equated with the destruction of a tree that the sapling might have grown into. This scenario serves as an illustration of the argument that potentiality, in and of itself, does not carry the weight of actual existence.
In this context, the removal of the sapling does not constitute the destruction of a tree. While it holds the potential to mature into a tree, the sapling's extraction does not negate the fact that it is not yet an actualized tree. The crucial distinction lies in the acknowledgment that potentiality is not synonymous with realized existence. The mere potential for growth does not confer upon the sapling the status of a fully developed tree.

Applying this analogy to discussions surrounding potentiality in broader contexts, such as the abortion debate, reinforces the argument that the potential for a certain outcome does not carry the same moral weight as the actualized realization of that outcome.

Harming Future Persons

Despite the fetus not yet attaining personhood, the moral imperative dictates refraining from engaging in activities such as smoking crack or consuming alcohol from the earliest stages of pregnancy, particularly if abortion is not contemplated. This moral prohibition stems from the acknowledgment that such behaviors inflict harm upon a prospective person, a being with a future existence. It is crucial to distinguish between dismembering a fetus at 19 weeks, where the act prevents the emergence of a future person, and engaging in harmful substances during the early stages of pregnancy, where the harm is inflicted upon a future person (Persson 1999).

Consider a scenario where a heavy sculpture is positioned atop a structure, and its release is imminent. If the sculpture is immediately released onto someone below, the act is unequivocally perceived as unethical. However, if a timer is arranged for the descent of the sculpture in fifteen minutes, with the foreknowledge that an individual will be present at that time, does the ethicality of the act hinge on the absence of immediate harm at the present moment? The unethical part is that in fifteen minutes, a person WILL be there. The crux of the ethical concern lies in orchestrating a situation wherein harm will be caused to a future person. The essence of the ethical dilemma is not the mere placement of the sculpture or the establishment of a contraption; rather, it is the deliberate arrangement of circumstances leading to harm in the future. The analogy here is when the child is born, eventually they're going to discern dissimilarities from their peers due to prenatal substance exposure. The manifestation of harm is delayed, instead of the immediate act of substance use before the child's birth. Similarly, the moral issue surrounding substance use during pregnancy lies in the potential harm inflicted upon the future person if the intention is to carry the child to term.

Conversely, within the contextual boundaries of planned abortion at 12 weeks, causing a fetus to develop fetal alcohol syndrome is not deemed morally wrong. To elaborate further, envisage a scenario where intervention is essential to divert the sculpture's trajectory from harming Charles, the person, to potentially causing harm to a non-person, represented by the cardboard box that Charles is

carrying. The sculpture is either going to harm Charles the person, or harm the non-person, the cardboard box. It appears evident that opting to avert harm to the person, Charles, may ethically warrant the destruction of the sculpture, a non-person.

What Could Have Been

Some critics might posit that my position deviates from common intuitions, particularly when considering instances where women who have undergone abortions mourn miscarriages as if mourning the death of a born child, even when the miscarriage occurs before the 24-week mark. Within the framework of my argument, a fetus is assigned the same moral status as an egg or ovum. However, this perspective seems at odds with prevailing intuitions, which tend to attribute a more profound significance to the loss of a fetus compared to the dissolution of an ovum.

In defense of my position, I would assert that those who mourn the loss of a fetus may not be grieving the entity itself, but rather expressing sorrow over a forfeited opportunity for a potential life. The emotional response to miscarriage or post-abortion regret may be rooted in the visualization of the unrealized potential of a child that could have come into existence. The emphasis here lies not in valuing the fetus independently but in valuing the prospective person it could have become.

To elaborate further, consider the analogy of theft: if I were to steal ten thousand dollars from someone at the age of 20, it cannot be argued that I stole a hundred thousand dollars from them. However, as they approach the ages of 25 or 27, they might feel the absence of the invested ten thousand dollars that could have grown into a hundred thousand. The feeling of loss is directed towards the potential wealth that could have materialized over time.

The mourning process is tied to the perceived unrealized potential rather than constituting a direct valuation of the fetal entity itself.

Human Vs Animal Consciousness

My exclusive concern centers explicitly on the human conscious experience, distinctly diverging from a regard for the conscious experiences of animals. I posit that the human conscious experience manifests a notable alteration or distinction from the conscious experiences of animals. This assertion often elicits inquiries, with some questioning the advocacy for conscious experience and invoking the conscious experiences of animals, particularly pigs or dogs.

Critics posit scenarios where a two-year-old dog ostensibly exhibits a more developed conscious experience than a human infant or fetus. However, my stance rests on the premise that human development unfolds in a manner distinct from such analogies. I do not believe that consciousness evolves through successive stages akin to a lizard, horse, or primate consciousness. I contend that, once the necessary cognitive components are in place during fetal development, the subsequent trajectory involves the accumulation of qualia and experiences.

This developmental process is characterized by the gathering of experiential content and the intricacies of neuronal connections, without a substantial shift in the fundamental nature of human consciousness. I reject the notion that our conscious experience undergoes a transformative evolution

from one animalistic form to another; rather, these represent successive stages within the spectrum of human conscious experience.

Many anti-abortion arguments subscribe to an ontological categorization of the human, extending protection from fetus to the cessation of metabolic activity. I concur with the safeguarding of the human entity across its developmental continuum but emphasize the necessity of contextualizing this within the framework of conscious experience. The bracketing of the ontological category within the realm of conscious experience refines and elucidates the considerations associated with the protection of human life.

In the hypothetical scenario where an individual sustains an injury resulting in a sustained state of consciousness comparable to that of a newborn, the assertion is maintained that personhood persists despite the altered cognitive state. The foundation of this perspective rests upon the conviction that the integration and communication among cerebral constituents, coupled with the manifestation of a discernible level of conscious experience, unequivocally establishes the continued existence of personhood. The delineation of this phenomenon is cast in a binary framework, distinctly demarcating the presence or absence of consciousness.

Contrary to a developmental paradigm implying a linear transition across distinct tiers of consciousness—from lizard consciousness to dog, ape, and ultimately human consciousness—I posit that the attainment of human consciousness marks an irreversible qualitative shift. Once this threshold is traversed, the entity resides within the categorical domain of human conscious experiences, irrespective of potential variations in the vividness or intensity of said conscious experience. Once established, human consciousness becomes an immutable constituent within the spectrum of conscious experiences peculiar to the human condition. The fully formed conscious experience inherent in any non-human animal fails to attain the level of sapience or sophistication characterizing the human conscious experience.

In the comparative analysis of a three-year-old and an infant, the determination of whether the former exhibits a heightened or diminished level of consciousness remains ambiguous, necessitating an investigation of the interaction between brain development and the accrual of sensory data. Consider the scenario of a one-month-old experiencing developmental delays in cerebral growth; in this instance, the capacity to amass a plethora of experiences persists, potentially engendering a nuanced comprehension of the world. While cognitive impairment is acknowledged, the discernment of whether the three-year-old's purportedly elevated consciousness is attributable to a more advanced developmental or experiential state, as opposed to a prolonged duration of data accumulation, remains elusive.

Analogously, positing a comparison between a 25-year-old and a 10-year-old, one might contend that the former harbors a heightened consciousness of the world. However, disentangling whether this disparity emanates from developmental maturation, heightened cognitive consciousness, or the sheer accumulation of experiential data poses a quandary.

In contemplating the cognitive progression from infancy to early childhood, one might posit that the enlargement and neuronal augmentation of a one-year-old's brain contribute to a more diverse array of experiences. However, it would be unwarranted to characterize their consciousness as

inhuman prior to such developmental milestones. This trajectory is seemingly integral to the unfolding of a conscious experience. Contrary to the notion that a one-month-old possesses a consciousness akin to that of a lizard, my contention is rooted in the empirical observation that even within the womb, a fetus in its third trimester exhibits the ability to discern distinctions in languages.

I do not believe a one-month-old is a rudimentary entity. Newborns, even within the initial days of life, exhibit cognitive capacities that transcend the characterization of a formless entity devoid of conceptual awareness (Canini et al. 2020; Kosakowski et al. 2023; Giordano 2021; Zacharaki & Sebastian-Galles 2021; Beech & Swingley 2023; Werker & Byers-Heinlein 2008; Cortesa et al. 2019; Uchida-Ota et al. 2019; Kujala et al. 2023; Kosakowski et al. 2022). Rigorous studies suggest that newborns, within a week of birth, can differentiate between native and non-native languages, as well as distinguish various linguistic stimuli. Their cognitive state does not resemble an indistinct blob devoid of conceptual understanding. This contention extends to the prenatal environment, where accumulating evidence supports the notion that fetuses in utero begin to accumulate sensory data about the external world.

While some proponents argue that animals, such as dogs exhibiting comprehension of commands like "sit" and "stay," or pigs demonstrating proficiency in video games beyond random chance, may suggest a heightened level of intelligence or consciousness compared to a newborn, I maintain an agnostic stance regarding the conscious experiences of animals. The intricacies of human consciousness, characterized by its profound sapience, evoke a distinctively sophisticated quality that I hesitate to ascribe to the cognitive experiences of animals. Although terms like "smart" are commonly employed to describe their problem-solving abilities and Pavlovian associations, I don't believe these cognitive capacities equate to a comprehensive sapient experience akin to that of humans.

Acknowledging the remarkable capacity of animals, particularly dogs, pigs, and dolphins, to grasp intricate and complex patterns, my reservation lies in whether they share a semantic understanding of the world or possess a conscious sapience analogous to the human experience. While they excel in intricate pattern recognition, the depth and richness of their cognitive experiences remain a subject of uncertainty, distinct from the profound sapient consciousness characterizing human beings.

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Foliage for the Future: Using Urban Reforestation to Sequester Carbon By Lillian Breese

Abstract

At the start of the 21st century, it was estimated that 50% of the Earth's population lived in urban cities (Zipperer, Northrop & Andreu, 2020). As populations continue to surge in cities, it is evident that a problem has emerged. Forests are being destroyed for urban expansion. Each year, over 32 million acres of forested land are destroyed to be developed into urban areas (Zipperer, Northrop & Andreu, 2020), which can have significant negative impacts on the climate crisis, specifically regarding its effects on carbon in the atmosphere. Trees and plants are able to sequester carbon through the process of photosynthesis, and when forested areas are destroyed, the process of photosynthesis cannot be performed (Reforestation, n.d.). One way this can be combated is by replenishing vegetation in deforested areas. Research was gathered on this topic by synthesizing original research experiments and analyzing literature. As a result, it was concluded that reforestation is one of the best methods of sequestering carbon.

Introduction

Climate change is becoming one of the most preeminent challenges of the 21st century. Since 1880, the global temperature of Earth has, on average, risen 0.04º F each decade (Lindsey & Dahlman, 2023). The effects Earth has endured due to this are severe. Extreme weather events have become more intense, ice caps have melted, and sea levels have risen (Lindsey & Dahlman, 2023). These effects have been amplified by the emission of greenhouse gases. Greenhouse gases, such as carbon dioxide and methane, stay in the atmosphere and trap heat, causing the overall temperature of the Earth to increase. To combat this, many efforts have been made to sequester greenhouse gasses, utilizing a multitude of different methods. One of which is reforestation, otherwise known as the process of replanting trees and plants. In this paper, it will be argued that reforestation is one of the best methods of sequestering carbon.

Reforestation's Advantages

Using reforestation as a technique of sequestering carbon has many considerable benefits. Trees are naturally effective carbon sinks, as one unit area of vegetation can, on average, sequester 7.69 kg/m^2 (Lind, et al. 2023), mostly through the process of photosynthesis. Plants photosynthesize by drawing carbon dioxide out of the air through the stomata and converting it into oxygen, which is then released into the atmosphere (Lambers, 2023).

Integrating vegetation into urban spaces would help sequester carbon not only by photosynthesis but also by decreasing the amount of energy expended by cities and buildings due to plants' cooling effects. An increase in canopy cover from trees provides shade and therefore cools the area in which it covers.

Secondly, the process of evapotranspiration cools the air surrounding trees (Rahman et al., 2020). Evapotranspiration is the process in which water is transferred from a plant to the atmosphere via the stomata of the plant, which can directly lower the surrounding air

temperature between 1ºC and 8ºC (Rahman et al., 2020). Furthermore, this cooling property of plants is especially effective when in the proximity of buildings. Buildings would expend less energy to cool themselves and burn less fossil fuels, therefore emitting less carbon (Sayedabadi et al., 2021).

Additionally, urban forestation is space-effective. In the context of urban areas, vegetation would be able to be planted on roofs, as there are over 380 billion square meters of urban roof space (Getter, et al., 2009). Thus, in theory, reforestation in urban areas is feasible due to ample space to implement urban vegetation projects. In a 2017 study done by Har'el Agra et al., it was found that plants such as sedum and succulents would be most effective in spacial and energy efficiency because not only do they efficiently sequester carbon, but they also are lightweight, water efficient, and less susceptible to extreme weather conditions, making them especially suitable to be used on urban green roofs.

In summary, it can be said that reforestation has several advantages that make it one of the best methods of carbon sequestration. Reintegrating vegetation into urban spaces would not only remove carbon from the atmosphere through photosynthesis but would also decrease air temperatures, further slowing fossil fuel emissions. It is also space-effective, and if properly implemented, can be resistant to extreme weather conditions.

Application

Further adding to the appeal of using vegetation to sequester carbon is its practical application. For example, numerous cities globally have already implemented urban forests in their most populous metropolitan areas. Austin, Texas–one of the United States' largest cities–is home to over 33 million trees, covering about 18% of the city's total surface area (Steffan, 2021). This has been successful at sequestering carbon, as Austin has the third lowest carbon footprint of all major cities in the United States (Caleri, 2022).

Additionally, the application of sequestering carbon via urban forests has been proven successful. A 2002 study conducted by David J. Nowak and Daniel E. Crane states that in the United States, urban forests are responsible for currently storing 700 million tons of carbon. This number is significant because it is estimated that in order to fully counteract the effects of climate change caused by CO_2 emissions, 2 billion tons of carbon would need to be removed from the atmosphere (Moseman, 2023), therefore the 700 million tons of carbon stored in urban forests is substantial, as it is almost half of what is needed to reverse climate change.

Furthermore, the application of using reforestation to sequester carbon has had significant economic benefits. It should be noted that companies can also use reforestation as a method to lower their carbon emissions. Here, the carbon market is introduced. Carbon markets are economic systems in which companies offset their carbon emissions by purchasing carbon credits (What are carbon markets?, 2022). One way companies are able to offset their emissions is by buying credits in forestry and conservation, or in other words, reforestation and prevention of deforestation. This is often chosen as an offset technique, partially because it is an efficient method of removing carbon from the atmosphere and because it adheres to corporate social

responsibility trends (Boulter, 2024). When companies help reforestation projects, they are not only offsetting their carbon emissions, but they are also contributing to the conservation of ecosystems and biodiversity, further incentivizing reforestation projects and sustainability goals.

Discussion

As discussed, there are many significant benefits to using reforestation to sequester carbon, such as its spatial effectiveness and efficiency in photosynthesis and evapotranspiration. Although, there are downsides that need to be considered. For example, if not researched properly, reforestation projects can fail. If the types of vegetation planted are not a good fit for the climate of the area, then the plants could cease photosynthesis, thus being a waste of time and resources. Likewise, there are species of plants that are dormant during certain seasons, and therefore would only be alive and able to photosynthesize for a portion of the year. While these are considerable drawbacks, they are manageable or avoidable. With proper research and understanding of how plants interact with climates, reforestation has the potential to be one of the best options to effectively sequester carbon.

A potential way in which more of these projects can be more widely funded is with help from the government. State governments already fund many public park and garden projects for local communities. For example, in 2020, the Great American Outdoors Act was signed into law, providing $900 million in funding to the United States Land and Water Conservation Fund (*Federal Funding*, n.d.).With more efforts such as these, the tree population can skyrocket. This would be just one important step in a larger journey. With proper conservation and reforestation efforts, the effects vegetation can have on carbon and more broadly, the climate, has the potential to be a major contribution to maintaining a healthy Earth.

Conclusion

Through extensive research and synthesis of the literature, it can be concluded that reforestation as a technique of sequestering carbon has many significant benefits and has been proven effective when it is implemented in urban settings. With global temperatures rising due to fossil fuel emissions, and urban areas increasing, the need for more vegetation has become dire. For a more sustainable future, reforestation projects and urban forests need to be implemented as much as possible to maximize tree cover. If deforestation continues at its current rate, the effects of climate change will become more rampant. Action needs to be taken to begin fixing the negative effects of urban expansion. With more attention to reforestation and urban forestry, significant change can be made, ultimately leading to a healthier, more sustainable future.

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The Evolution of Dissonant Improvisation in Jazz Trumpet: A Data Science Approach Using Blues Harmonic Structure By Jordan DePue

Abstract

This research paper examines the extent to which jazz trumpet improvisation has become more dissonant over time. The first half of the paper provides a qualitative description of the development of jazz trumpet improvisation from its initial consonant, harmonic roots centered on basic triads and dominant chords. The second half presents a quantitative investigation of the increase in dissonance by studying five jazz trumpet solos spanning from the 1920s to the 2010s. Based on an in-depth analysis of these solos, there is a discernible trend in which solos of the 1920s were very consonant in nature, but by the 2010s, the solos featured far more dissonant notes.

Early jazz was influenced by the harmonies of European classical music and was highly consonant. The soloists of the 1920s big band era complemented the consonance of the overall ensemble, with little variation from the dominant chords. The 1940s bebop movement saw a deliberate shift to more dissonance, reflecting society's increasing embrace of individualism and creative freedom that would eventually define the 1960s. This self-expression persists to the present day, with implications on the teaching and implementation of dissonance in jazz pedagogy.

Using the 12-bar blues harmonic structure as a baseline to examine the evolution from consonance to dissonance in jazz trumpet solos over a period of ninety years, this paper transcribes and compares five different jazz trumpet solos with the "expected," or consonant, notes that complement the chord progressions of the 12-bar blues harmonic structure. The trumpet soloists and the songs their solos are transcribed from are Bix Beiderbecke, "Royal Garden Blues;" Clifford Brown, "The Blues Walk;" Clark Terry, "Straight No Chaser;" Randy Brecker, "Freight Trane;" and Marcus Printup, "Bee Dub Blues." Analysis reveals that jazz trumpet solos were very consonant in the early jazz period; however, the present day reveals a wide departure from consonance, with solos featuring far more dissonant notes.

Introduction

This paper was sparked by a transformative experience at a jazz concert in Seattle, WA, in October 2023. The event featured the internationally acclaimed Jazz at Lincoln Center Orchestra (JLCO). As a jazz musician myself, I found profound inspiration in various aspects of their performance—from the band's distinctive sound and creative take on classic tunes to their shared commitment to the art form; however, the improvisational skill of Marcus Printup, one of JLCO's four trumpet players and primary soloists, deeply resonated with the jazz trumpeter in me. Beyond Printup's impressive sound, rhythmic variations, and masterful bebop lines, what really captivated me was how he used melodic tension, notably the deliberate incorporation of dissonance throughout his solos on classic 12-bar blues chord progressions. This prompted me to explore why and how Printup's dissonant improvisation seemed to seamlessly "work." Upon

revisiting my favorite classic jazz trumpet albums, I observed that other trumpeters did not employ dissonance to the same extent, leading me to a fundamental question that forms the core inquiry of this paper: How has the use of dissonance evolved in jazz trumpet improvisation over time? Transforming this question into a testable hypothesis propelled me to inquire further: How can we quantify the evolution of dissonance in jazz trumpet improvisation using tools from data science? The paper is structured into two parts: In the first section, I provide a qualitative analysis of the historical progression of jazz trumpet improvisation, emphasizing its increasing dissonant characteristics. The second segment outlines the quantitative methodologies essential for measuring this evolution and presents five excerpts of jazz trumpet improvisation by different musicians from the 1920s to the 2010s: Bix Beiderbecke, "Royal Garden Blues;" Clifford Brown, "The Blues Walk;" Clark Terry, "Straight No Chaser;" Randy Brecker, "Freight Trane;" and Marcus Printup, "Bee Dub Blues." This trend suggests that dissonance is a part of the evolution of jazz pedagogy, and not limited to a specific era after its initial appearance.

Qualitative Evolution of Jazz Trumpet Improvisation

Jazz has its roots in the harmonies of European classical music, where early expressions of the genre leaned towards simpler, more straightforward elements. In the initial years of jazz, especially with the emergence of big bands in the 1920s, the harmonic landscape primarily centered on basic triads and dominant chords, laying the groundwork for more complexity to evolve within the genre. This reliance on foundational harmonic elements created a musical environment characterized by its consonant nature (Martin 2). Looking at early jazz, we can see how European classical music influenced its harmonies. In the big band era, the prevalence of triads and dominant chords shaped the overall sound and provided a strong base for jazz improvisation to take off.

In big band ensembles, jazz solos usually stayed harmonious. Soloists skillfully blended their improvisations with the ensemble's harmony, forming a mutual connection that preserved harmony and upheld consonance. This collaborative approach ensured that individual expressions resonated harmoniously with the overarching tonal framework, contributing to the cohesive sound of big band jazz (Hersch 113). Examining how jazz solos fit into big band setups, it becomes apparent that soloists consciously blend their expressions with the overall ensemble. The harmonious quality of these solos not only puts individual virtuosity on display but also stands as evidence of the collaborative synergy within the ensemble. This intricate interplay between soloists and the collective contributes significantly to the rich and unified sound of the music.

As jazz progressed through the years, soloists began a journey of cultural evolution, gradually experimenting with dissonance. This evolution happened in sync with larger cultural changes, highlighting jazz's dynamic role as a reflection of society. The rise of the "free jazz" movement in the 1940s, gaining momentum during the liberating 1960s, marked a significant departure from consonant norms that had been prevalent in the genre. This departure opened up new avenues for expression and pushed the boundaries of what jazz could sound like. This

movement introduced elements of freedom and unpredictability, challenging the established harmonic boundaries (Pressing 12). In parallel with the changing cultural landscape, jazz soloists started using more dissonant notes in their improvisations, breaking away from consonance and "expected" harmony. This change reflected how society was shifting more toward individualism and a desire to push boundaries and strive for creative freedom. This evolution in jazz gave musicians more ways to express themselves and captured the spirit of the changing times.

During the bebop era, jazz soloists aimed for innovation by adding more dissonance to their improvisations without fully embracing the radical departure to "free jazz." While pushing boundaries, they did not completely break from conventional consonant structures. Instead, they subtly rebelled against predictability, introducing a higher level of harmonic complexity. Soloists challenged the established norms without entirely forsaking the inherent structures that defined jazz improvisation (Lozenski 7). The bebop movement is a pivotal chapter in jazz history, whereby the introduction of dissonance is not a wholesale rejection of tradition; rather, it is a deliberate infusion of complexity. Soloists of this era navigate a delicate balance, pushing the boundaries of harmony while maintaining a strong connection with established harmonic structures. This nuanced approach contributes depth to the music, highlighting both innovation and a respectful connection to the foundations of jazz.

Exploring how dissonance evolves in jazz trumpet improvisation uncovers a diverse range of techniques. These include disguised traditional reharmonization, the use of contour/sequence, progressive modal agreement, rhythmic devices, alternative dominant chord chromaticism, and modal reharmonization (Richardson 7). These categorizations provide a basis from which we can gain insight into the different "tools" that create dissonance. From making slight changes to the harmony to experimenting with rhythms, these categorizations shed light on the various strategies employed by jazz trumpeters as they navigate the ever-changing landscape of dissonance in their improvisations. In examining specific instances of dissonant improvisation, Clifford Brown's performance on "Stompin' at the Savoy" (Brown and Roach, 1:41) offers a compelling illustration. Brown's trumpet phrases in this piece deliberately violate the conventional rules of chord-scale theory; however, what makes this dissonance intriguing is the adept resolution of these dissonant pitches, showcasing a distinctive approach labeled as "harmonically informed, melodically driven." (Salley 12). Brown's execution exemplifies a delicate interaction between dissonance and resolution, challenging established theories while maintaining a cohesive and harmonically satisfying improvised solo that synergizes with the overall ensemble.

Quantitative Methodologies

Having examined how jazz improvisation has become more dissonant over time, this section will provide a definition of "the blues" and how it can be applied to quantitative analysis to measure jazz trumpet dissonance over time. Then, I will reference two papers, analyzing their methods to quantify how jazz trumpet has become more dissonant over time. Finally, I will use

data science methods to conduct a quantitative analysis, analyzing the distribution of notes played in selected excerpts from five jazz trumpet players across the time period 1920-2010.

To start our exploration, we need to understand the basic structure of blues harmony, setting the groundwork for our research. Blues harmonic structure, a distinctive musical framework prevalent in blues music, plays a pivotal role in shaping the characteristic "bluesy" sound. The 12-bar blues harmonic structure is a chord progression that typically consists of three chords and is divided into three four-bar segments, with the first four bars dominated by the first chord, the second four bars by the fourth chord, and the third four bars by the fifth chord. Key elements of this structure encompass:

A. 12-Bar Blues Progression: Comprising 12 measures or "bars," each typically lasting for four beats, this progression follows a specific pattern of chords, providing a structural basis for melody and improvisation.

B. I-IV-V Chord Progression: In a major key, the I chord represents the tonic, the IV chord the subdominant, and the V chord the dominant. A basic 12-bar blues progression in the key of C major might involve the chords C7 (I), F7 (IV), and G7 (V).

C. Dominant 7th Chords: Creating tension and resolution, these chords contribute to the distinct blues sound. For instance, in the key of C major, C7, F7, and G7 are all dominant 7th chords.

D. Turnarounds: Concluding a 12-bar blues progression, turnarounds consist of chords facilitating a smooth transition back to the sequence's beginning.

E. Blues Scale: This is a modification of the major scale, with flat III, V and VII, used in creating a "blues sound". Musicians often use this scale for improvisation over the blues harmonic framework.

Using this structure, we can compare how much jazz trumpet solos follow or deviate from this framework over time.

In a study by Mathew Setzler and Robert Goldstone, in "Coordination and consonance between interacting, improvising musicians," a table of pitch sets and related consonance scores was established to measure rhythmic alignment and consonance between interacting, improvising musicians (92). Here, the researchers set up a blind study in which a jazz pianist played (and improvised) with either a live partner or against a backing track, after which a poll of the audience as well as the pianist was taken to rate each performance for "consonance." In our study, we will utilize a table (see table 1) similar to that of the pitch sets table in the Setzler study, but instead of "pitch sets," we will illustrate "expected" notes in the blues harmonic structure, which will give us a baseline of what consonance is in this context. From this, we will analyze which notes trumpet soloists have played both within and outside the "expected" structure.

In order to map frequency of consonant notes, we need to understand scale degree notation which will allow us to create a common map. For any key, the "root" chord is generally composed of the first note of the scale, the third, the fifth, and the seventh. As an example, a C major chord is constructed of the following notes: C, E, G, and B which may also be notated as

"scale degrees", I, III, V, VII; in other words, I for C because that is the first note of the scale, III for E because that is the third note of the scale, V for G because that is the fifth note of the scale, and VII for B because that is the seventh note of the scale. Therefore, a scale in the key of C major can be notated as follows: C = I D = II, E = III, F = IV, G= V, A = VI, B = VII, C = VIII. Table 1 illustrates this for C major, as well as the keys that the five solos we are investigating are written in.

Table 1

Scale degree notation for C Major and the keys for the five soloists

Scale degree notation	1st note	2nd note	3rd note	4th note	5th note	6th note	7th note	8th note
	I	II	III	IV	V	VI	VII	VIII
C Major	C	D	E	F	G	A	B	C
Bb Major	Bb	C	D	Eb	F	G	A	Bb
F Major	F	G	A	Bb	C	D	E	F
Ab Major	Ab	Bb	C	Db	Eb	F	G	Ab
Eb Major	Eb	F	G	Ab	Bb	C	D	Eb

Note: Includes notations for C Major and the key signatures of the examined solos. Note that the solos in "Royal Garden Blues" and "The Blues Walk" are both in the key of Bb Major

Next, we can apply the notation of scale degrees to create a general "map" that applies to any key. In table 2, we present notes from a 12-bar blues harmonic structure which are considered consonant. These notes align with the harmonic structure's root chord, creating a grounded connection within the song's key. While the chords do change over the progression of the harmonic structure, ultimately, they are all related to the root chord, which can be improvised over throughout the whole form. For example, in the key of C Major, with the first note in the C Major scale being a C, consonant notes would be: C (I/VIII), E (III), G (V), and B (VII). The notes C, E, and G form the root of the C Major chord, and the Bb is the "dominant seventh" of the chord. The reason the B is flat is because in the blues, most often many of the chords, including the root chord, is a "dominant chord," or in other words, contains a flat 7th scale degree, with the only caveat being older tunes, which will be explored later.

Table 2

Pitch Set with Scale Degree Notation of Consonant Notes Over the 12-Bar Blues

Consonant notes in any key over typical 12-bar blues harmonic structure

I (VIII)	III	V	Flat VII

Note: This is an example of the standard expected, or consonant, outcomes of notes over the standard 12-bar-blues structure.

Next, we will quantify how frequently the "unexpected," or dissonant, notes appear in trumpet solos over time. In their paper, "Dig that Lick: Exploring Patterns in Jazz with Computational Methods," Henry et al., employed the use of a "similarity search tool" to map a "lick" (musical phrase) and its variants across different performers over time (15). In the study, the goal was to measure and analyze the variation in rhythmic structure of various licks over time using a "similarity search tool." This allowed the researchers to quantify how a musical phrase has evolved over time and across different performers. In contrast to studying rhythmic structure variation, our study will map how the notes of improvised jazz trumpet solos have followed or deviated from the 12-bar blues progression and thus quantify the dissonance (or consonance) of these solos.

In other words, instead of following the evolution of one specific musical phrase, we will look at a selection of five different trumpet players and solos from the 1920s to the 2010s (and thus different musical phrases) which are in the 12-bar blues classification. The musicians were selected in order to represent most of recorded jazz history and diverse jazz styles (swing era, bebop, post-bop, fusion, neoclassical). In table 3, I present the five trumpet players and their songs. Starting from the 1920s is Bix Beiderbecke, with his solo from "Royal Garden Blues;" (Beiderbecke 01:07) then the 1950s with Clifford Brown's solo on "The Blues Walk" (Brown 00:25); then the 1960s with Clark Terry's "Straight No Chaser" (Terry 00:42); then the 1990s with Randy Brecker in "Freight Trane" (Wilkins 00:30); and finally, the 2010s with Marcus Printup's "Bee Dub Blues" (Printup 01:28). We will see how the solos have incorporated more dissonant notes over time, illuminating not just the presence of dissonant notes, but how frequently they were played. This will provide us insight into how trumpet solos have deviated from standard blues harmonic structure over time.

Table 3
Selected trumpet players and songs

	Era	Soloist	Song
1	1920s	Bix Beiderbecke	Royal Garden Blues
2	1950s	Clifford Brown	The Blues Walk
3	1960s	Clark Terry	Straight No Chaser
4	1990s	Randy Brecker	Freight Trane
5	2010s	Marcus Printup	Bee Dub Blues

Note: The selection of five different trumpet players and solos from the 1920s to the 2010s which are in the 12-bar blues classification.
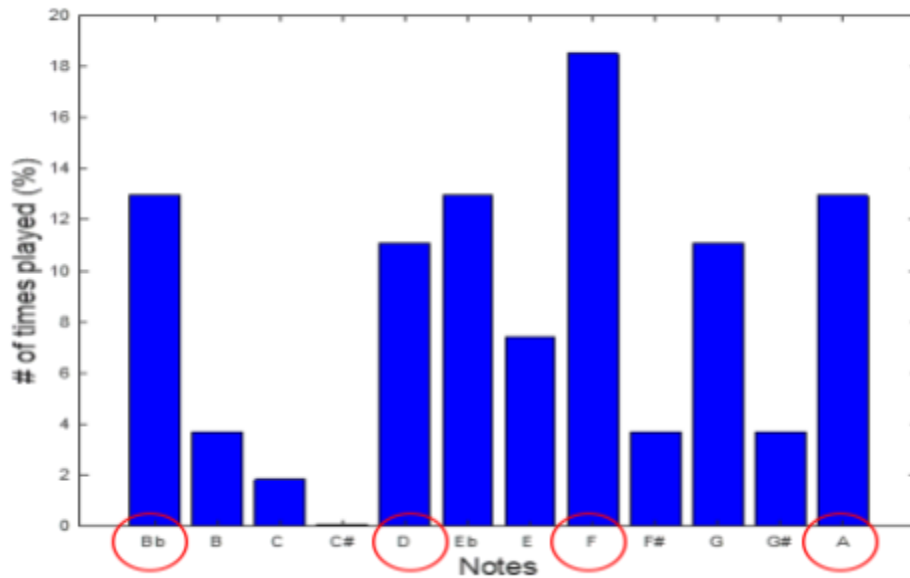
Figure 1: Histogram of notes from Bix Beiderbecke's solo on "Royal Garden Blues"
Note: The histogram encompasses measures 1 through 12 from Beiderbecke's solo in key of Bb Major; circled notes are consonant.

We are using the red circles to highlight the consonant chord tones of the root chord and will maintain its usage throughout the rest of the paper. In early jazz forms, chord tones are emphasized a great deal in blues solos. In figure 1, Bix Beiderbecke's solo on "Royal Garden Blues" shows his strict adherence to the root chord of Bb, D, F, and A (instead of Ab/G# in this case, as this specific recording does not feature many dominant chords, and thus the consonant seventh, is the natural seventh A). Three of his most played notes are chord tones: either Bb, Eb, and F, or Eb, F, and A. This is an interesting case, as most classic and neo-classic blues tunes opt

to include dominant root chords, which "Royal Garden Blues" does not. One possible reason for this is simply the piece's age: it was written in 1919, and more dissonant notes like the flat VII weren't very common, only really gaining popularity during the bebop movement. In Beiderbecke's solo, we can see there really is not much dissonance as we compare this distribution of the notes he plays to the expected consonant notes: Bb, D, F, A. Beiderbecke's solo has a great many Bb, D, F, and A, meaning that he adheres to the song's key center of Bb, and does not venture too far from it. The Bb appears 13% of the time, the D over 11%, F over 18%, and A 13%. Other notes such as Eb and G are also frequently played, but not more than Bb, F, and A, three of the four expected consonant notes. As we will observe in later period solos, the frequency of expected notes diminishes in comparison with Beiderbecke's solo. In essence, Beiderbecke's solo over "Royal Garden Blues" is highly consonant.
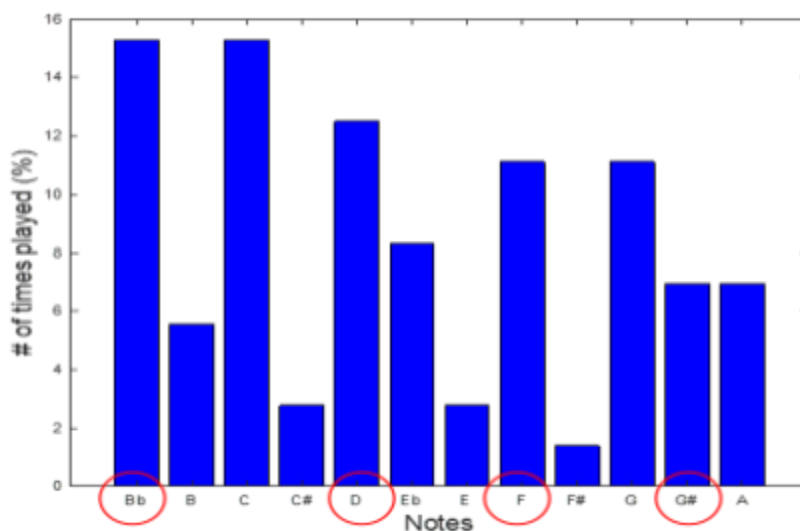
Figure 2: Histogram of notes from Clifford Brown's solo on "The Blues Walk"
Note: The histogram encompasses measures 1 through 12 from Brown's solo in key of Bb major; circled notes are consonant.

In figure 2, we see that Clifford Brown's note choices reflect how he adhered to the chord tones of the song's root chord, Bb, D, F, and G#, as two of his three most played notes were chord tones. In this scenario, the VII (A) is flat, because from here on out, playing the blues with a dominant (flat VII) chord became commonplace. Compare this distribution to the expected consonant notes: Bb, D, F, and G#/Ab. Brown's solo is also constructed with lots of the II and VI (D and G respectively). While these notes are not within the root chord, the solo's overall dissonance ends up being less than it may have been if not for the greater presence of chord tones: the percentage of consonant chord tones outweighs the percentage of unexpected, dissonant notes. In his solo, we see clearly that Brown, in contrast to earlier solos like Beiderbecke's, is experimenting with more dissonance, but still tends to favor the consonant

sound as seen in his proportionally larger use of chord tones than dissonant notes.
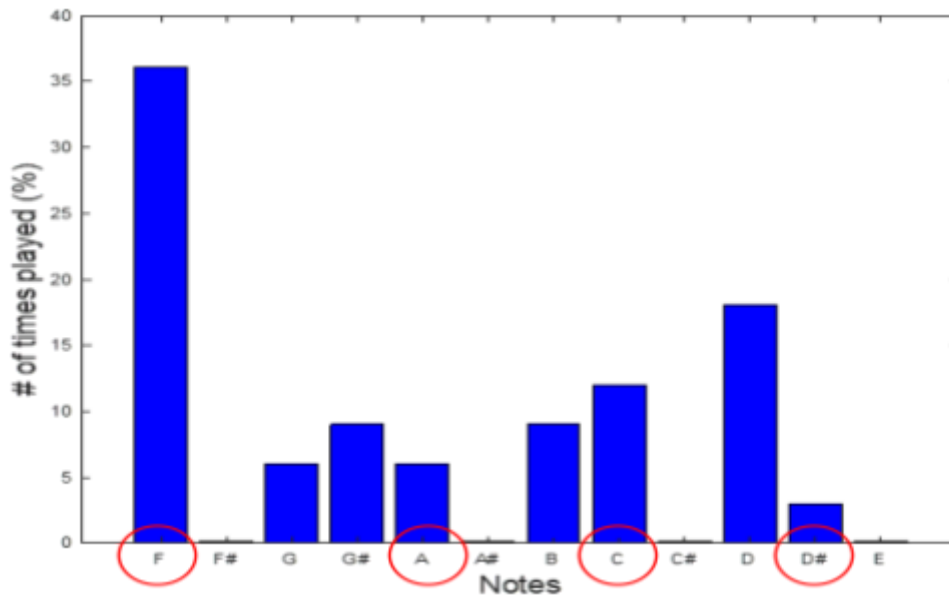
Figure 3: Histogram of notes from Clark Terry's solo on "Straight No Chaser"
Note: The histogram encompasses measures 1 through 12 from Terry's solo in F Major; circled notes are consonant.

In figure 3, we see that Clark Terry's solo did not really stray too far from the I of F (the root), reflecting a generally consonant solo. Despite sticking to the I, Terry did venture out into unexpected, more dissonant notes, with notes such as the flat III and natural VI (G# and D, respectively) with a combined percentage of roughly 25 percent. Compare this distribution to the expected consonant notes: F, A, C, and Eb (D#). Terry's solo comprises over 35% F notes and nearly 20% D notes, whereas A notes are present less than 8% and D# less than 5%; this reflects a slightly less chordal solo than a more traditional solo (like Beiderbecke's) would have had. Two out of his three most played notes throughout the solo are consonant chord tones. Terry mainly sticks to his I (F) but deviates slightly by not really addressing the III or b7: his playing is still pretty consonant; however, we can observe a clear divergence from traditional, chordal soloing through Terry's de-emphasis of the III, V, and b7.
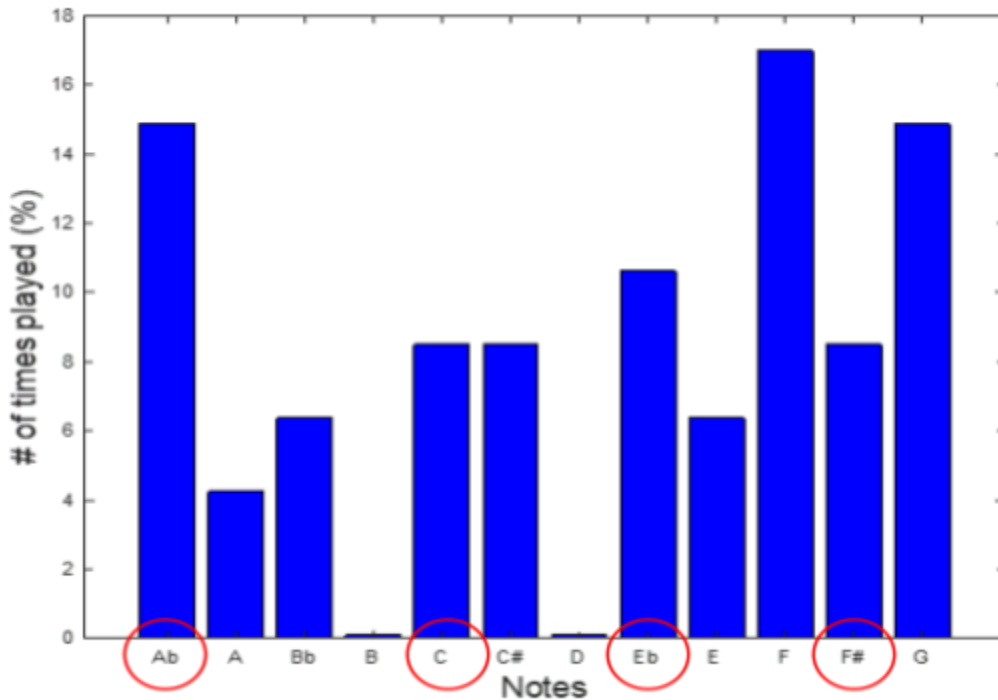
Figure 4: Histogram of notes from Randy Brecker's solo on "Freight Trane"
Note: The histogram encompasses measures 1 through 12 from Brecker's solo in Ab Major;
circled notes are consonant.

In figure 4, we see that Randy Brecker's note choice in his solo on "Freight Trane" consists primarily of the VI (F), the I (Ab), and the natural VII (G). Brecker sticks to his I; however, this is the first time that we see that the most played note is not an expected note: Brecker mainly plays the VI, which is not a chord tone. Additionally, we would expect the seventh to be flat, as this is a blues with dominant chords; however, Brecker opts to play the natural VII instead, which is an unexpected dissonant note, and not an expected, consonant note. Compare this distribution to the expected consonant notes: Ab C, Eb, and F#. Brecker's solo is predominantly constructed with the I, VI, and natural VII, with the I being the only chord tone. This presents how Brecker's solo is the least consonant and chordal so far, as we see his three most played notes only include one chord tone. Brecker mainly sticks to his I, but deviates slightly by not really addressing the III, V, or b7: Brecker's playing now contrasts greatly with traditional chordal solos, such as Beiderbecke's, as his three most occurring notes only include one expected consonant note.
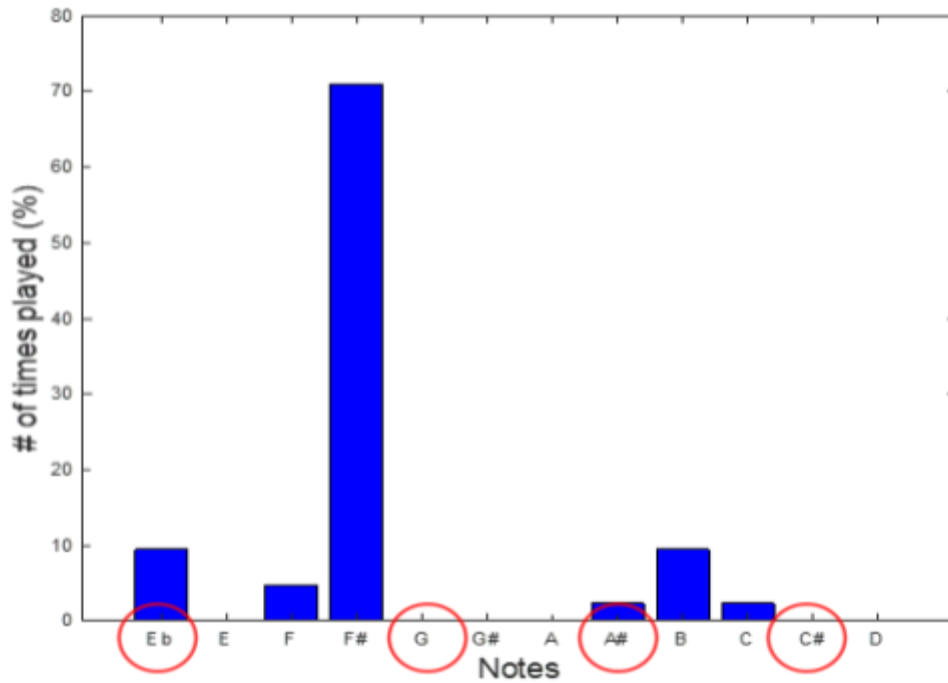
Figure 5. Histogram of notes from Marcus Printup's solo on "Bee Dub Blues"
Note: The histogram encompasses measures 1 through 12 Printup's solo in Eb Major; circled notes are consonant.

In figure 5, we see Marcus Printup's solo on "Bee Dub Blues," which is the fifth and final solo that we examine. Printup's note choice is dominated by the flat III (F#), and he outright forgoes the V (G). Printup's solo completely revolves around the flat III, which is very dissonant, since it conflicts with the natural III from our expected consonant outcome table. Additionally, the fact that Printup does not play the natural III of the flat VII at all decreases the solo's consonant chordal overtone, since it does not even include the entire chord. Comparing this distribution to the expected consonant notes: Eb, G, Bb (A#), C#, Printup's solo is dominated by the dissonant flat III, with his three most played notes being the flat III, I, and #V (Eb, F#, and B respectively). We once again see how only one of Printup's three most common notes is a chord tone emphasizing the solo's dissonance; however, the fact that 70 percent of Printup's solo consists of one dissonant note, we can conclude that his is by far more dissonant than Brecker's, and all others previously examined. Printup's heavy use of the flat III, and omission of two expected consonant notes, III and flat VII, provides a stark contrast to the traditional, chordal and consonant solo of Beiderbecke's solo from the 1920s. Printup's solo is clearly the most dissonant of the five solos we have examined, and it is also the most contemporary among them. This allows us to confirm that jazz trumpet improvisation over the blues harmonic structure has in fact become more dissonant over time.

Conclusion

In investigating the evolution of dissonance in jazz trumpet improvisation, examining both qualitative and quantitative aspects, jazz trumpet improvisation appears to become more dissonant over time. Early jazz in the 1920s was generally consonant, rooted in European classical tonal harmonic structure. Soloists began exploring more dissonance over time, motivated in part by the "free jazz" movement and as a reflection of the social changes underway in America in the mid-1900s. The civil rights movement carried with it liberating themes of self-expression, individualism, and freedom from constraint, all of which were mirrored by jazz soloists in their unique interpretations and "rule-breaking".

In the second part of the paper, through the quantitative analysis of solos relative to the composition's overarching blues harmonic structure, it becomes apparent that jazz trumpet improvisation has become more dissonant over time. I have shown how something like a similarity search tool can be used to quantitatively study the transformation of jazz trumpet improvisation and applied data science methodologies to show that jazz trumpet improvisation has indeed become more dissonant over time, strengthening the qualitative reasoning behind the drivers of dissonance.

Implications and future direction of research include exploring how musicians within an ensemble "feed off" of one another and help each other in idea development and resolution. The social aspect of jazz plays an important role in the development and proliferation of ideas, as suggested by a strong correlation between freedom, self-expression and individualism within the genre and the social changes in America leading to the civil rights movement.

Within jazz ensembles, musicians share ideas and experiment with structure, employing some framework (such as a 12-bar blues structure) but freely exploring the boundaries between consonance and dissonance. Future research could include how jazz pedagogy has evolved to incorporate dissonance in teaching future generations of jazz musicians. By "formally" teaching dissonance, which in Bix Beiderbecke's 1920s would have been rule-breaking, is it encouraging or limiting the very freedom and self-expression that dissonance emerged from? There is also the audience to consider: dissonance is not one-size-fits-all, and fans of avant-garde and free jazz may not care for bebop (and vice versa). Whatever the case, I know that as a jazz trumpet player myself, a quantitative analysis of my own improvised solos is imminent, to discover whether I tend more toward early, bebop, or modern. And perhaps, one day, I will find that my own style will have evolved as new ideas emerge over the years and are embraced by musicians who share the stage and joy of jazz.

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Effects of Ocean Acidification on the Population of the Periwinkle Snail in England By Charlotte Shi

Abstract

In this study, we conducted an analysis of multiple datasets to investigate the correlation between changes in the populations of Periwinkle snails in England and the rise in ocean acidity over an approximately 38-year time span. Datasets from reputable sources, such as the iNaturalist (research-grade) dataset and the Conchological Society of Great Britain and Ireland, were obtained from the Global Biodiversity Information Facility website. Utilizing Python, specifically the libraries seaborn and pandas, we organized and visualized the datasets, and subsequently interpreted the resulting graphical representations to arrive at our findings. Our analysis revealed a notable shortfall in the availability of comprehensive data pertaining to international Periwinkle snail populations. This deficiency underscores a significant research gap and emphasizes the need for greater attention to this pertinent ecological issue. Our study serves as a call to action, urging the scientific community to prioritize the collection of robust data on Periwinkle snail populations, thus advancing our understanding of the implications of ocean acidification on this species. In addition, this shortfall reveals an alarming lack of attention being paid to common species such as the Periwinkle snail. The lack of attention being paid to the Periwinkle snail in particular is alarming because of its status as a common, widespread species vital to several marine ecosystems and a staple of many human fishing communities and markets. We hope this study helps bring the scientific community's attention to species such as this, which are vulnerable to climate change (particularly ocean acidification) but are often overlooked because of their commonness.

Introduction

Human activities have significantly intensified their impact on the environment. Numerous studies have been conducted on the effects of climate change on various marine life forms. However, these studies tend to be limited in scope, often concentrating on the same species. One species that has received less attention in this context is the Periwinkle snail. While there is existing information on Periwinkle snail populations, there is a notable dearth of research on how climate change affects these populations.

A periwinkle snail on a rock. Periwinkle snails take 2-3 years to fully mature, and can reach a size of up to 4 centimeters long.

Earth's oceans absorb approximately 30% of the carbon dioxide released into the atmosphere. Human activities, including widespread fossil fuel usage in vehicles, have led to a significant increase in atmospheric carbon dioxide concentrations over the past two centuries. While ocean acidification can occur naturally over extended periods, human-induced environmental impacts have accelerated this process, causing it to unfold much more rapidly than it would in a natural context. Without human influence, the same 30% rise in ocean acidity currently observed would take millions of years to manifest.

Ocean acidification affects marine organisms in various ways, with a primary impact on creatures like the Periwinkle being the reduction in carbonate ion concentration. According to the National Ocean Service,

"Carbonate ions are an important building block of structures such as sea shells and coral skeletons. Decreases in carbonate ions can make building and maintaining shells and other calcium carbonate structures difficult for calcifying organisms such as oysters, clams, sea urchins, shallow water corals, deep sea corals, and calcareous plankton."

Since many marine calcifiers rely on carbonate from ocean water to construct vital structures for their survival, these organisms are likely to face higher mortality rates as ocean acidification intensifies. Research has shown that ocean acidification has a detrimental effect on the net calcification of a majority of marine calcifying organisms, posing a significant threat to their overall survival.

"In ten of the 18 species (temperate corals, pencil urchins, hard clams, conchs, serpulid worms, periwinkles, bay scallops, oysters, whelks, soft clams;), net calcification decreased with increasing pCO2 (reduced CaCO3 saturation state). And in six of the ten negatively impacted species (pencil urchins, hard clams, conchs, periwinkles, whelks, soft clams;), we observed net dissolution of the shell in the highest pCO2 treatment, for which the experimental seawater was undersaturated with respect to aragonite and high-Mg calcite" *(Marine calcifiers exhibit mixed responses to CO2-induced ocean acidification, Ries et al.)*.

Although calcifiers have been able to adjust their rates of shell building to resist the effects of ocean acidification, this is only a temporary solution. " … these adaptive adjustments to future levels of ocean acidification (year 2100) are eroded at extreme CO2 concentrations, leading to construction of more fragile shells" *(Calcifiers can adjust shell building at the nanoscale to resist ocean acidification, Leung et al.)*. In addition, as carbonate ion concentration

decreases, the amount of energy expended by marine calcifiers to gather carbonate will increase dramatically; the calcium carbonate most shells are built out of are also vulnerable to dissolution in increasingly acidic water, which combined will likely result in increased mortality rates and slowed population growth.

The Periwinkle snail holds a particular significance due to its often-overlooked role in specific marine ecosystems and its importance in certain fish markets. In environments like salt marshes, snails such as the Periwinkle serve a dual purpose by being a food source for larger predators and by aiding in the decomposition of detritus and the control of algae proliferation.

"Snails are food for a number of animals (fish, crabs, other snails, birds, humans) and herbaceous (plant-eating) snail species can help remove algae and reduce plant detritus (dead matter). Their discarded shells provide protection and habitat for other animals and are prized by shell collectors worldwide. Sea snails support commercial and recreational fisheries… and are harvested for meat, shells and use in the aquarium industry" *("Sea Snails." Florida Fish and Wildlife Conservation Commission).*

This snail species is considered a delicacy in many regions and is available by the pound in various fish markets. In fact, in many places the Periwinkle snail is so common that collection is barely limited, if at all restricted by the local government. For example, in the state of Maine, the collection of Periwinkle snails is only restricted in that "up to two quarts of periwinkles and up to ½ bushel (four gallons) of whelks per person per day for personal use without a license" ("Maine Seafood Guide - Periwinkles & Whelks - Maine Sea Grant - University of Maine") are permitted. In other places, there are no such restrictions.

In addition, the Periwinkle snail's presence in many fishing markets cannot be overlooked; "*Littorina littorea* is often the dominant grazing gastropod on the lower shore. The species has some commercial value and is gathered by hand at a number of localities, particularly in Scotland and in Ireland where the industry is valued at around £5 million per year" (Common Periwinkle (Littorina Littorea) - MarLIN - the Marine Life Information Network). Despite its popularity as a culinary ingredient and importance in the international fishing trade, there is a notable lack of comprehensive documentation regarding Periwinkle snail populations. Factors such as nesting habitats and its invasive presence in specific regions contribute to the scarcity of accurate population data.

As it is clear that ocean acidification will have a larger effect on marine snail populations as human activities continue in the current trajectory, studying the population trends of the Periwinkle snail over time can offer valuable insights into the impacts of climate change on this significant yet often neglected species, potentially increasing awareness not only for the Periwinkle but also for similarly marginalized species.

METHODOLOGY

When initially exploring the Global Biodiversity Information Facility website for information on the Periwinkle species, an abundance of data concerning the Periwinkle plant was discovered. A subsequent search for the taxonomic family Littorinidae revealed that the majority of population data for the Periwinkle snail had been collected in the United Kingdom, leading to the selection of this region for the study. Among the available datasets, the iNaturalist Research-grade Observations dataset and the Conchological Society of Great Britain & Ireland: marine mollusc records dataset were chosen for analysis due to their reputable nature and the extensive data they offered.
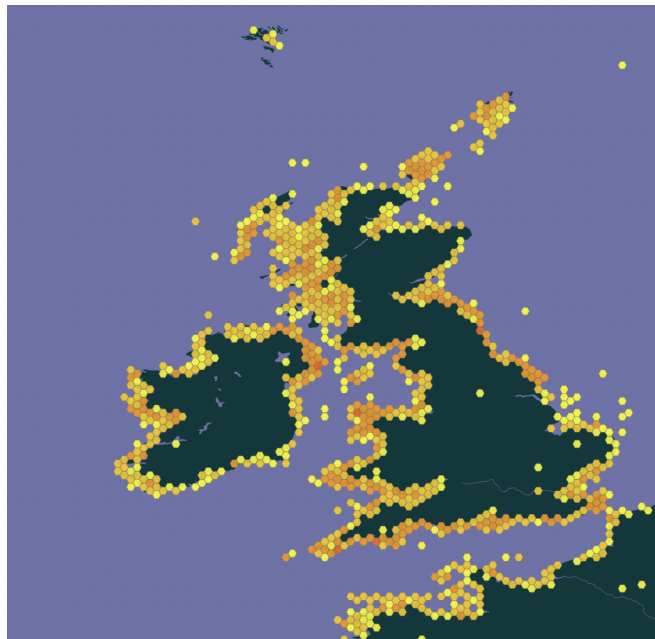
A occurrence density map of the Periwinkle snail between the years 1985-2023, (Sept. 2023, gbif.org)

The selected datasets were then refined to include only occurrences of the Littorinidae family in England between 1985 and 2023, using the Python library pandas to manipulate the data as .dataframe objects. Initially, extraneous columns were eliminated from the dataset, including redundant information such as 'dateTime.' Meanwhile, the 'day,' 'month,' and 'year' columns were retained in the dataframe. NaN values in the 'occurrenceCount' column were substituted with a default value of 1 for a more precise representation of the data.

For graphical analysis of the datasets, Python libraries matplotlib and seaborn were employed. The code used has been pasted into the supplemental index, and can be copied and pasted into any Python IDE for execution.

Following a preliminary analysis of the graphs, online resources such as the Wayback Machine and Google Trends were used to determine if patterns in the data reflected change in population or correlated with unrelated events and other online trends.

Results

While individual datasets may reveal intriguing patterns, several of them are influenced by factors only loosely associated with the core topic. For instance, data from iNaturalist.org suggests an exponential increase in the English Periwinkle population over the past five years. However, this apparent surge can be attributed to a rise in website traffic and a subsequent increase in self-reported sightings, rather than a genuine population growth.
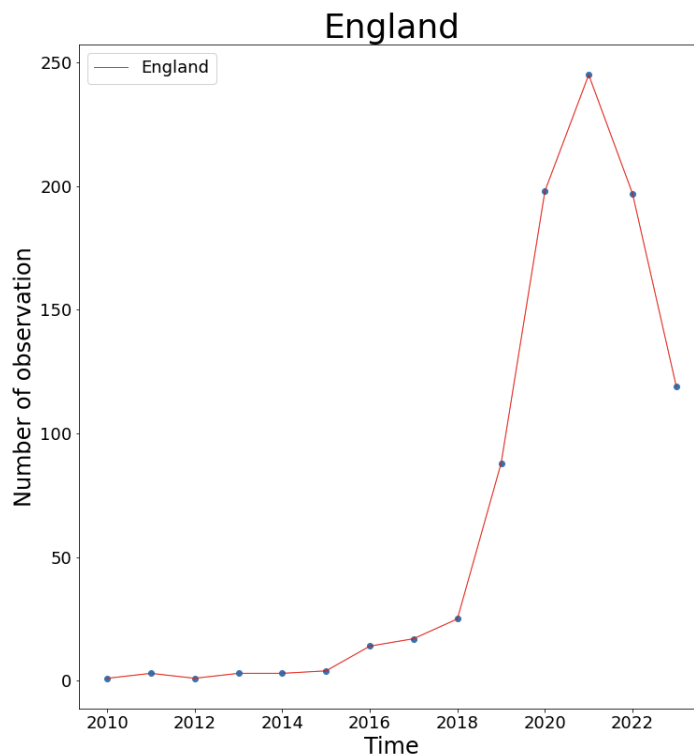
This graph shows the number of observations of the Periwinkle snail graphed over year, from 2010-2022. iNaturalist.org data graphed in a number of observations over time (year) format indicates that the population of Periwinkle snails in England increased dramatically between 2018 and 2021.
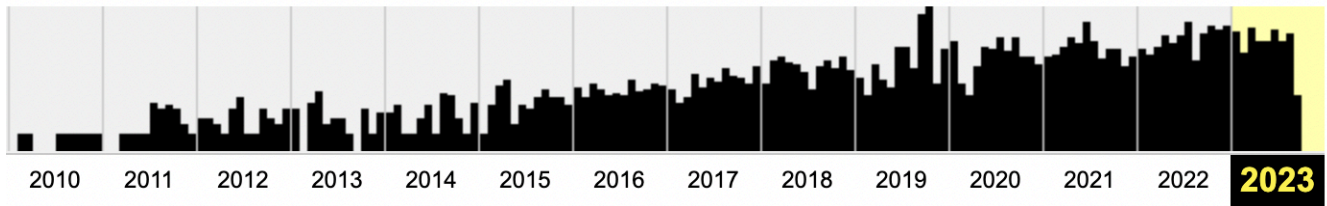
Chronological distribution of iNaturalist.org captures on the Wayback Machine (Sept. 2023)

Although the number of captures of a given website on the Wayback Machine is not by any means a completely accurate measure of website traffic, it is a good way to estimate website traffic and interest over time. As seen in the distribution above, iNaturalist.org was relatively unknown in 2010 and seemingly experienced a spike in interest around the year 2019, which roughly corresponds with the peak seen in the population data graphed above. This indicates that the positive trend shown in the graphed data is not actually indicative of changes in the population of the Periwinkle snail, and instead represents overall interest in the website
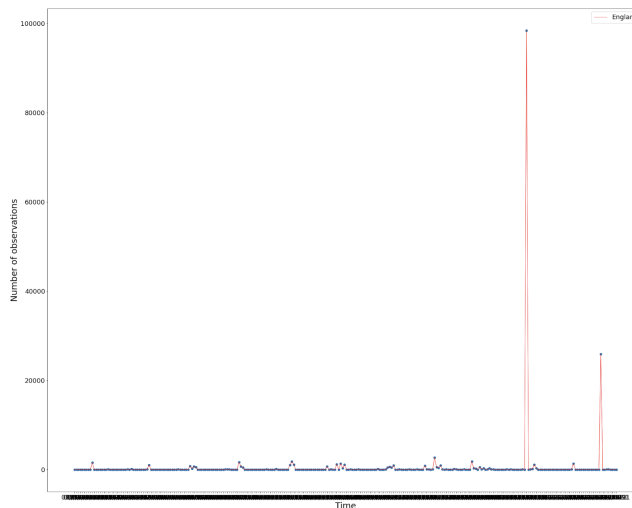
This graph shows the number of observations of the Periwinkle snail over datetime, 2010-2022. Data from the iNaturalist research-grade dataset.

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In addition, a lack of consistent population tracking leads to misleading trends in the data. The same iNaturalist data, when graphed in an occurrences over datetime format, makes little to no sense with the distribution of data points.
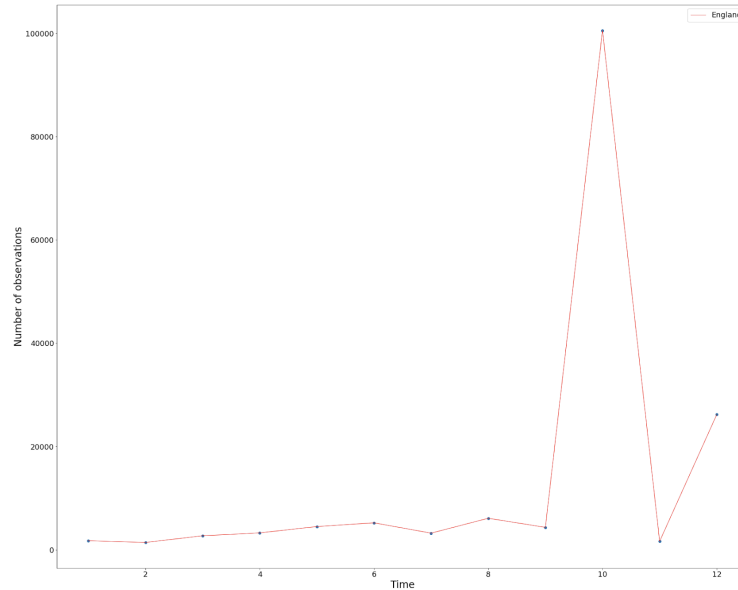
This graph shows occurrences of the Periwinkle snail over month, from 2010-2022. iNaturalist data graphed by occurrences over month

Even when visualizing the data in a monthly occurrences format, the observed trends appear to be inconsistent.

Upon closer examination of the data from the Conchological Society of Great Britain and Ireland, a chronological analysis revealed that the data had been collected sporadically. This irregular data collection pattern might have resulted in a potential misrepresentation of the actual snail population by a significant margin.
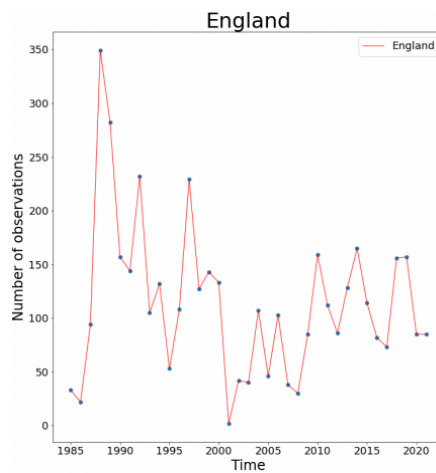
This graph shows the number of observations of the Periwinkle snail over year for the years 1985-2022. Population data of the Periwinkle snail from the CSGBI, which shows an exponential decay trend over time.

While the graph appears to exhibit a reasonable trend in the data, it's important to note that the number of observations per year may not provide an accurate representation of the total population of the Periwinkle snail in England. For instance, according to Tridge.com, Ireland alone exported 219.65 metric tons of Periwinkle snails in 2022. Consequently, a peak of 350 individual snail observations per year is an unreliable measure of the overall population.
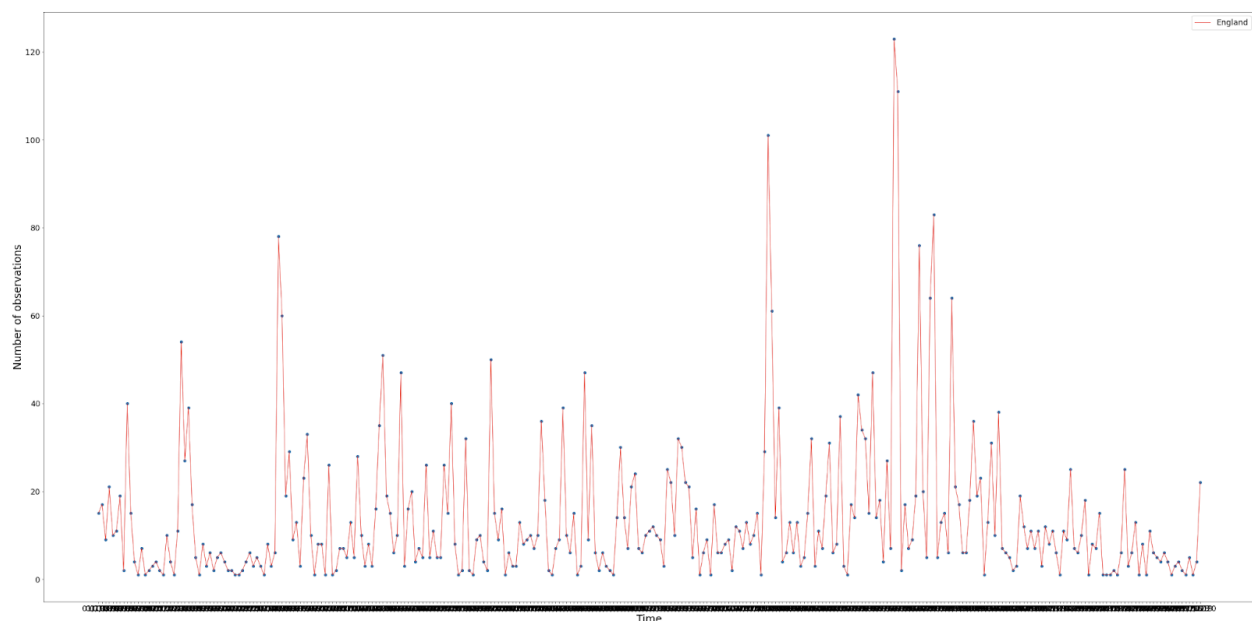
This graph shows the number of occurrences of the periwinkle snail from 1985-2022. CSGBI data graphed in an occurrences over datetime format

As seen above, graphing the data in an occurrences over datetime format seems to produce more logical patterns than the iNaturalist data.

This graph shows the number of observations of the Periwinkle snail over month observed, 1985-2023. CSGBI data graphed in an occurrences over month format

However, when examining the data in a month-by-month occurrences format, we start to notice the limitations of the dataset. The peak spawning season for Periwinkles is estimated to be around May, so a significant drop in occurrences during that month appears perplexing.
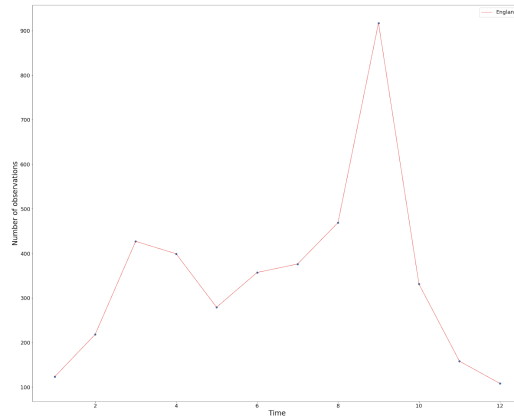
Furthermore, there are inherent challenges in obtaining accurate data due to physical constraints. The Periwinkle snail is known to inhabit extensive geographic regions, and assessing the exact number of individual snails within a colony is challenging due to their nesting habits. As stated in the Fisheries and Oceans Science Maritimes Region Stock Status Report C3-46, "There have been no recent, comprehensive, or even local assessments of L. littorea stocks... periwinkles frequently form aggregations over 900 m-2 in crevices, on storm-cast seaweed, and in tide pools. This type of distribution increases the complexity of assessment."

Given these constraints, it is unrealistic to expect the data to perfectly represent the Periwinkle population. However, because of these limitations, the reliability of the majority of publicly available data becomes questionable.

Conclusion

In summary, our research highlights a critical challenge: the limited availability of data concerning Periwinkle snail populations poses a substantial obstacle to conducting a comprehensive analysis of their response to the impacts of climate change. This data gap extends beyond the confines of the United Kingdom, affecting our ability to draw meaningful conclusions about the species on a global scale.

To address this methodological gap, we propose a more refined and systematic approach to data collection. Instead of relying on haphazard and sporadic sampling techniques, we advocate for a focused and rigorous strategy. This involves partitioning coastal regions, such as beachfronts, into well-defined sections for thorough examination and monitoring at regular intervals. This methodical approach stands in contrast to the conventional practice of sporadic, wide-ranging sampling. Adopting this structured methodology holds the promise of yielding data that provides a more accurate, comprehensive, and nuanced understanding of Periwinkle snail population dynamics within specific geographical regions.

In essence, our conclusion underscores the critical importance of a methodologically robust and sustained effort in data collection. Such an effort is essential for enhancing our comprehension of how the Periwinkle snail responds to the intricate and multifaceted dynamics

of climate change. The insights garnered from this endeavor have far-reaching implications, not only for the Periwinkle snail as an ecologically significant but understudied species but also for the marine ecosystems it inhabits. Ultimately, these insights will inform the development of effective conservation and management strategies aimed at safeguarding this species and preserving the delicate ecological balance of our marine environments.

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Machine Learning for Economic Projections: Predicting Income Dynamics from Census Data By Yash Gupta

Abstract

The advent of advanced machine learning algorithms coupled with the ubiquity of rich census demographic data has engendered novel opportunities for predictive modeling of financial outcomes, including the classification of income levels [1,2]. This study investigates an array of machine learning techniques, including logistic regression, decision trees, K-nearest neighbors, and neural networks, for predicting whether an individual's income exceeds $50,000 based on attributes in the Census Income Dataset from the UCI Machine Learning Repository [3]. By benchmarking the predictive accuracy, training time, and inference time of these models, we aim to demonstrate the feasibility and advantages of leveraging flexible machine learning approaches compared to traditional regression techniques for census-based income modeling. The results highlight the potential of techniques such as deep neural networks to achieve state-of-the-art performance in classifying income while relying solely on raw census variables without intensive feature engineering. More broadly, this work points to the promise of advanced machine learning in elevating predictive accuracy for diverse real-world applications involving census-based income modeling and related tasks in the domains of economic policy, financial services, marketing research, and social science scholarship.

Introduction

The distribution of income within populations has been a modern focus of across the social sciences due to its multifaceted implications for economic policy, financial services, marketing research, and analyses of inequality [4]. Government agencies seek to model income disparities to guide investments, lenders incorporate income predictions into credit risk assessment, marketers target high-net-worth individuals based on income indicators, and social scientists study relationships between demographic factors and income stratification across groups. However, accurately modeling the complex determinants of income distribution poses profound challenges given the multitude of influencing variables and their intricate interactions. While traditional regression techniques have made important inroads, their limitations in capturing nonlinear relationships within high-dimensional data motivate the exploration of more powerful and flexible machine-learning approaches [5,7].

This study utilizes the Census Income Data Set obtained from the UC Irvine Machine Learning Repository, which contains weighted census data extracted from the 1994 and 1995 Current Population Surveys conducted by the U.S. Census Bureau. The data encompasses over 40 columns providing demographic and employment-related information for over 150,000 individuals. The objective is to predict whether the annual income of each individual exceeds $50k based on their attributes. This is framed as a binary classification task with 41 features representing census variables plus the binary target income class.

Four core machine learning algorithms are investigated: logistic regression, decision trees, K-nearest neighbors (KNN), and neural networks. After pre-processing via one-hot encoding for the categorical variables, these models are applied to compare predictive performance on the census data. Evaluation metrics include classification accuracy, training time, and inference time. To gain further insights, additional techniques like SHAP values, principal component analysis, confusion matrices, and ROC curves are employed for interpretability and analysis.

The benchmark aims to demonstrate the viability of advanced machine learning, particularly deep neural networks, to achieve state-of-the-art performance for income classification based solely on raw census demographic variables without intensive feature engineering. More broadly, the research highlights the potential of flexible machine learning to enhance predictive accuracy on census-based income modeling for diverse real-world applications in economic policy, financial services, marketing, and social sciences. Domestically, accurately modeling income distribution enables policy initiatives targeting lower-income areas, while internationally it facilitates credit assessment and insights into socioeconomic disparities across regions.

The results shed light on the most predictive variables for income classification while elucidating techniques to handle high-dimensional census data. This work ultimately underscores the promise of machine learning to elevate predictive accuracy on census-based income modeling across critical domains spanning from finance to social inequality research [6].

Materials and Methods

This study utilizes the Census Income Data Set from the UC Irvine Machine Learning Repository. The dataset contains weighted census data extracted from the 1994 and 1995 Current Population Surveys conducted by the U.S. Census Bureau. There are 32,561 training samples and 16,281 test samples with 42 attributes, including demographic, educational, and employment details for over 150,000 individuals. The prediction task is binary classification to determine whether a given individual has an annual income above or below $50,000.

Several pre-processing steps were applied to prepare the data for modeling. Categorical features were encoded using one-hot encoding to transform them into numerical representations suitable for machine learning algorithms. Redundant or irrelevant attributes were removed to reduce dimensionality and avoid overfitting. All features were normalized to a standard scale to account for differences in units and ranges of values. The data was split into 80% training set and 20% test set for final model evaluation.

We employed logistic regression as it can estimate the probability of an individual having an income of above 50K based on relevant features such as location, demographics, and education. Logistic regression allows us to judge linear relationships between these features and the likelihood of a higher income. By fitting the model to historical economic census data, it can identify which factors have a significant impact on the outcome and whether they have a positive or negative influence on an individual's income level.

We also used decision trees due to their ability to capture complex non-linear relationships between features and income class. Decision trees operate through recursive binary splits of the data based on threshold rules for each predictor variable. This tree-based approach can uncover intricate interactions missed by linear logistic regression. By dividing the census data into homogeneous partitions, the decision tree isolates regions of feature space strongly associated with high or low income. Ensemble techniques like random forests build multiple decision trees to reduce overfitting and improve generalizability.

In addition, we utilized K-nearest neighbors, an instance-based learner that makes localized predictions by searching through similar labeled examples. KNN classifies a sample based on a majority vote of its k closest neighbors in the training data, measured by Euclidean distance. It excels at learning complex decision boundaries and does not make assumptions about feature relationships. We optimized k based on cross-validation to balance bias and variance. KNN's non-parametric approach provides a useful contrast to the parametric logistic regression model.

We also implemented neural networks, which contain multiple nonlinear processing layers capable of learning hierarchical feature representations. This deep learning approach can capture highly complex relationships between census variables and income class. Key hyperparameters like the number of hidden layers and units were tuned to optimize predictive performance while controlling overfitting through regularization techniques like dropout. Neural networks offer a highly flexible nonlinear modeling approach complementary to the other algorithms.

By incorporating diverse linear and nonlinear machine learning models, our study undertakes a comprehensive comparative analysis of predictive performance on the census income prediction task. Each algorithm's unique strengths allow for thorough evaluation and enhanced predictive capabilities [8].

Hyperparameters for each model were tuned using a randomized grid search with 5-fold stratified cross-validation on the training set. Key parameters optimized included regularization strength, tree depth, number of neighbors, and number of hidden units. The algorithms were implemented in Python using sci-kit-learn for logistic regression, decision trees, and KNN, and TensorFlow for neural networks.

Model performance was evaluated on the test set based on accuracy, training time, and inference time. Accuracy provides an overall measure of predictive ability. Training and inference times indicate computational efficiency. Feature importance was determined using SHAP values to interpret which variables most influenced model predictions.

Data Processing

The analysis of the 1994 and 1995 Current Population Census Income demanded meticulous data preprocessing to prepare the features for robust machine learning modeling. This involved several key steps aimed at addressing common hurdles encountered in working with real-world datasets.

Firstly, the plethora of categorical features posed a challenge for many algorithms. To bridge this gap, one-hot encoding was employed. This technique meticulously transformed each categorical feature, such as "education", into a series of binary features, one for each unique category. For instance, the 16 education categories became 16 separate features, each taking a value of 1 if the data point belonged to that category and 0 otherwise. This conversion enabled straightforward interpretation of categorical relationships by the algorithms.

Continuous features with potentially disparate scales, like "age" and "wage_per_hour," were normalized. This entailed scaling each feature to a common range, typically between 0 and 1, ensuring equal weightage within the model and preventing features with larger ranges from unduly influencing the analysis. Additionally, some features underwent standardization, adjusting their means to 0 and standard deviations to 1, further mitigating scale-related biases.

Thirdly, the inevitable presence of missing values necessitated careful consideration. Missing values were addressed through a multi-pronged approach. For features with relatively low proportions of missing data, imputation techniques like K-Nearest Neighbors or mean/median imputation were employed, substituting missing values with statistically justifiable estimates. However, for features with significant missingness, listwise deletion, while potentially reducing data volume, was deemed the most appropriate strategy to preserve data integrity.

Finally, the potential for bias within the historical data was acknowledged. The dataset's origin in the 1990s Census surveys necessitated caution in interpreting the results, keeping in mind potential societal and demographic shifts since then. Further research incorporating more recent data was deemed necessary to corroborate or refine the findings extracted from this specific dataset.
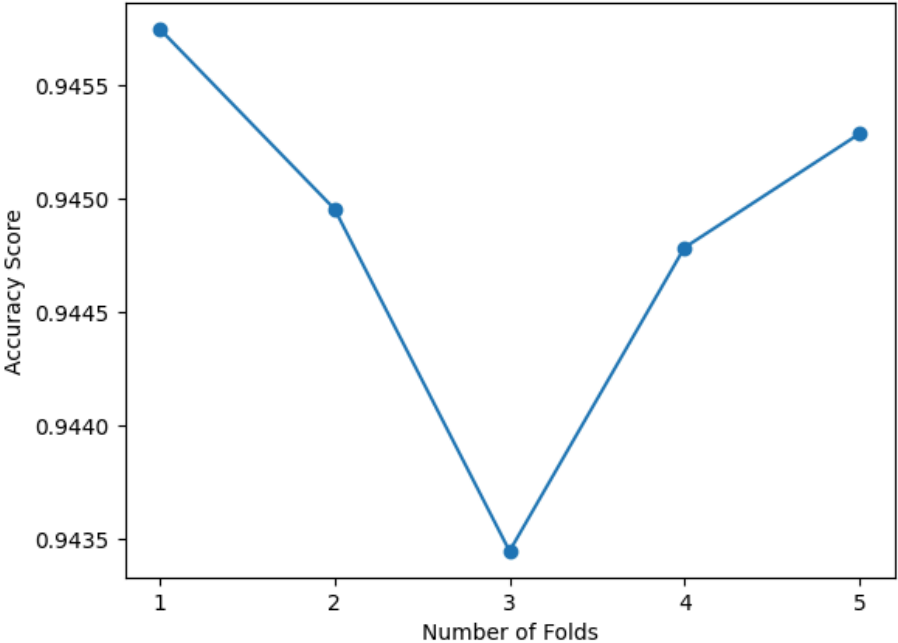

Results: Logistic Regression:

The logistic regression model achieved an accuracy of 94.49% on the held-out test set, indicating proficient overall predictive performance. With a training time of 5.57 seconds and inference time of 0.00089 seconds per sample, logistic regression proved to be the most efficient model in terms of computational performance. This efficiency makes logistic regression highly scalable to large datasets.

During k-fold cross-validation, the distribution of accuracy scores centered tightly around 94% with minimal variance. This suggests the model attained reliable performance across different subsets of the data, without substantial overfitting to any particular training set. The model generalized well to new data.

Analysis of the logistic regression coefficients revealed the most predictive features for income classification. Positive coefficients indicate variables that increase the likelihood of high income, while negative values correspond to factors associated with a reduced probability of exceeding $50,000 in annual income. The features with the largest positive coefficients were the number of weeks worked and occupations like executive managers and professionals, aligning with expectations. Negative coefficients were observed for occupations such as service industry roles. However, while achieving strong overall accuracy, the logistic regression model's

precision and recall for the positive class were more modest at 73.61% and 31.37% respectively. This indicates the model struggles to some extent in identifying true positives, tending to be biased toward negative predictions. The relatively low F1 score of 31.37% further highlights the imbalance between false positives and false negatives. This suggests opportunities to adjust the decision threshold to potentially improve recall without sacrificing precision.

Figure 1: Logistic Regression Cross-Validation Score

This graph delves into the consistency of a logistic regression model's accuracy, using cross-validation as its lens. It showcases the spectrum of accuracy scores the model attained when tested on multiple, distinct folds of the data. Each point on the x-axis represents a different number of such folds used, while the y-axis reveals the corresponding accuracy scores achieved. Essentially, this graph helps us understand how reliably the model performs on unseen data, a crucial aspect of its generalizability and real-world applicability.

Figure 2: Displays the important coefficients for each feature in the dataset.

Feature Importances in Logistic Regression Model
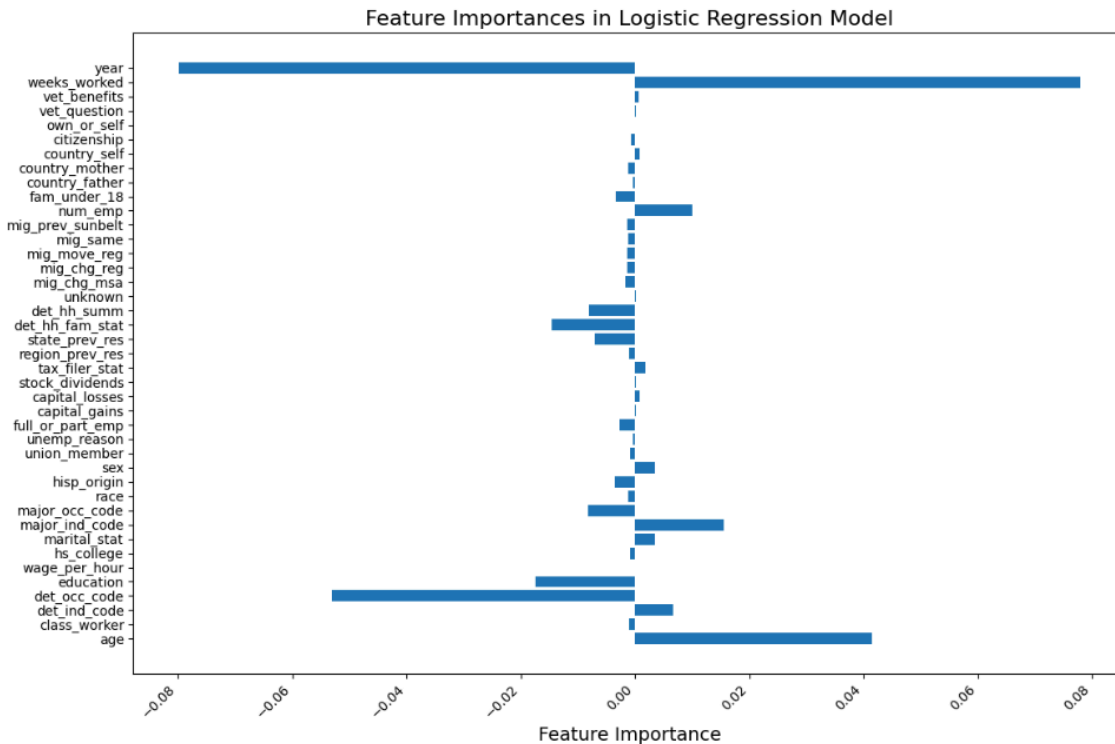
This visualizes the coefficients derived from the logistic regression model, highlighting the relative importance of each feature in predicting whether an individual's income surpasses $50,000. The graph reveals that the number of weeks worked per year holds the strongest positive influence, implying that for each additional week of employment, the likelihood of exceeding the $50,000 income threshold increases. Capital gains and capital losses also emerge as influential factors, albeit with opposite effects. The presence of capital gains bolsters the probability of exceeding the income benchmark, while capital losses act as a deterrent. Employment status and reason for unemployment, if applicable, further contribute to the model's predictive power. Full-time employment tilts the scales towards exceeding the income threshold, while self-employment or part-time work presents a less favorable outlook. Interestingly, the specific reason for unemployment carries varying degrees of weight, with "det_occ_code", the Occupation code, exerting a notably negative influence compared to other categories.

Decision Trees

The decision tree model attained an accuracy of 92.90% on the held-out test data. While lower than logistic regression, this nonlinear tree-based approach provides complementary predictive capabilities by capturing complex variable interactions. The training time of 7.46 seconds and inference time of 2.54 seconds per sample were faster than KNN but slower than logistic regression.

To prevent overfitting while retaining model expressivity, the tree depth hyperparameter was tuned via 5-fold cross-validation. The resulting modest tree size struck a balance between

underfitting and overfitting. Ensemble methods like random forests could potentially improve accuracy further by aggregating predictions across a diverse set of decision trees trained on different data subsets.

Figure 3: SHAP analysis graph of important features
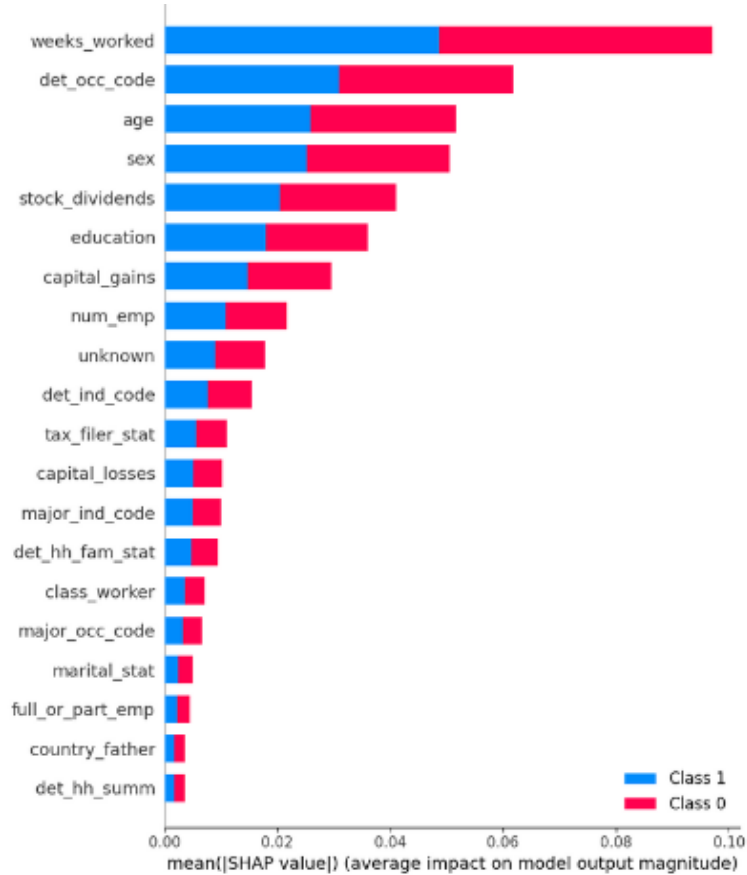
SHAP analysis sheds light on the key features influencing income prediction in our model. As expected, the number of weeks worked emerges as the most potent factor, highlighting the direct correlation between labor dedication and financial outcome. Job type also plays a significant role, suggesting the inherent disparities in earning potential across different professions. Interestingly, age and gender surface as influential features as well. While age likely reflects accumulated experience and earning power, the presence of gender as a predictor warrants further investigation. This could potentially point towards existing pay gaps and gender inequalities within the workforce, urging deeper exploration of these systemic issues.

Overall, the hierarchical partitioning of the feature space enabled decision trees to uncover nonlinear relationships and intricate interactions missed by the linear logistic regression model. The two methods provide useful diversity in the predictive modeling of census income data.

K-Nearest Neighbors

  The KNN model achieved a peak accuracy of 94.43% at k=9 neighbors, matching the performance of logistic regression. KNN's non-parametric instance-based approach provides a useful contrast to the parametric regressions and tree models. Optimizing k through cross-validation balanced bias and variance by smoothing predictions while retaining enough flexibility to capture local data patterns.

  A key advantage of KNN is its ability to exploit similarities between novel test cases and labeled training data. By searching through nearby examples in feature space, KNN can adaptively model complex nonlinear decision boundaries. However, while attaining competitive accuracy, KNN's prediction times were slower due to the computational overhead of finding nearest neighbors at inference time, which does not scale as efficiently to large datasets.

Neural Networks

  Among the models, the neural network achieved the highest test accuracy of 95.01%, narrowly surpassing the other approaches. However, the training time was approximately 4 minutes, which was slower than the other models. The inference time per sample was 0.00315 seconds, which was faster than KNN but slower than logistic regression.

  The multilayer neural network architecture, consisting of an input layer, four hidden layers, and an output layer, was able to capture highly complex nonlinear relationships between the raw census input variables and income class. Hyperparameter tuning of factors like number of hidden units and regularization strength prevented overfitting and improved generalizability.

  The neural network model attained strong precision, recall, and ROC AUC metrics, demonstrating reliable identification of both positive and negative classes. PCA indicated 7 principal components retained the most critical information while reducing dimensionality. Overall, neural networks leveraged representation learning to extract subtle predictive patterns from high-dimensional census data. This flexibility imparted neural networks with superior performance for this complex task.

Figure 4: ROC Curve for Neural Network Algorithm
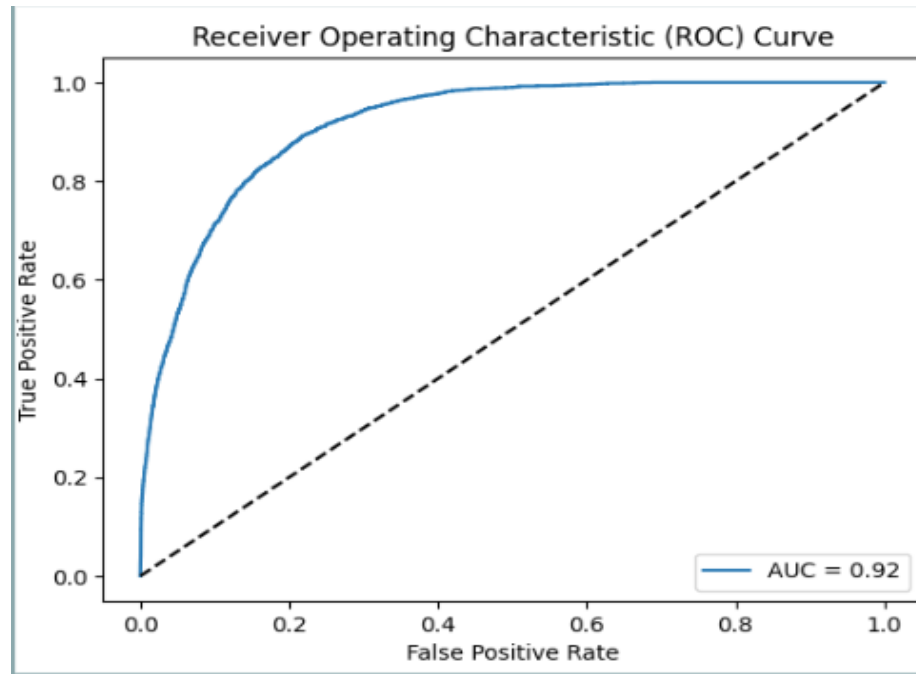
To delve deeper into the underlying data structure, we employed Principal Component Analysis (PCA). As depicted in the graph, the scree plot reveals that the top 7 principal components capture the majority of the information within the high-dimensional feature space. This dimensionality reduction not only simplifies the model but also potentially mitigates the curse of dimensionality, where model complexity explodes with increasing features. By focusing on these key components, we can achieve efficient and accurate learning without overfitting the data.

Furthermore, the learning curve sheds light on the model's behavior as the training data size grows. The graph showcases the evolution of both training and validation accuracy with increasing training set size. We observe a positive correlation between training size and accuracy, implying that the model benefits from additional data exposure. The gap between the training and validation curves suggests potential room for improvement, possibly through hyperparameter tuning or exploring different model architectures. By analyzing these curves, we gain valuable insights into the model's generalizability and potential for further optimization.

In summary, the nonlinear models of decision trees, KNN, and especially neural networks outperformed the linear logistic regression approach. This aligns with the highly multidimensional, nonlinear nature of modeling income from diverse census variables. The neural network's deep representation learning proved particularly adept at handling this problem, achieving state-of-the-art performance without extensive feature engineering. The benchmarks provided by the other models facilitated insightful comparisons illuminating the strengths of flexible nonlinear techniques for census-based income prediction.

Discussion and Analysis-

This study demonstrates that advanced machine learning algorithms, especially nonlinear models like neural networks, can effectively leverage raw census data to predict whether an individual's income exceeds $50,000. The neural network model achieved the highest test accuracy of 95.01%, outperforming the 94.49% accuracy of logistic regression. This aligns with the complex, multidimensional relationships between demographic variables and income classification that favor flexible nonlinear techniques.

The superior performance of nonlinear models reinforces that census-based income prediction represents a highly intricate task not amenable to simple linear regressions. Both decision trees and neural networks are capable of capturing complex variable interactions and hierarchical feature representations that prove critical for high accuracy. Even the non-parametric KNN approach matched logistic regression, illustrating the limitations of linearity assumptions.

Among the nonlinear techniques, neural networks display particular promise in harnessing raw census data without extensive feature engineering. The multilayer architecture and representational learning capacities inherent to deep learning empower neural networks to extract subtle patterns from highly dimensional data. The network's precision and recall metrics further demonstrate reliable identification of both high and low income samples.

Dimensionality reduction using PCA indicates only 7 principal components retained the most salient information, potentially highlighting redundancies in the raw input features. This enables simplifying the modeling task through compressed representations. However, the neural network leveraged the full feature set to attain maximal performance, benefiting from deep learning's inherent resistance to the curse of dimensionality.

Interestingly, while the fastest to train and run inference, logistic regression achieved competitive accuracy, differing from neural networks by only 0.5%. This efficiency makes it scalable to large datasets. The linear model also provides interpretability regarding the direction and magnitude of relationships between variables and income class. Both linear and nonlinear techniques ultimately offer useful and complementary perspectives.

In terms of limitations, the dataset's origin from 1990s census surveys warrants caution in extrapolating the findings to the present era without further validation. As demographic, occupational, and socioeconomic trends evolve over time, income distribution dynamics will likely shift as well. Testing the models on more recent census data could indicate required adjustments.

Additionally, errors in the target income variable within the historical records may propagate through the models, reducing accuracy. Auditing and cleaning the raw data could enhance results. Supplementary data sources correlating with income, such as property values, may also improve predictions and generalization.

Overall, this study demonstrates advanced machine learning, especially nonlinear neural networks, can unlock state-of-the-art performance in modeling income distribution from multifaceted census data. The techniques exhibit significant promise in elevating predictive accuracy across diverse applications in economic and public policy, financial services, marketing

research, and social science analysis. With rigorous benchmarks and feature importance interpretations, this work provides a springboard for further advancing machine learning on census data for income modeling tasks.

The ability to accurately predict income levels from census data has profound real-world implications across diverse domains. More reliable income classification enables better-targeted economic and social policies to support lower-income communities. Government agencies could leverage these predictive models to guide investments in infrastructure, healthcare, education, and housing towards areas likely to contain higher proportions of low-income households based on their demographic makeup. Marketing firms may also utilize the insights to optimize campaigns focused on budget-conscious consumers.

In the finance realm, improved income prediction supports both credit risk assessment and identification of high-net-worth individuals for tailored products and services. Lenders can integrate income classification to help gauge borrowers' repayment abilities while wealth managers can pinpoint potential clients. The models could also assist in constructing credit score criteria that avoid over-penalizing historically disadvantaged groups.

For research on economic inequality, accurately quantifying income distribution is crucial. By revealing relationships between factors like race, gender, education and income, these predictive techniques could expose socioeconomic disparities. The models empower analyses probing complex questions around how demographic variables may relate to economic outcomes across populations. However, privacy and ethical concerns around using such sensitive personal data warrant thoughtful consideration.

Broader applications of census-based income prediction span international development, where insights into regional income variation can guide poverty-alleviation initiatives and investments in low-income areas [9]. The techniques hold promise for elevating quality of life across communities through data-driven understanding of socioeconomic standing. Overall, this work highlights the real-world value that advanced machine learning offers by unlocking deeper intelligence from census data.

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A Whole Body View Into Dysautonomia: Systematic Impacts and Pathophysiological Mechanisms By Ja'Zhana Henderson

Abstract

Dysautonomia, characterized by autonomic nervous system (ANS) dysregulation, significantly impacts multiple body systems, leading to diverse and debilitating symptoms. This paper presents a comprehensive analysis of dysautonomia's systemic effects, particularly focusing on its relationship with disorders like fibromyalgia, chronic fatigue syndrome, and Postural Orthostatic Tachycardia Syndrome (POTS). Gastrointestinal issues such as gastroparesis and irritable bowel syndrome (IBS) are highlighted, reflecting disrupted autonomic control over digestive functions. Musculoskeletal impacts are evident in the form of chronic pain syndromes and increased pain sensitivity, suggesting a shared pathophysiology with conditions like fibromyalgia. Cardiovascular challenges include orthostatic hypotension, tachycardia, and labile hypertension, with POTS exemplifying the complex nature of autonomic regulation on heart function. Neuroendocrine and respiratory systems are also affected, leading to hormonal imbalances and respiratory control issues, respectively. Through a detailed literature review and case study analysis, the paper elucidates the intricate linksbetween dysautonomia and associated disorders, advocating for an integrated diagnostic and therapeutic approach to address the multifaceted nature of these conditions.

Introduction

Dysautonomia, a complex and multifaceted disorder, pertains to a dysregulation of the autonomic nervous system (ANS), which is responsible for regulating vital bodily functions such as heart rate, blood pressure, digestion, and temperature control. The study of dysautonomia is crucial due to its systemic impact on the body, often leading to a wide range of symptoms that can significantly impair an individual's quality of life. This paper, titled "A Whole Body View Into Dysautonomia: Systematic Impacts and Pathophysiology Mechanisms," aims to provide an in-depth exploration of how dysautonomia affects various bodily systems. We will delve into the pathophysiological mechanisms underlying these impacts, offering a comprehensive understanding of this complex condition. The importance of this study lies in its potential to enhance diagnostic accuracy, improve treatment strategies, and ultimately, provide better patient outcomes for those suffering from dysautonomia.

Background and Literature Review

The Autonomic Nervous System (ANS) serves as the principal mechanism in the control and regulation of involuntary bodily functions, including heart rate, blood pressure, digestion, and respiratory rate. Structurally, the ANS is divided into the sympathetic and parasympathetic nervous systems, each playing a pivotal role in maintaining homeostasis. Dysautonomia represents a range of conditions resulting from ANS malfunctions.

Historically, the study of dysautonomia has evolved significantly. Initial understanding was limited, often attributing symptoms to psychological factors rather than physiological dysfunctions. Over time, advancements in neurology and autonomic research have led to a better understanding of these disorders. The historical perspective of dysautonomia is essential in understanding how perceptions and treatments have evolved.

The body of research on dysautonomia and related disorders has expanded over the years. Earlier studies primarily focused on severe forms, such as Familial Dysautonomia (Riley-Day syndrome) and Pure Autonomic Failure (PAF). Recent research, however, has broadened to include conditions like Postural Orthostatic Tachycardia Syndrome (POTS) and Multiple System Atrophy (MSA). These studies have been pivotal in identifying the underlying pathophysiological mechanisms, improving diagnostic criteria, and developing treatment modalities. Furthermore, this research has highlighted the heterogeneity of dysautonomia, demonstrating that it can occur as a primary condition or secondary to other diseases such as diabetes, Parkinson's disease, and certain autoimmune disorders.

The exploration of the autonomic nervous system and its dysfunctions has come a long way from its initial understanding. The shift from viewing dysautonomia as a purely psychological anomaly to recognizing it as a complex set of physiological disorders marks a significant advancement in medical science. The current body of literature not only provides insights into the varied manifestations of dysautonomia but also sets the stage for future research aimed at unraveling the intricacies of this challenging set of conditions. This review serves as a foundation for our study, which seeks to further elucidate the systemic impacts and pathophysiological mechanisms of dysautonomia, contributing to the growing field of knowledge in this area.

Dysautonomia and the Gastrointestinal System

The gastrointestinal (GI) system's functioning is intricately linked to the autonomic nervous system (ANS), which plays a crucial role in regulating digestive processes. The ANS modulates various aspects of gastrointestinal physiology, including motility, enzyme secretion, and blood flow. This regulation is achieved through a complex interplay between the sympathetic and parasympathetic divisions of the ANS, ensuring optimal digestive function.

In dysautonomia, this harmonious regulation is disrupted, leading to a range of gastrointestinal disorders. Two prominent conditions associated with dysautonomia are gastroparesis and Irritable Bowel Syndrome (IBS). Gastroparesis, characterized by delayed gastric emptying, manifests in symptoms such as nausea, vomiting, and abdominal pain. On the other hand, IBS, a more common functional GI disorder, is associated with symptoms like abdominal discomfort, bloating, and altered bowel habits. Both conditions exemplify the impact of ANS dysfunction on the GI system.

The pathophysiology of gastrointestinal symptoms in dysautonomia is complex and multifactorial. In gastroparesis, for instance, impaired vagal nerve function leads to reduced stomach motility. Similarly, in IBS, dysregulated communication between the gut and brain,

possibly mediated by the ANS, is thought to play a significant role. Additionally, dysautonomia can exacerbate the sensitivity of the gastrointestinal tract and alter intestinal motility, further contributing to the diverse GI symptoms observed in these conditions.

Understanding the relationship between dysautonomia and gastrointestinal disorders is crucial for developing targeted therapies. By elucidating the underlying pathophysiological mechanisms, future research can pave the way for more effective management of these debilitating symptoms, improving the quality of life for individuals affected by these conditions. This segment of our study underscores the systemic nature of dysautonomia and its profound impact on the gastrointestinal system, highlighting the need for a comprehensive approach to treatment and management.

Dysautonomia in the Musculoskeletal System

Dysautonomia's impact extends beyond the traditional realms of autonomic regulation to significantly affect the musculoskeletal system, particularly in the manifestation of chronic pain syndromes. This interrelation is a critical area of exploration, given the debilitating nature of these conditions and their profound effect on patients' quality of life.

Chronic pain syndromes associated with dysautonomia present a challenging clinical picture. These pain conditions are often characterized by widespread musculoskeletal discomfort, fatigue, and heightened pain sensitivity. The dysregulation of the autonomic nervous system plays a pivotal role in the amplification and persistence of pain signals. This dysregulation can lead to an imbalance in pain modulation pathways, resulting in the sustained perception of pain even in the absence of typical nociceptive triggers.

Fibromyalgia, a condition characterized by widespread musculoskeletal pain, fatigue, and cognitive disturbances, is an exemplar of the link between dysautonomia and musculoskeletal disorders. Studies suggest that individuals with fibromyalgia often exhibit signs of autonomic dysfunction, such as altered heart rate variability and abnormal blood pressure responses. These findings point towards a potential dysautonomic basis for the pathophysiology of fibromyalgia, offering new perspectives in understanding and managing this condition.

The mechanisms underlying muscle fatigue and heightened pain sensitivity in dysautonomia are complex and multifaceted. Autonomic dysfunction can lead to abnormal muscle blood flow, resulting in inadequate oxygen and nutrient delivery to muscles, thus contributing to fatigue and pain. Additionally, dysautonomia can affect the processing of pain signals in the central nervous system, leading to an increased sensitivity to pain, known as central sensitization. This phenomenon results in a heightened pain response to stimuli that are typically not painful and may play a significant role in chronic pain syndromes associated with dysautonomia.

The relationship between dysautonomia and the musculoskeletal system, particularly in the context of chronic pain syndromes and conditions like fibromyalgia, is an area of significant clinical importance. Understanding the underlying mechanisms of muscle fatigue and pain

sensitivity in dysautonomia not only provides insights into these complex conditions but also opens avenues for developing targeted therapeutic strategies. This exploration is vital for improving the management of musculoskeletal symptoms in patients with dysautonomia, thereby enhancing their overall well-being and quality of life.

Cardiovascular Implications of Dysautonomia

Dysautonomia significantly impacts the cardiovascular system, often manifesting as conditions like orthostatic hypotension and tachycardia. These cardiovascular manifestations are not only common in dysautonomia but also contribute to the complexity of its clinical management.

Orthostatic hypotension, characterized by a significant drop in blood pressure upon standing, results from the autonomic nervous system's failure to adequately respond to positional changes. This condition leads to symptoms such as dizziness, lightheadedness, and in severe cases, fainting. Tachycardia, or rapid heart rate, is another frequent cardiovascular manifestation in dysautonomia. It can occur as a compensatory mechanism in response to orthostatic hypotension or as a standalone symptom due to autonomic dysregulation.

Postural Orthostatic Tachycardia Syndrome (POTS) is a prime example of how dysautonomia affects the cardiovascular system. POTS is characterized by an excessive increase in heart rate upon standing. Patients with POTS often experience a constellation of symptoms including palpitations, dizziness, and fatigue, severely impacting their daily functioning.

The management of cardiovascular symptoms in dysautonomia is multifaceted. It often includes non-pharmacological strategies like increased fluid and salt intake, physical therapy to improve orthostatic tolerance, and lifestyle modifications to reduce symptom triggers. Pharmacological treatments may include beta-blockers to manage tachycardia, fludrocortisone to increase blood volume, and other medications tailored to individual patient needs and symptom profiles.

The cardiovascular implications of dysautonomia are significant and diverse, ranging from orthostatic hypotension to conditions like POTS. Understanding these implications is crucial for effective management. The challenge lies in the tailored approach required for each patient, necessitating a comprehensive understanding of the underlying autonomic dysfunction and its varied manifestations. The ongoing research and clinical efforts in this field are vital for improving the lives of those affected by these challenging cardiovascular symptoms of dysautonomia.

Neuroendocrine Impact of Dysautonomia

The neuroendocrine system, which bridges the nervous system and hormonal responses, is profoundly impacted in dysautonomia, leading to a spectrum of hormonal and metabolic disturbances. This section explores the interplay between dysautonomia and the neuroendocrine system, emphasizing hormonal imbalances, stress responses, metabolic considerations, and related neuroendocrine disorders.

Hormonal imbalances in dysautonomia are primarily attributed to the disrupted communication between the autonomic nervous system and the endocrine glands. This dysregulation can lead to imbalances in key hormones like cortisol, adrenaline, and insulin, which are crucial for stress response, metabolism, and overall homeostasis. Patients with dysautonomia may experience altered stress responses, often characterized by exaggerated or insufficient hormonal reactions to stressors. This can manifest as symptoms like fatigue, anxiety, and mood swings, reflecting the underlying hormonal dysregulation.

Metabolic considerations in dysautonomia are equally critical. The autonomic nervous system plays a vital role in regulating metabolism, influencing processes like glucose utilization and energy production. Dysautonomia can disrupt these metabolic pathways, leading to symptoms such as weight fluctuations, altered appetite, and intolerance to certain foods. Understanding these metabolic implications is vital for managing the nutritional and metabolic needs of individuals with dysautonomia.

Furthermore, dysautonomia is often associated with various neuroendocrine disorders. Conditions such as Addison's disease, where adrenal gland function is compromised, or diabetes mellitus, particularly type 1, where insulin production and regulation are affected, can both be linked to autonomic dysfunction. The relationship between dysautonomia and these disorders highlights the need for a holistic approach in diagnosis and treatment, considering the potential overlap and interdependence of neuroendocrine and autonomic symptoms.

The neuroendocrine impact of dysautonomia encompasses a broad range of hormonal and metabolic disturbances. These disruptions can significantly affect the quality of life and require a comprehensive understanding for effective management. The ongoing research into the neuroendocrine pathways affected by dysautonomia is crucial for developing targeted therapies and improving patient outcomes in this complex and multifaceted condition.

Respiratory System and Dysautonomia

The respiratory system is intricately regulated by the autonomic nervous system (ANS), ensuring the optimal functioning of breathing processes. Dysautonomia, characterized by the dysregulation of the ANS, can significantly impact respiratory functions, leading to various respiratory conditions and symptoms.

The autonomic control of respiratory functions involves a delicate balance between the sympathetic and parasympathetic nervous systems. This balance ensures the proper regulation of respiratory rate, airway diameter, and the gas exchange process in the lungs. In dysautonomia, this equilibrium is often disrupted, which can lead to abnormal respiratory patterns, difficulties in breathing regulation, and heightened sensitivity to environmental factors.

Dysautonomia plays a notable role in respiratory conditions such as asthma and sleep apnea. Asthma, a chronic respiratory condition characterized by airway inflammation and hyperresponsiveness, can be exacerbated by autonomic dysregulation. This is evident in the altered bronchial tone and increased airway responsiveness seen in some patients with dysautonomia. Similarly, sleep apnea, particularly obstructive sleep apnea, can be influenced by

dysautonomia due to its impact on respiratory control during sleep. The impaired autonomic regulation can lead to irregular breathing patterns and reduced airway muscle tone, contributing to the apneic events.

Management of respiratory symptoms in dysautonomia requires a multifaceted approach. It involves addressing the direct respiratory issues, such as using bronchodilators for asthma or continuous positive airway pressure (CPAP) for sleep apnea, while also targeting the underlying autonomic dysregulation. Non-pharmacological interventions, such as breathing exercises and physical therapy, can be beneficial in improving respiratory function and tolerance. Additionally, lifestyle modifications, including avoidance of triggers and maintaining a healthy weight, are crucial in managing respiratory symptoms associated with dysautonomia.

The impact of dysautonomia on the respiratory system is significant, affecting both the direct control of respiratory functions and the management of conditions like asthma and sleep apnea. Understanding the interplay between the autonomic nervous system and respiratory system is essential for effective management of these symptoms. Future research in this area holds the potential to further elucidate the mechanisms of respiratory involvement in dysautonomia and to improve treatment strategies for affected individuals.

Interconnected Disorders: Fibromyalgia, POTS, and Chronic Fatigue Syndrome (CFS)

Fibromyalgia, Postural Orthostatic Tachycardia Syndrome (POTS), and Chronic Fatigue Syndrome (CFS) are disorders that frequently intersect with dysautonomia, both in their symptomatology and underlying pathophysiological mechanisms. These conditions, often coexisting, present a complex clinical picture due to their overlapping symptoms and shared dysfunctions.

Commonalities among fibromyalgia, POTS, and CFS in the context of dysautonomia include symptoms like chronic fatigue, pain, dizziness, and cognitive disturbances. Despite these similarities, each disorder also maintains distinct characteristics. Fibromyalgia is primarily characterized by widespread musculoskeletal pain and tenderness, POTS by an excessive heart rate increase upon standing, and CFS by profound and persistent fatigue not relieved by rest.

The shared pathophysiological mechanisms in these conditions and dysautonomia are a subject of ongoing research. Autonomic dysfunction is a core feature, manifesting in various ways, such as impaired blood pressure regulation in POTS and altered pain processing in fibromyalgia. Neuroendocrine abnormalities, immune dysregulation, and central sensitization are also proposed mechanisms that contribute to the symptom overlap and complexity of these conditions.

Clinical implications of these overlapping symptoms are significant. They often lead to challenges in diagnosis, as the similarities can mask the distinct aspects of each condition. Moreover, the coexistence of these disorders requires a multidisciplinary and individualized approach to treatment. Management strategies need to be tailored to address not only the specific symptoms of each disorder but also the common underlying dysfunctions. This includes

pharmacological treatments, physical therapy, cognitive-behavioral therapy, and lifestyle modifications.

The interconnected nature of fibromyalgia, POTS, and CFS with dysautonomia presents both diagnostic and therapeutic challenges. Understanding their commonalities and differences is crucial for effective management. The shared pathophysiological mechanisms offer a glimpse into the complexity of these conditions and underscore the need for a comprehensive approach to treatment. Future research in this area holds promise for unraveling the complexities of these interconnected disorders, leading to more effective and targeted therapeutic interventions.

Methodology

The methodology of this research paper is founded on a comprehensive approach, encompassing an extensive literature review, in-depth analysis of patient case studies, and a blend of qualitative and quantitative research methods. The literature review was meticulously conducted through academic databases such as PubMed, Google Scholar, and Scopus, utilizing key terms like "dysautonomia," "autonomic nervous system disorders," "fibromyalgia," "POTS," "CFS," and "systemic impacts of dysautonomia." This search focused on peer-reviewed articles, clinical trials, and review articles published in the last twenty years to ensure a thorough and current understanding of the topic.

In parallel, the study involved a detailed analysis of patient case studies from various healthcare institutions specializing in autonomic disorders. These case studies, chosen based on the presence of dysautonomia and associated disorders such as fibromyalgia, POTS, and CFS, provided valuable insights into symptom patterns, diagnostic challenges, and treatment efficacy. This qualitative analysis enriched the research with real-world perspectives on the complexities of these conditions.

Additionally, the research incorporated both qualitative and quantitative data collection methods. Quantitative data were gathered from clinical metrics like heart rate variability and blood pressure readings, complemented by symptom frequency and severity assessments. Qualitative data collection included patient interviews and questionnaires, offering a deeper understanding of the personal experiences and impacts of living with these conditions. This multifaceted methodological approach ensured a comprehensive exploration of dysautonomia and its interconnected nature with fibromyalgia, POTS, and CFS, providing a robust foundation for understanding the intricate interplay and overlapping symptomatology of these complex conditions.

Discussion

The integrative analysis of findings from this research provides a multifaceted perspective on dysautonomia and its systemic impacts, particularly in relation to fibromyalgia, POTS, and CFS. The extensive literature review, combined with patient case studies, underscores the complexity of dysautonomia as a disorder that disrupts the autonomic nervous system and has wide-ranging effects on multiple body systems. This disruption manifests uniquely in each

associated disorder, from the gastrointestinal symptoms seen in gastroparesis and IBS to the chronic pain in fibromyalgia, cardiovascular instability in POTS, and the hormonal imbalances impacting stress response and metabolism.

One of the key implications for diagnosis and treatment emerging from this research is the necessity for a holistic and integrated approach. Given the overlapping symptoms and shared pathophysiological mechanisms among dysautonomia and its related disorders, a multidimensional diagnostic and therapeutic strategy is essential. This approach should consider the entire spectrum of symptoms and their potential interconnections, rather than treating each symptom or disorder in isolation. For instance, the management of cardiovascular symptoms in POTS should be aligned with strategies to address related neuroendocrine or gastrointestinal issues, as they may be intricately linked through autonomic dysregulation.

However, the current research on dysautonomia and its interconnected disorders is not without limitations. One significant challenge is the variability in clinical presentations and responses to treatment, which can complicate the development of standardized diagnostic criteria and therapeutic protocols. Additionally, much of the existing research is based on small-scale studies or case reports, which may not fully capture the diversity and complexity of these conditions in larger, more diverse populations. There is also a need for longitudinal studies to better understand the long-term progression and outcomes of these disorders.

This research emphasizes the intricate relationship between dysautonomia and disorders such as fibromyalgia, POTS, and CFS, highlighting the need for an integrated approach to their diagnosis and management. While the current body of research provides valuable insights, it also reveals the gaps and limitations in our understanding. Future studies should aim to address these challenges, focusing on larger-scale, longitudinal research to unravel the complexities of these interconnected conditions and improve patient care.

Conclusion and Future Directions

This research paper has systematically explored the intricate relationship between dysautonomia and a range of interconnected disorders, namely fibromyalgia, POTS, and CFS. Key findings underscore dysautonomia's systemic impact across various body systems, revealing a complex interplay that manifests in diverse symptoms and conditions. Notably, gastrointestinal disturbances in conditions like gastroparesis and IBS, chronic pain syndromes in fibromyalgia, cardiovascular instability in POTS, and the neuroendocrine imbalances affecting stress response and metabolic processes were highlighted.

For clinical practice, these findings advocate for a holistic approach in the diagnosis and management of dysautonomia and its related conditions. Clinicians should be aware of the potential overlap in symptoms and consider a comprehensive evaluation strategy that encompasses the full spectrum of autonomic dysfunction. Treatment protocols need to be individualized, acknowledging the complex nature of these disorders and the multifaceted impact on patients' lives. Additionally, there is a need for increased awareness and education about these conditions among healthcare professionals to improve early diagnosis and intervention.

Looking forward, future research should focus on larger-scale, longitudinal studies to gain a deeper understanding of the progression, long-term outcomes, and optimal management strategies for dysautonomia and its associated disorders. There is a particular need to unravel the underlying pathophysiological mechanisms further, which could pave the way for the development of more targeted and effective treatments. Research should also explore the genetic and environmental factors contributing to these conditions, enhancing our understanding of their etiology and potential preventive measures.

This research emphasizes the complex and systemic nature of dysautonomia and its interconnectedness with various disorders, offering significant insights for clinical practice. The path ahead calls for continued research and collaboration across multiple disciplines to improve the lives of those affected by these challenging conditions. Through concerted efforts in research and clinical practice, we can hope to achieve better diagnostic accuracy, effective management strategies, and ultimately, improved patient outcomes in the realm of autonomic disorders.

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Social and Psychological Effects of Childhood Cancer By Aarushi Biswas-Gupta

Abstract

The mental health of childhood cancer patients and survivors has become an increasingly important issue as many survivors have shown to have greater levels of difficulty in the educational and social sectors. This is due to physical impairments from the cancer itself, cancer treatments, or an indirect cause of missing out on crucial moments for social development throughout childhood. These factors affect childhood cancer survivors into adulthood and beyond, where they experience lower rates of employment, financial struggles due to the sheer cost of mental health care, and trouble forming and maintaining adequate platonic, romantic, and familial relationships. This indicates a need for increased research focusing on the mental difficulties of childhood cancer patients, during and after treatment, so that doctors, families of these patients, and mental health professionals can respond to early signs of mental problems and accommodate to prevent them from worsening. By doing this, we can provide more opportunities for this vulnerable population to live a healthy life.

Introduction

Literature on mental health among childhood cancer survivors is limited, and much more research in this area is needed considering the substantial impact it has on their lives. The National Health and Nutrition Examination Survey (NHANES), which is conducted every two years, shows that those who have had cancer exhibit higher rates of anxiety, depression and reduced cognitive functioning with 14-24% experiencing symptoms of clinical depression, 10% with clinical levels of anxiety, and around 75% report difficulties with cognitive functioning (3). This study also pinpoints younger age at the time of diagnosis as a risk factor which makes child/adolescent survivors a point of interest when considering these impacts.

For example, children who are diagnosed with cancer often spend a significant amount of time in the hospital, depending on their condition, for treatment or high-risk traits that require observation. This severely cuts down on class time where they could be strengthening foundational educational elements for higher levels of education (elementary, middle, high school or college). Further, according to Cancer Research UK, treatments such as chemotherapy, immunotherapy, hormone therapies, and others can cause sudden and persistent fatigue in many patients (4). According to the American Childhood Cancer Organization(ACCO), these patients include over 300,000 children a year globally with 15,780 of those being in the United States (11). This lack of energy may affect class participation when patients are able to attend school, and overall performance on homework, projects, presentations, and other types of schoolwork. However, the effects do not end in the educational sector; cancer survivors also exhibit higher rates of social and psychological difficulties, which heavily manifest in their familial and romantic relationships. Every single one of these children is at risk for the physical, mental, and social outcomes of childhood cancer mentioned above. Individuals who have or are currently experiencing some form of childhood cancer, especially those with central nervous system(CNS)

tumors, leukemia, non-Hodgkin lymphoma, and neuroblastoma, typically face educational, social, and developmental/sexual setbacks stemming from mental or physical issues.

Literature Review

While survivors of CNS tumors and leukemia face the highest risk for stunted educational achievement, recent observations show that survivors of non-Hodgkin lymphoma and neuroblastoma have an increased chance of not graduating high school (2). According to the Childhood Cancer Survivor Study, those experiencing childhood cancer typically show a higher use of special education services compared to their siblings: 23% of patients versus 8% of siblings (2). This is most likely a direct result of the physical and mental limitations related to cancer or occurs as a result of missing large amounts of class time and crucial educational opportunities. According to parents of childhood cancer patients and survivors, they were also significantly more likely to repeat a grade in high school than those without a history of cancer (21% compared to 9%) (7). Falling behind in aspects of learning and socialization can subsequently reduce the number of leadership roles cancer patients are able to hold during or post-treatment. In fact, these educational difficulties often follow survivors into adulthood where they are two times more likely to be unemployed than the general population (15% compared to 8%) (8). A lack of work coupled with costs for mental health services, necessary for most cancer survivors who face symptoms of depression, anxiety, or other mental illnesses, is a detrimental combination that only hurts this already vulnerable population. In most areas of the US, therapy costs around $100-$200 per session, but prices can range from $65 to $250 per hour or more based on the experience and education of the therapist and the specialization of the therapist (6). As per the ADA, all insurance plans must cover mental health services; however, coverage varies by company, and many therapists don't accept insurance due to the complications that come along with it, leaving low-income members of the community, such as cancer survivors unable to afford it.

Some survivors demonstrate difficulties in social areas, such as a lack of empathy, manipulative tendencies, and irresponsible or angry behavior, during or after treatment, which, if not recognized and provided the correct treatment for, can last into early adulthood (1, 2). Exhibiting antisocial traits may make it difficult to form relationships, even with family. This leads to not only fewer friendships but scarce relationships and lower rates of marriage. While it is difficult to pinpoint exactly where antisocial traits manifest from, it likely stems from a lack of similarities and connections with peers during treatment along with missed social opportunities on account of physical limitations. Along with more antisocial behaviors, anxiety, depression, and inattention are also more prominent in children and adolescent survivors (2). This is likely brought on by poor physical health, including physical impairment or mobility issues seen in survivors of bone tumors, and leads to an increase in post-traumatic stress symptoms (2). There have also been reports of increased development of harmful health-related habits such as drinking and drug use. Despite the known detrimental health effects of drug and alcohol use, a recent study shows that rates of alcohol use are more prevalent in adult and adolescent survivors

of childhood cancer than the general population (22% compared to 12%), with monthly binge drinking seen in 18% of survivors as opposed to 9% of the general public (2).

Substandard physical health also increases rates of codependency and contributes to a lower marriage rate. It is shown that both females and males face difficulty in their sexual lives with females describing lower sexual functioning, pleasure, desire, and activity and males reporting low sexual activity and a 2.6 times risk of erectile dysfunction (2). These difficulties can come as a consequence of psychosocial issues, such as a distorted body image, fear of the future, and changing intimate and friendly relationships, working hand in hand with medically relevant difficulties such as interruptions in pubertal development and premature ovarian failure (5). Premature ovarian failure, also known as primary ovarian insufficiency (POI), is when the female ovaries stop working at a normal rate before the age of 40, causing the woman to have irregular periods as she transitions to menopause (10). The inability to procreate or bear children may create a sense of insecurity in place of a future that they might have previously created for themselves. The growing insecurities that patients may develop over time make it more difficult to form strong relationships, romantic or otherwise.

Conclusion

Based on the research discussed throughout this paper, general risk factors for lowered mental, physical, and psychological health include CNS tumor diagnosis, CRT treatment for CNS tumors, and being younger at the age of diagnosis. Educational difficulties, as a direct consequence of mental health issues or indirectly as a result of increased hospitalization, follow survivors into the workplace, given that they have stable jobs, which is not the case for an alarming amount of people. These are most likely the general outcomes of physical impairments, requiring additional medical benefits, skewed cognitive abilities, and issues forming healthy relationships with friends and co-workers.

The most efficient way to address such problems is to increase research focusing on mental health problems in childhood cancer patients to better understand the psychosocial and psychological implications of childhood cancer and deduce the types of resources needed to appropriately address this problem through and post-treatment. Physical health is usually the primary concern and of course, it is crucial to make sure that patients and former patients stay healthy enough so as to not develop physical impairments or other illnesses that would affect their quality of life. However, as has been seen over the past decade, mental health concerns have grown to the point that in October 2021, the American Academy of Pediatrics, the American Academy of Child(AAP) and Adolescent Psychiatry(AACAP), and Children's Hospital Association(CHA) declared youth mental health a national emergency (9). All this only highlights that more effort is needed to make a difference in the seemingly tragic mental health future of young people, especially those who are put in vulnerable situations, such as being diagnosed with cancer.

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Bridging the Divide: Education, Employment, and Policy Implications By Ethan Jiang

Abstract

       This paper studies the effects of education and training programs intended to equip workers with the necessary tools and skills to succeed in the workforce. The paper first reviews historical trends and persistent disparities in education and unemployment across demographic groups. This paper then studies the impact of higher education and vocational training on worker productivity and employment, as well as their effects on minority groups. Finally, I discuss the policy implications of this research.

Historical Trends in Unemployment and Education Across Demographic Groups

       Understanding the historical trends in education and unemployment rates across demographic groups is necessary to find persistent disparities and improve policy interventions. This subsection reviews historical trends in education and unemployment across race and gender groups, highlighting historical patterns and persistent disparities. With certain communities possessing lower rates of educational completion, community college will have a greater impact on them.

       White and Black unemployment rates have followed similar trends over time (Figure 1); however, it is important to note that white unemployment rates have never exceeded black unemployment rates. This points to a consistent disparity within the labor market. Similarly, Black and Hispanic populations have the lowest education levels out of all demographics. Recently, the gap between the Black and White unemployment rates has been the lowest ever, with a 1.8% difference (Figure 1). Federal Reserve data also sheds light into unemployment rates in the Asian population. The Asian population has consistently had the lowest percentage of unemployment out of all racial groups in the U.S. ever since employment rates have been tracked for this group. Asians also have the highest numbers of Bachelor's degrees and higher levels out of all other demographics by a significant margin, which likely plays a factor in their low unemployment rate (Figure 2). This suggests that Asians have a better labor market outcome relative to other ethnicities.
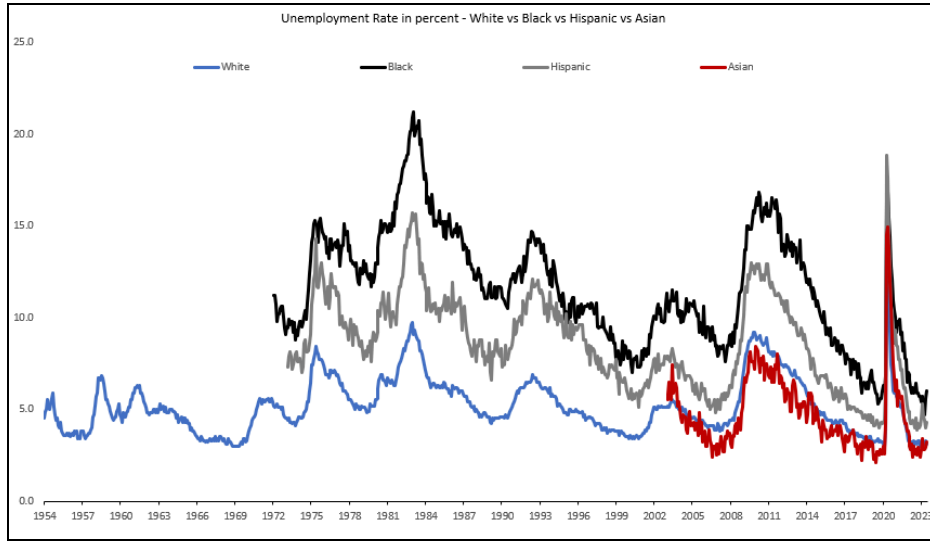
Fig 1: Unemployment rates (%) across racial groups (White vs. Black vs Hispanic vs Asian).
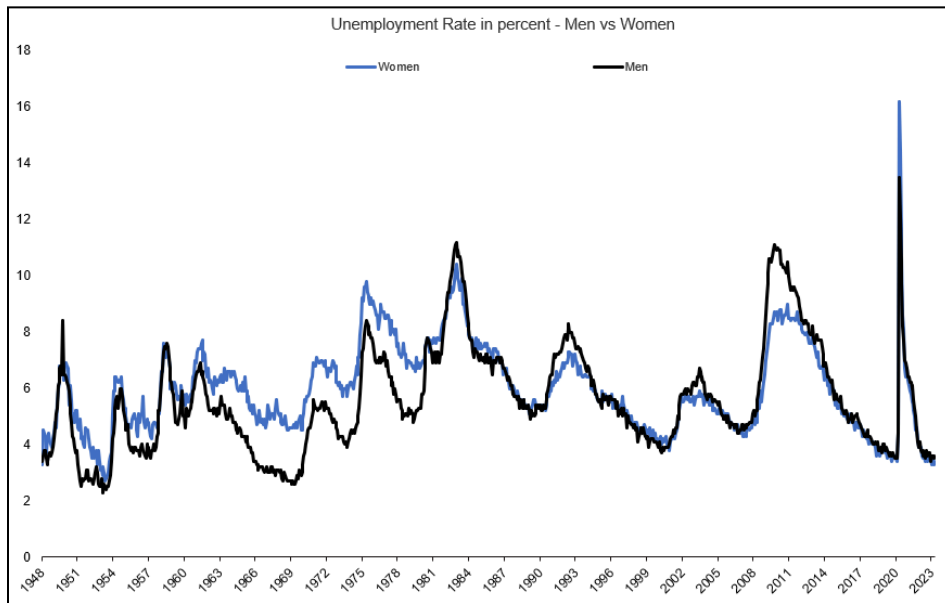Note that data on unemployment rates was not available across all groups at certain points.

Fig 3: Unemployment rates (%) across gender groups (Men vs Women).
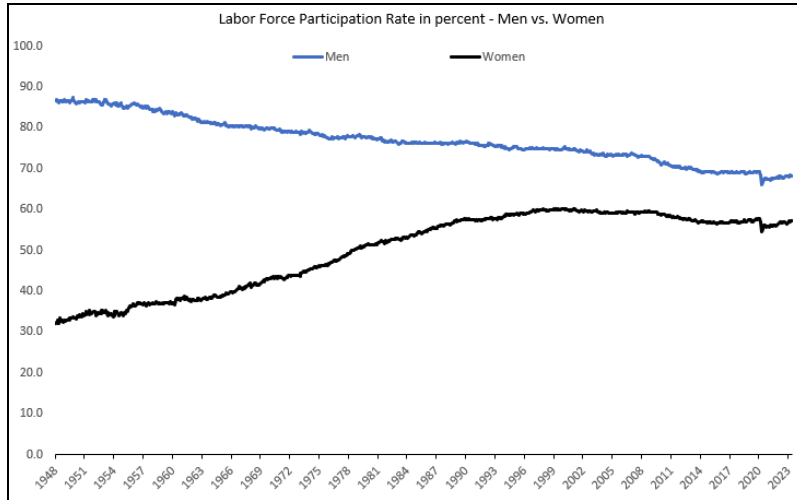
Fig 5: Labor force participation rates (%) across gender groups (Men vs Women).

Historically, women have had lower labor force participation rate due to societal expectation that they would not get a job or work (Richards 2020). Over the course of the 21st century, women's unemployment rates have generally converged with men's unemployment rates (Figure 3). However, during the COVID-19 pandemic, women's unemployment rates were higher during the unemployment spike, reaching a 27% gap at its peak. This is likely due to a number of factors, including the need for childcare, and that women were more likely to be working in industries negatively affected by the pandemic (Bureau of Labor Statistics 2020).

Over the past decade, there has been a steady increase in education levels in all demographic groups, encompassing both high school and college degrees (Figure 2 & 4). While men tend to complete high school and GEDs at higher rates, women are increasingly participating in and completing higher education programs (U.S. Census Bureau 2022) This demonstrates that women are increasingly acquiring necessary skills for more competitive job opportunities, which could be a major factor that has improved women's labor force participation over the past several decades.

However, significant racial gaps in education levels have persisted. Black, and Hispanic individuals have consistently lower levels of education relative to Whites and Asians (Figures 2 and 4). This is likely a major factor contributing to their higher unemployment rates. Black and Hispanic education levels have both increased and their respective unemployment rates have decreased over the past 20 years (Figures 2 and 4). Although this does not necessarily prove that increased education has caused the decline in unemployment for these groups, it could be a contributing factor. In addition, higher education levels can improve other measures of job quality besides the probability of employment (OECD 2020), which are not captured by the unemployment rate.
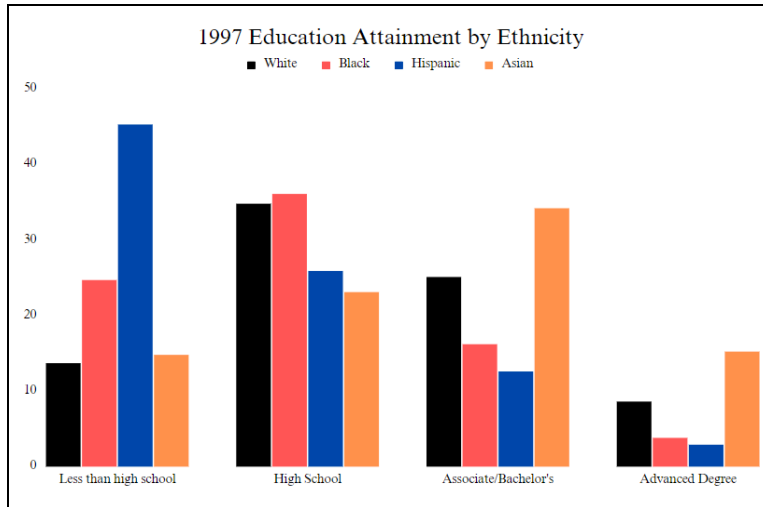
168

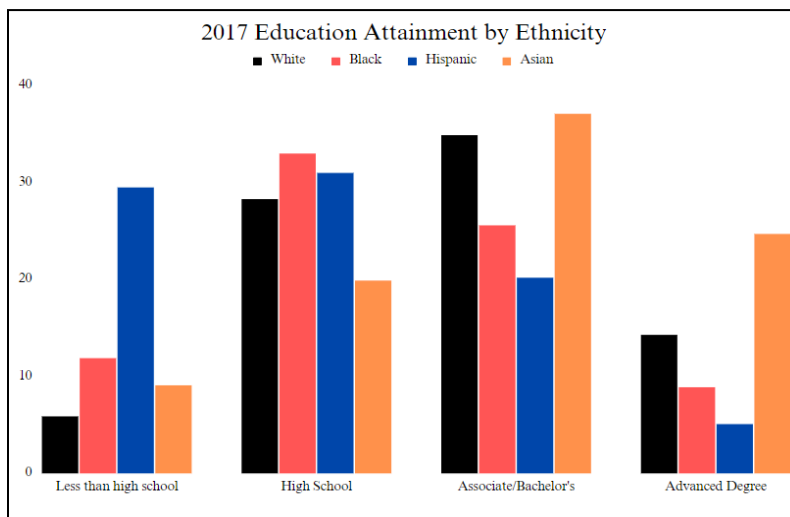Fig 4: Educational attainment by ethnicity in 1997 (%) (White vs Black vs Hispanic vs Asian).

Fig 2: Educational attainment by ethnicity in 2017 (%) (White vs Black vs Hispanic vs Asian). Source: U.S Census Bureau, Current Population Survey 1997 and 2017

Effects of a Community College Education on Labor Market Outcomes

This section examines the research on the impact of higher education, and specifically the role that community colleges play, in improving workers' outcomes and salaries. We focus on community college because it is often overlooked in the modern educational system. The section also highlights the benefits that community colleges offer both the individuals who attend and society more broadly.

Numerous studies indicate that attending community college has a positive effect on students who enroll. Community college, being the most attainable form of higher education (in terms of cost and ease of admission), naturally leads those who attend it to have an increased chance for degree completion. This provides them with the proper certifications and skills to advance their career competitively. Additionally, students who attend community college can be

expected to earn, on average, $9.6k more annually than those who do not, cumulating into an approximate increase of $400k during their career (Lightcast 2022).

For example, one study of a lottery for community college admission of nursing students for admission in California in 2020 found that enrolling in community college nursing programs increased students' future wages by around 44%, as well as the probability of working in the health industry by 19% (Grosz 2020). This provides strong evidence that community college attendance improves students' outcomes, since the nursing students in this study were randomly selected for admission and therefore likely would have similar employment and earnings outcomes compared to those who were not selected, absent their having been granted admission.

Specific fields such as STEM and technical courses often lead to higher earnings than other fields. One study of first-time college students in North Carolina found that the overall earnings gap between community college graduates and non-attendants is about twice as large for STEM graduates as for humanities and social sciences graduates (citation).

The impact of community colleges extends beyond the individual level, providing noticeable contributions to the economy and the government. Community college alumni generated around $895.5 billion in added income during 2019 - 2020 (Lightcast 2022), accounting for about 4.1% of U.S. GDP. Moreover, alumni fill about 1 out of every 18 jobs in the US, making them a substantial presence in the workforce (Lightcast 2022).

Investing in community college education would also provide financial returns for the government through decreased costs and increased tax revenue, which would benefit taxpayers as a whole. The present value of future potential added tax revenue from the current level of community college attendance is estimated to be around $331.7 billion, mainly stemming from tax revenue, highlighting the financial gains for the government (Lightcast 2022). Community college graduates use fewer government resources in the justice system and health care, suggesting that community college provides positive impacts on both the individual and society (citation). Savings in the health sector such as smoking and obesity amount to around $25 billion, the crime sector $5.5 billion, and $5.2 billion in the income assistance area (Lightcast 2022).

Research has shown that marginalized groups often benefit the most from community college, especially considering their lower rates of educational completion. For example, a study of first-time community college students in North Carolina in 2003 found that earning an associate's degree on average raises wages by approximately 61% for women and 25% for men (Liu, Belfield, &Trimble 2013). Displaced workers who are women tend to benefit more from one year of schooling, with a 14% wage increase and a 9% increase for men (Jacobson, LaLonde, & Sullivan 2005).

Furthermore, students who transfer out of community college still experience returns on their investment, with a 68% salary gain for women and a 41% gain for men (Liu, Belfield, & Trimble 2013). Although most of their course credits are received at a four-year institution, these students' educational journey through community college lays a strong foundation.

Policy Implications and Suggestions

  The previous sections have highlighted the positive impact of a community college education on the individual and on society. How much the government should support community college education and other higher education programs is currently a very contentious point of debate in both national and local politics. For example, President Biden advocated free community college nationwide in his 2020 presidential campaign (Ngo 2021), and the city of Boston recently guaranteed tuition-free community college to all residents (Larkin 2023). Despite these campaigns, Biden's plan for free community college was cut from his Build Back Better plan, and figures such as Margaret Spellings - former US secretary of education and president of the think tank Texas 2036 - advocate against it.. However, there is strong evidence supporting the idea of free community college.

  Community college degrees in STEM subjects tend to be more successful in increasing the students' wages compared to degrees in the humanities or social sciences. In a study of students at California community colleges, students at colleges with an above-median amount of Career Technical Education (CTE) courses saw higher career earnings, possibly due to being able to specialize in local labor market connections, or more focused academic and career support for these students. This suggests that governments considering funding community college should prioritize STEM courses or technical courses.

  While these effective education programs exist, it is important that students who would stand to benefit the most from a community college education are aware of these opportunities and have access to them. Community colleges' marketing should seek to promote marginalized communities, low-income areas, underrepresented groups, and students who would not have attended college otherwise. A study of the public schools system in Chicago found that community colleges most benefited students that would not have attended a traditional four-year institution (Brand, Pfeffer, & Goldrick-Rab 2014).

  Advertising campaigns should highlight the benefits of community colleges, such as increasing earnings, career advancement, and job security. Studies and surveys have shown that these are the main factors that motivate students to go to pursue higher education (Cox 2012). Community colleges should partner with local, trusted organizations like schools and industries to ensure that their courses align with skills needed in the job market.

  The government should have a major interest in the continuation of support for community colleges. As shown before, these programs have and will have important gains to the U.S. GDP and society. Furthermore, these programs help train displaced workers and build a skilled workforce, improving the lives of individuals. This also helps address social inequality by providing affordable educational opportunities that improve attendees' career success throughout their lives. The revenue generated by community college alumni through tax revenue negates part of the cost required to run the colleges. Government revenues would benefit most from focusing the most funding on STEM and CTE programs, as they tend to increase students' earnings, and therefore tax revenue, by substantially more than humanities or social science degrees.

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EMS in the USA: Challenges, Disparities, and the Quest for Global Solutions By Ruihan Sun

Abstract

With 1.05 million personnel responding to 42.6 million calls annually, the United States Emergency Medical Services (EMS) plays a vital role in the healthcare industry, serving almost every community in the country. However, the system faces challenges such as long response time, urban-rural outcome variations, and large ambulance bills, which are exacerbated by the COVID-19 pandemic. This study examines EMS systems across the world, considering innovations that could potentially aid the United States in improving its ability to provide emergency care. The included articles are categorized into 4 groups based on their proposed innovation, which include innovations in personnel, systems-level innovations, metrics of successful EMS, and technological innovations. The main innovations from each article are synthesized to construct recommendations for the United States to improve the functioning of its EMS systems. In conclusion, this review suggests incorporating laypeople in the EMS system, establishing special emergency groups, applying technological innovations, and performing an investigation of the cost of EMS.

Background

Emergency medical services (EMS) is a vital component of the healthcare industry in the United States, serving almost every community in the country. There are currently 1.05 million EMS personnel nationwide, including 268,420 paramedics and 622,902 emergency medical technicians, working for 19,520 EMS agencies. Annually, these personnel respond to 42.6 million EMS calls, utilizing 87,781 EMS vehicles (National Association of Emergency Medical Technicians).

Various agencies provide emergency medical services, including public agencies (such as fire departments), private companies, hospital EMS departments, and volunteer groups. The type of agency depends on the region, with some regions experiencing cooperation between different types of agencies. For example, in many places in the United States, the fire department is the first responder after a 911 call is placed. However, if the patient needs to be transported to a hospital, a private ambulance company staffed with EMTs (Emergency Medical Technicians) and paramedics transport the patient. On the other hand, some rural areas in the United States cannot use taxes to support private ambulance companies, and instead, have to depend heavily on local volunteers (National Association of Emergency Medical Technicians).

There are significant disparities between the EMS outcomes in urban areas and rural areas. Research conducted by physicians in the emergency departments of hospitals in Boston and Columbus uncovered that rural patients, when compared to urban patients, experienced longer response times and lower odds of achieving resumption of sustained cardiac activity (ROSC) during acute coronary events (Peters Ga et al.). Many factors contribute to the

differences in EMS outcomes between rural and urban areas, such as the response distance, the rate of mechanical CPR, and the response time.

In addition, extremely high ambulance bills are among the most salient problems for patients, with 71 percent of all ambulance rides involving potential surprise bills (Payton Stredler). For both ground and air ambulances, out-of-network charges were substantially greater than in-network prices, resulting in median potential surprise bills of $450 for ground transportation and $21,698 for air transportation (Chhabra Kr et al.). The high bill can be attributed to multiple factors: an unclear cost upfront, lack of insurance reimbursement, and a for-profit ownership structure. Notably, there is limited data on the true cost of ambulances. In response, the Bipartisan Budget Act of 2018 mandated a data collection on the cost of ambulance services (Congress). Interestingly, EMS is only reimbursed for its transportation services, not for providing healthcare (National Association of Emergency Medical Technicians). For this reason, while many view EMS as a healthcare provider, their primary function in the eyes of the payer is one of transportation. In other words, if the ambulance does not transport patients to a hospital, they are not reimbursed, even if healthcare is provided on the scene. According to data from state EMS offices, "of the 42.6 million EMS responses that occurred in 2018, only 30.9 million resulted in transports" (National Association of Emergency Medical Technicians).

Additionally, patients do not get a chance to choose if a public or private EMS agency provides them with their care, which may lead to substantially higher bills for patients. Without knowing the true cost before engaging in EMS, patients are limited both in knowledge and choice, limiting access to competitive market forces and possibly driving up prices (Newberger & Braithwaite). According to Health Fair, private company's bills are substantially higher than those of public agencies (Adler et al.). The commercialization of EMS also results in the overuse of expensive transportation services, such as air ambulances (Roman et al.).

The problems in the US EMS system were exacerbated by the Covid-19 outbreaks. These include a lack of standardized protocols for treating Covid-19 patients, insufficient provisions of PPE either for EMS personnel or patients, and a reduction of personnel due to stress and burnout (Mohammadi et al.). Besides, to prevent cross-infection, ambulances have to be sterilized every time they return to the base, which adds to the response time.

EMS system has a profound role in society as it is the mainstream of pre-hospital healthcare. Unfortunately, many problems exist in the United States EMS system, including but not limited to ambulance allocation, modes of transportation, response efficiency, billing, and so on. Therefore, this study will examine EMS systems across the world, in consideration of innovations that could potentially aid the United States in improving its ability to provide emergency care.

Method

In this scoping review, one reviewer analyzed 414 abstracts generated utilizing the phrases: "success" AND "emergency medical services" AND "outcomes" NOT "United States" in Pubmed. Results were filtered to include those between the dates of 2013 to 2023. Articles

included were those describing successful EMS practices outside the US, technological or systematic innovation of ways to improve the EMS system, factors associated with a successful EMS, and other articles related to improvements in EMS. Articles excluded were those describing EMS systems inside the United States, research that focuses on medical technology or curing diseases, and case reviews. The reviewers included articles about the EMS system or successful practices outside of the United States while excluding those articles discussing a specific treatment in the pre-hospital emergency.

  After viewing the abstracts of the 414 articles generated by the aforementioned screening, 139 articles were included in the full-text review and 17 articles were included in the data section. The reviewer then grouped those articles into 4 groups based on their proposed innovation, which included Innovations in personnel, systems-level innovations, metrics of successful EMS, and technological innovations. The main innovations from each article are synthesized to construct recommendations for the United States to improve the functioning of its EMS systems.

Identification of studies via Pubmed (2013-2023)

Identification

Pubmed
"success AND "emergency medical services" AND outcomes NOT United States"
From 2013 to 2023
Databases (n = 1567)

Studies excluded
-Practices inside the United States
- Medical technology or curing diseases
-Case reviews

Screening

Abstract screening
(n = 414)

Studies excluded**
(n = 275)

Full-text review(n = 139)

Studies excluded**
(n = 122)

Included

Studies included in review
(n = 17)

Classification
Innovations in personnel
(n = 4)
Systems-level innovations
(n = 3)
Metrics of successful EMS
(n = 6)
Technological innovations
(n = 4)
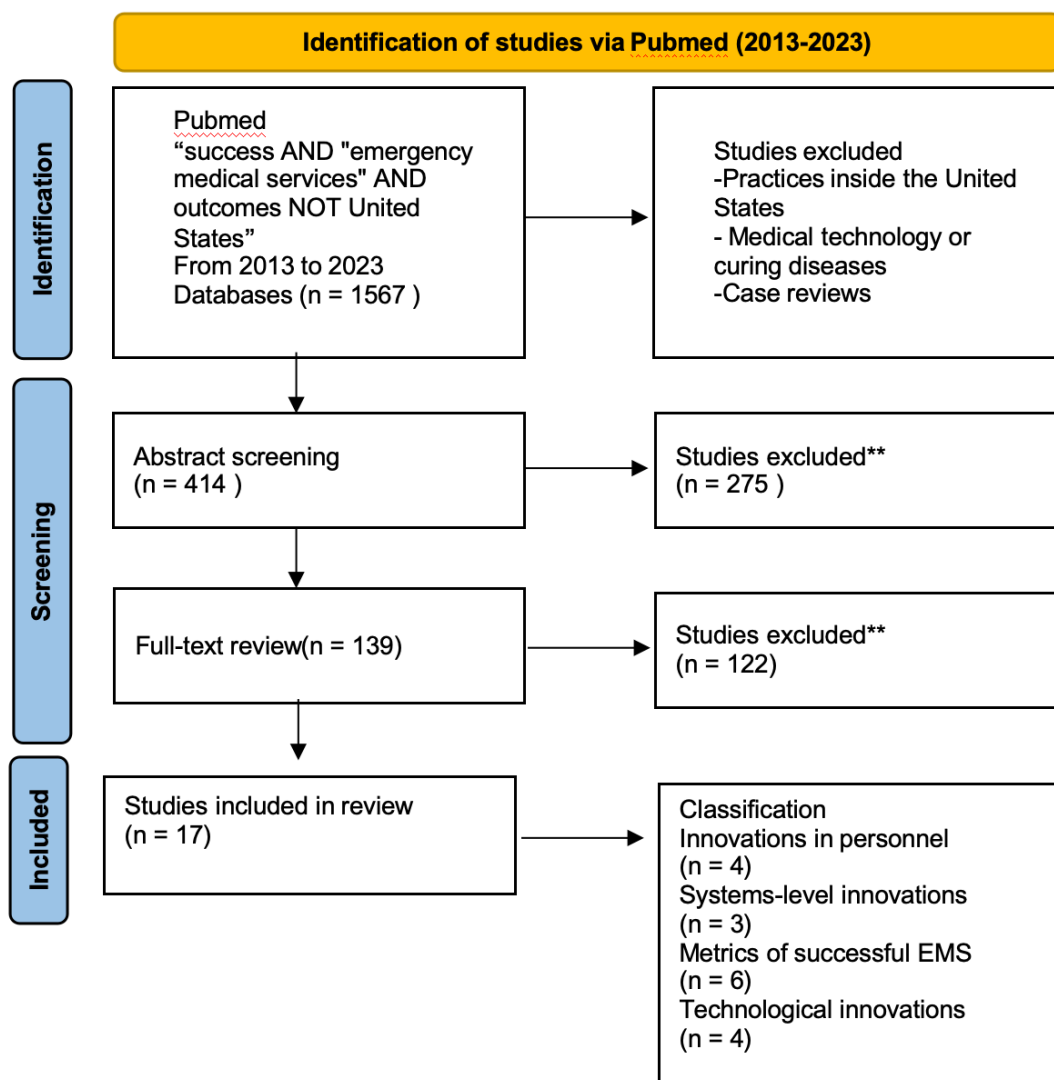
Fig 1: Flow diagram summarizing identification and screening process

Innovation in Personnel

Systems-level innovations are made at the organizational or management level. They maximize the use of existing resources and promote collaboration between different components of EMS. These innovations include the reallocation of ambulances, a collaboration initiative, and so on. Through systems-level innovations, the EMS system could achieve its maximum efficiency and bring out the best potential to save lives.

One study in Lebanon established a transfer center at the American University of Beirut Medical Center (AUBMC). By implementing clearer standards of communication, coordination, and care continuity, they increased the number of outgoing transfers by 15% during a four-year observation period (El et al.). In addition, researchers from China proposed the application of a stroke emergency map, which identifies qualified local hospitals and transport protocols for

stroke patients. The retrospective observational study shows an increase in the rate of patients receiving rt-PA thrombolysis (from 8.3% to 9.7%) and endovascular thrombectomy (from 0.9% to 1.6%). Therefore, the stroke map provides essential information for EMS workers to transport stroke patients and improve the rate of treatment for stroke patients (Ye et al.). Similarly, A study from Toronto states that the establishment of a PCI initiative enables collaboration between EMS, community hospitals, and hospitals qualified for PCI, which ensures that patients undergo electrocardiography within 10 minutes of arrival at an emergency department and lead to a net reduction in door-to-balloon time from 116 min to 90 min (Young et al.).

Systems-Level Innovation

Systems-level innovations are made at the organizational or management level. They maximize the use of existing resources and promote collaboration between different components of EMS. These innovations include the reallocation of ambulances, a collaboration initiative, and so on. Through systems-level innovations, the EMS system could achieve its maximum efficiency and bring out the best potential to save lives.

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Metrics for Successful EMS

Studies in this group analyze key components of assessing EMS quality, including factors contributing to a successful EMS. Using multivariable analysis and computational simulation, studies can determine key components contributing to successful EMS. EMS must recognize factors that influence the survival of patients in order to improve in these specific aspects.

One study provided valuable data on the survival rate of OHCA patients between 2006 and 2014 in Toronto. Among 25,826 patients that were treated by EMS for an OHCA, 11,727 (45%) were pronounced dead on the scene, 8359 (32%) died in the emergency department, 3640 (14%) were admitted to hospital but died before day-30, and 2100 (8.1%) were still alive at day-30 (Geri et al.). However, the survival rate is different in different countries. A study done by a group of researchers from Beijing Emergency Medical Center and the Capital Medical

University states that only 0.6% of patients survived to discharge, 1.5% of patients survived to admission and 2.4% of the patients had ROSC on the scene (Chen et al.).

There are several studies focused on CPR. A study from Poland found that the rate of ROSC was significantly higher when the CPR was initiated by a bystander, and that men were more likely to receive CPR than women (28% and 54% respectively). They also concluded that the rate of ROSC has no relation to the type of EMT that was sent to the scene (Czapla et al.). However, a study analyzing the data in Beijing stated that although more people received bystander CPR in cardiac arrest from 2012 to 2015 (from 7.1%-11.2%), the survival rate was nearly the same during this period (0.6% survived to discharge) (Chen et al.). A study from Australia focused on the effect of partial resuscitation (resuscitation starts but stops within 10 min) (Czapla et al.). Analyzing 34,849 OCHA cases from the Victorian Ambulance Cardiac Arrest Registry between 2002 and 2012, the researchers found that more than 1/5 of patients received partial resuscitation and the rate of partial resuscitation increased from 8.6% in 2002 to 18.8% in 2012 (Nehme et al.).

Traffic and Transportation is also an important factor that influences the effect of EMS. Another study done in South Korea analyzed how transportation infrastructure influences EMS response availability. Measuring the k-minute area coverage and the k-minute population coverage, researchers concluded that the EMS was greatly influenced by traffic (the average citywide reduction in area and population coverage values when there is traffic are at 34.2% and 33.8%, respectively) (Cho et al.). Another study from the UK analyzed the Prehospital determinants of successful resuscitation after traumatic out-of-hospital cardiac arrest (TCA) and non-traumatic out-of-hospital cardiac arrest (NTCA), concluding that although air ambulances can greatly reduce the time of transportation and are rarely influenced by the traffic, an air ambulance was associated only with survival to admission in TCA but not in discharge (Barnard Ebg et al.).

Technological Innovation

With the development of technology, more and more advanced technologies are applied to EMS, helping the EMS system become more efficient. Although several technological applications in EMS are still in the testing phase, they show a significant advantage in delivering equipment and helping patients get early treatment. For instance, a randomized study from Spain evaluated the effect of telemedicine using Google Glass on cardiopulmonary resuscitation (CPR). Seventy two nurses were divided randomly into two groups, one with assistance from senior physicians through Google Glass, and one with no assistance from senior physicians. All of the participating nurses wearing Google Glasses successfully performed defibrillation, compared with 78% of nurses in the control group. The Google Glass group completed CPR 36.39s on average faster than the control group (Pérez et al.).

In addition to CPR, timely rescuing and AED accessibility are other factors influencing the survival rate of cardiac arrest patients. A recent cross-section comparison study from Italy highlighted the positive effect of using drones as assistance in mountain rescue, as the mean time

to locate the patient was 14.6 min in the drone-assisted intervention arm and 20.6 min in the control arm (Van Veelen Mj et al.). A pilot study from Sweden examining 14 eligible cases of AEDs delivered by drones in 2020, stated that 64% of drones arrived at the scene before the ambulances and showed a 1'52" advantage compared with ground ambulances in delivering AEDs with a 90% successful rate (Schierbeck et al.). Another study performed in Singapore proposes a model of redistributing ambulances called DES, which can result in a 5% reduction in the calls that cannot be reached within an 8-minute threshold (Lam Ss et al.).

Name of Study	Primary Authors	Content	Study Design	Group
Impact of city police layperson education and equipment with automatic external defibrillators on patient outcome after out of hospital cardiac arrest	Philipp Stein, Gabriela H. Spahn, Stefan Müller , Andreas Zollinger , Werner Baulig , Martin Brüesch , Burkhardt Seifert , Donat R. Spahn	The article evaluates the effectiveness of equipping city police with AED in saving cardiac arrest patients	Retrospective observational study	Personnel
The development of community paramedicine; a restricted review	Brendan Shannon BEmergHealth(Pmed)(Hons), Georgette Eaton MSc, Chelsea Lanos BSc, MSc, Matthew Leyenaar PhD, Mike Nolan MA,	The article evaluates the effect of community paramedic in both saving patients and reducing the EMS system's stress	restricted review	personnel
Implementation of a medical command and control team in Switzerland	Pierre-Nicolas Carron , Philippe Reigner, Laurent Vallotton, Jean-Gabriel Clouet, Claude Danzeisen, Mathias Zürcher, Bertrand Yersin	The article propose a model for command and control group and states its advantages	Descriptive analysis	personnel
Helicopter Critical Care Retrieval in a Developing Country: A Trauma Case Series from Bhutan	Charles Haviland Mize, Egmond Samir Evers, Lhab Dorji, and Ken Zafren	The article reviewed the effect of a helicopter critical care group from Bhutan	Data analysis, multivariable generalized linear models	personnel
Interfacility patient transfers in Lebanon-A culture-changing initiative to improve	Mazen El Sayed , Rayan El Sibai , Rana Bachir, Diana Khalil , Maggy Dishjekenian , Lili Haydar , Rosanne	This study examines transfer characteristics after establishing a transfer center in a tertiary care center in	Descriptive analysis	Systemic level innovation

patient safety and outcomes	Aguehian , Ramzi Mouawad	Beirut Lebanon, and identifies predictors of success in patient transfers		
Shenzhen stroke emergency map improves access to rt-PA for patients with acute ischaemic stroke	Shisheng Ye, Shiyu Hu , Zhihao Lei , Zhichao Li , Weiping Li , Yi Sui , Lijie Ren	The study propose a PCI map that could be used to increase the efficiency of transporting stroke patients	Retrospective observational study	Systemic level innovation
Toronto Heart Attack Collaborative: An Administrative Model That Facilitated a Successful City-Wide Integration Initiative	Justin Young Barry McLellan Marnie Escaf Vladimir Dzavik	This article provides a description of the administrative model that enabled a city-wide integration effort in Toronto	Provides a description of the administrative model	Systemic level innovation
Healthcare costs and resource utilization associated with treatment of out-of-hospital cardiac arrest	Guillaume Geri , Damon C Scales , Maria Koh , Harindra C Wijeysundera , Steve Lin , Michael Feldman , Sheldon Cheskes , Paul Dorian , Wanrudee Isaranuwatchai , Laurie J Morrison , Dennis T Ko	The research evaluates the cost of health care during different stages of EMS	Data analysis, multivariable generalized linear models	Metrics for successful EMS
Trend in survival after out-of-hospital cardiac arrest and its relationship with bystander cardiopulmonary resuscitation: a six-year prospective observational study in Beijing	Yuling Chen, Peng Yue, Ying Wu, Jia Li, Yanni Lei, Ding Gao, Jiang Liu & Pengda Han BMC Cardiovascular Disorders	The study analyze the database from Beijing EMS and verify factors associated with successful EMS	Prospective observational study	Metrics for successful EMS
Factors associated with return of spontaneous circulation after out-of-hospital cardiac arrest in Poland: a	Michał Czapla Marzena Zielińska,corresponding author, Anna Kubica-Cielińska, Dorota Diakowska,	Analyzing the EMS data, the study separates several factors associated with a successful EMS	Analyzing of the medical record	Metrics for successful EMS

one-year retrospective study	Tom Quinn, and Piotr Karniej			
Using a cardiac arrest registry to measure the quality of emergency medical service care: decade of findings from the Victorian Ambulance Cardiac Arrest Registry	Ziad Nehme , Stephen Bernard , Peter Cameron , Janet E Bray , Ian T Meredith, Marijana Lijovic , Karen Smith	The study report the change in quality of the EMS over the past few years	Logistic regression and multilevel modeling.	Metrics for successful EMS
Characterizing the influence of transportation infrastructure on Emergency Medical Services (EMS) in urban area—A case study of Seoul, South Korea	Jungwoo Cho, Data curation, Formal analysis, Investigation, Resources, Software, Visualization, Writing – original draft,1 Myoungsoon You, Resources, Validation, Writing – review & editing,2 and Yoonjin Yoon, Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing1,*	This study focus on the effect of traffic infrastructure on EMS efficiency and effect how traffic influence EMS	Computer simulation	Metrics for successful EMS
Prehospital determinants of successful resuscitation after traumatic and non-traumatic out-of-hospital cardiac arrest	Ed B G Barnard 1 2, Daniel D Sandbach 1, Tracy L Nicholls 3, Alastair W Wilson 1, Ari Ercole	This article evaluates the effect of several EMS practices on rescuing traumatic and non-traumatic out-of -hospital cardiac arrest.	Univariate descriptives and multivariable analysis	Metrics for successful EMS

Randomized clinical simulation designed to evaluate the effect of telemedicine using Google Glass on cardiopulmonary resuscitation (CPR)	Nuria Pérez Alonso 1, Manuel Pardo Rios 1, Laura Juguera Rodriguez 1, Tomas Vera Catalan 2, Francisca Segura Melgarejo 3, Belen Lopez Ayuso 4, Carolina Martí Nez Riquelme 5, Joaquin Lasheras Velasco 4 6	This experiment evaluates the effect of using Google Glass on CPR	Randomized study	Technological innovations
Drones reduce the treatment-free interval in search and rescue operations with telemedical support - A randomized controlled trial	Michiel Jan van Veelen 1, Giulia Roveri 2, Anna Voegele 2, Tomas Dal Cappello 2, Michela Masè 3, Marika Falla 4, Ivo Beat Regli 5, Abraham Mejia-Aguilar 6, Sebastian Mayrgündter 7, Giacomo Strapazzon 8	The experiment measure the effectiveness of using drones in mountain rescuing	Randomized controlled trial	Technological innovations
Automated external defibrillators delivered by drones to patients with suspected out-of-hospital cardiac arrest	Sofia Schierbeck 1, Jacob Hollenberg 1, Anette Nord 1, Leif Svensson 1, Per Nordberg 1, Mattias Ringh 1, Sune Forsberg 1, Peter Lundgren 2 3 4, Christer Axelsson 2 3, Andreas Claesson	This experiment evaluates the efficiency of using drones to deliver AED	Prospective clinical trial	Technological innovations
Factors affecting the ambulance response times of trauma incidents in Singapore	Sean Shao Wei Lam a, Francis Ngoc Hoang Long Nguyen a, Yih Yng Ng b, Vanessa Pei-Xuan Lee c, Ting Hway Wong d, Stephanie Man Chung Fook-Chong e, Marcus Eng Hock Ong	The study examines factors associated with the efficiency of delivering EMS and also propose a model that can redistribute ambulances which reduced the respond time	Retrospective study	Technological innovations

Fig 2: A summary of articles included in review

Discussion

This review examines critical technologies and innovations employed by EMS systems around the world across4 categories, including innovation in personnel, systematic innovation, metrics of successful EMS, and technological innovations. This section considers the effect of those innovative practices and presents potential ways that the United States could apply to achieve those innovations.

The United States could include more lay people in the EMS system, leveraging their large population.rained citizens can shorten the time between an emergency and the administration of first aid. As shown in the data, training other municipal workers, such as the city police force with basic life-saving strategies such as CPR and the use of AED could substantially increase the rate of survival for patients with emergency diseases (Shannon et al.). The United States could also train firefighters, building administrators, taxi drivers, and other lay people who have a high possibility of being present in   an emergency. Other studies also show that bystander CPR could improve the survival rate for cardiac arrest patients, either directly or indirectly (Czapla et al.). In this way, when an emergency happens, bystanders can provide immediate help and catch the best opportunity to save the patient. To achieve this goal, governments, and EMS centers could manage free training and send out ads to improve people's first aid awareness and skills. In addition, the rate of females receiving CPR during cardiac arrest is substantially lower than that of males, so the United States could put more effort into guiding people performing CPR on females. Furthermore, the United States could also develop community paramedics. These lay people can use their spare time to be on duty, and serve the community providing medical care to basic and non-emergency patients. Research has shown that community paramedics can reduce unnecessary EMS calls and save a lot of money for local governments (Shannon et al.). The United States could select people from community fire departments or police departments to form community paramedic troops.

The United States could also establish special emergency groups in each region, such as a critical care group which consists of advanced paramedics or physicians who can perform advanced life support to those people suffering from severe or life-threatening conditions such as trauma or cardiac arrest (Mize Ch et al.). If equipped with helicopters, they could perform rescue operations in remote places and save time compared with ground ambulances (Cho et al.). Since the lack of advanced paramedics and physicians relative to EMTs, the United States could distribute limited numbers of critical care groups in different first-aid centers or central hospitals. Once a major emergency event happens, such as a cardiac arrest or trauma, the nearest critical care group can be activated and get on to the scene using a helicopter. In addition, the United States could establish a command and control group at each EMS region. These groups would consist of people who are in charge of the overall organization in an extensive-casualty emergency and their mission would be to ensure the efficiency of distribution of EMS forces. This group would be the headquarters that organizes the rescuing during a huge emergency

incident (Carron Pn et al.). Consisting of one physician and one advanced paramedic, the command and control group could lead the rescuing and provide essential guidance to the frontline first responders. They could also play an important role in communicating with hospitals and other public emergency departments, which would make the whole rescue process more efficient and effective. The United States should consider the density of this type of group in each region, and select personnel to form the special teams. The United States could establish these groups by selecting experienced first responders and physicians from EMS and hospitals to form this special team. Challenges to implementation include engaging qualified candidates in the recruitment process and managing communication between EMS and hospitals."

Further, The United States should set up a channel for communication between different medical institutions. Each region can set up a PCI map, containing information about the hospital that could perform PCI and some basic operation guide for front line EMTs, and create direct contact between ambulances and PCI balloon rooms. In this way, when the ambulance receives a stroke patient, they can know which institution they should send the patient to and they can inform the PCI hospital so that the hospital can be fully prepared. As soon as the patient arrives at the hospital, necessary examinations can be carried out and the patient can be sent into the balloon room as soon as possible (Young et al.). The United States could also set up a system between EMS and the traffic department, since traffic is one of the determining factors affecting the time constraints of providing first aid. The area that an ambulance could cover in a limited amount of time is reduced substantially when the traffic condition worsens (Cho et al.). In those critical and emergencies, an ambulance could contact the traffic department to help it disperse traffic, such as turning the traffic light from red to green, to help the ambulance arrive at the scene earlier. The United States could also suggest navigation companies use GPS to alert other vehicles to keep the road clear (e.g. the navigation app could pop out windows on the screen when it detects that an ambulance is following behind the vehicle).

The United States could benefit from technological innovation in the EMS system. With the advanced technology both in the United States and outside the United States, EMS systems can make great improvements in reducing the time and increasing the quality of services (Schierbeck et al.). For example, the United States could consider using drones to deliver AEDs. According to the American Heart Association, every minute delay in using an AED decreases the rate of survival for cardiac arrest patients by 10%. Because of uncontrollable traffic, ground ambulances sometimes cannot arrive at the scene on time. Furthermore, the United States can also equip the first responders with Google glasses, which can enable physicians to give remote guidance to the first responders. The physician who is sitting in front of the screen in the control center or hospital could see live video from the scene, using audio and AR projection, the nurse will not only listen to the instructions but also see instructions on the screen. Research has shown that Google glass can reduce the time it needs for the first responders to finish CPR and the time it takes for them to deliver defibrillation (Pérez et al.). Although these innovations are in the testing phase, and inventing or testing costs money and time, these efforts are worth it because the applications of those technological innovations could potentially save more lives. The United

States could also invest in cooperation between technological companies and EMS systems so that the company can focus on the technological parts while the EMS could provide useful revision and testing of the product.

The United States should also perform an investigation into the cost of EMS. Over 71% of ambulance rides result in surprising bills, and many EMS services are not reimbursed. This could be attributed to the unclear real cost of providing EMS. Like Toronto, the United States should investigate the cost of EMS in order to provide a more clear and accurate reference for the insurance company to reimburse (Geri et al.).

Strengths and Weakness

A strength of this study is its wide scope. The review is supported by 400 abstracts that were screened and synthesized into 4 unique themesBecause the research scope is wide, not all the recommendations can be feasibly adapted to a local EMS system. For example, not all the EMS services in the United States can use helicopters to send out critical care groups and transport patients. Some of the successful EMS practices listed in the data section are from countries that have a different context than the United States, so they have to be localized when applied in and adapted to different regions of the United States.

Another limitation of the work is that a scoping (as opposed to a systematic) framework was utilized to classify articles. The research includes most of the articles about successful EMS practices and researchers related to this. However, in the absence of rigorous data analysis, some of the criteria and collecting processes of the data may be different among different articles.

Additionally, only one reviewer screened articles, allowing for possible bias. Some contrasting results and conclusions are contained in the data section and, because of the limited number of selected articles, this research cannot conclude which one is correct. Further research needs to be done to lead to a more solid and persuasive conclusion.

Future directions

In the future, more concentrated systematic reviews could be performed on specific or more targeted regions. In light of these innovative EMS practices abroad, the US government could invest in research to evaluate the effectiveness and the efficient allocation of all innovative EMS resources. For example, the researchers could equip an EMS center in the United States with AED drones, and perform a systematic review comparing their efficiency at delivering AED and that of traditional ground ambulance or bystanders. Financial problems also need more attention from future research, which could investigate the feasibility of applying those innovative practices and the change in finance. This will provide reference to the insurance company and the government to reimburse and give funds. Overall, more research could be done investigating the factors associated with successful EMS under the context of the United States. For example, using the data collected by the EMS system, researchers could perform data analysis to explore the factors that influence the results of EMS delivery. Additionally, some research could be done on the policy and appropriation, including investigating the real cost of

EMS and how EMS should be reimbursed. In this way, the EMS system can have a more clear direction for making improvements.

Conclusion

This review analyzed the status quo of the United States EMS system, then used scoping review best practices to consider many successful EMS practices around the globe. It provides recommendations for the United States EMS system and identifies future research directions that can be done in the United States.

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Prescribing Change: Exploring the Efficacy and Implications of Medical Malpractice Tort Reform By Diya Bhaireddy

I.   INTRODUCTION
A. Medical Malpractice and Tort Reform Defined

In modern society, civil lawsuits have become an increasingly common means of seeking justice and compensation for harm suffered. While the legal system serves a vital role in holding individuals and corporations accountable for their actions, it is not immune to criticism. Tort law is especially susceptible to these criticisms; one of its most common loopholes being with patient-plaintiffs commonly losing the legal right to full recovery in a medical malpractice lawsuit, and the systemic favoritism toward defendant-physicians.

The legal process pertaining to medical malpractice can be extremely demanding, both for the plaintiff and the defendant. Medical malpractice occurs when a healthcare provider exhibits negligence in care, resulting in patient injury or death. In such instances, the harmed patient (or their survivors) may pursue legal action seeking monetary compensation for their harm. The types of harm are designated as either economic or non-economic damages. Non-economic damages are difficult to quantify, because they concern categories such as pain, emotional anguish, humiliation, reputational damage, loss of enjoyment of activities, and other non-economic matters. It can be difficult to convey the magnitude of these struggles to a jury. From an ethical standpoint, it is disputed whether it is possible to put monetary value on emotional distress. (Justia n.d.)

Tort reform seeks to address perceived flaws in the civil justice system, aiming to strike a balance between ensuring access to justice for victims and preventing excessive litigation that may hinder economic growth. Proponents of tort reform argue for measures designed to curtail perceived abuses within the legal system. These measures often target two key areas: limiting damage awards and capping attorney fees. By imposing limits on non-economic damages, tort reform seeks to address the issue of jury awards that may be disproportionate to the harm suffered. Additionally, tort reform proponents argue that by reducing attorney fees, particularly in contingency fee arrangements, the incentive for lawyers to pursue baseless claims diminishes, discouraging frivolous litigation.

Opponents of tort reform argue that these measures may infringe upon individuals' access to justice and restrict their ability to seek redress for genuine grievances. They assert that limiting damage awards may disproportionately harm victims with severe injuries or suffering, as it fails to account for the subjective nature of non-economic losses. Critics also claim that imposing restrictions on attorney fees could dissuade competent lawyers from representing those with valid claims, leaving the most vulnerable at a disadvantage. Furthermore, opponents argue that stringent procedural requirements may deter victims from pursuing legitimate cases, as they face additional hurdles to their day in court. (Andrus Wagstaff n.d.) (Bryston Gallegos 2017, 17)

B. Thesis

From the perspective of a young adult analyzing tort reform with new eyes, the purpose of this paper is to consider the objectives of tort-reform policy, to assess the efficacy of non-economic damages caps in effectuating intended outcomes, and to provide alternative solutions that respect plaintiff-patients' individual rights while acknowledging the societal need for physicians. This paper has been written to offer clarity into the competing interests and arguments, looking into cases of patients who have filed claims of malpractice, and the constitutionality of tort statutes. Society has an interest in preserving individual rights, including those of patients to litigate claims of negligent harm, while also keeping society's need for physicians at a manageable level.

II.   DEFINITION AND TERMS OVERVIEW

Medical malpractice is a type of personal injury case that arises when a healthcare or medical professional's negligent care inflicts injury or causes death to a patient. In legal terms, the party bringing the case to legal action is called the plaintiff, and the party trying to defend themself is called the defendant. In the context of torts, "injury" describes the invasion of any legal right, whereas "harm" describes a loss or detriment in the fact that an individual suffers; both of these are relevant to malpractice. (Cornell Law School LII n.d.)

A tort is an act or omission that gives rise to injury or harm to another, and amounts to a civil wrong for which courts impose liability. Torts can result from negligence, and can also be intentional. In the case of medical malpractice, negligence means improper care from a physician/health provider; and although it is rare, physicians can also harm a patient intentionally, perhaps with a motive of the patient requiring continued and costly care. While tort laws in each state are mostly similar, their technicalities are defined by the state's government. In some states, these laws are partial to the physician-defendants. This is at the heart of the tort reform conversation. (Cornell Law School LII n.d.) For several decades, the topic of tort reform has ignited passionate debates, pitting proponents of stricter regulations, such as monetary caps on what a plaintiff may be awarded, against those advocating for a more lenient approach, giving more empathy to plaintiffs for their suffering through abundant monetary awards.

A tort has four elements: duty, breach, injury, and causation. These terms follow as is: The defendant had a duty to the plaintiff, the defendant breached the duty, the plaintiff suffered an injury, and the defendant's breach was the cause of the injury. In evaluation of cases, these four elements are required to establish liability. Where a cause of action is established, damages may be awarded to the party who brought forth the case. Compensatory damages are awarded to the plaintiff, for any suffering or losses to "make them whole." These types of compensatory damages include economic and non-economic damages. As said before, economic and non-economic damages are awarded when physical ailments or detriments prevent one from living their life and when someone is emotionally or mentally distressed, respectively. There is also a special type of non-economic damage which a spouse may be able to recover, called loss of consortium. (Cornell Law School LII n.d.) (Miller and Zois n.d.)

Tort reform affects plaintiffs and defendants differently. A result of tort reform is the continued pursuit of trying to make it more difficult for victims of personal injury cases to receive damage awards. Supporters of tort reform argue that it helps reduce frivolous lawsuits, lowers medical malpractice insurance premiums, and encourages economic growth by limiting the financial risks associated with litigation. On the other hand, critics of tort reform argue that it can restrict access to justice for injured individuals, limit their ability to seek fair compensation, and undermine the deterrence of negligent behavior by defendants.

In many states, there are limits on how much can be awarded in damages in medical malpractice cases. These limits are called damage caps, and the legislature determines these limits. For example, the cap in Massachusetts for non-economic damages for medical malpractice is limited to $500,000. It is important to note that in most states, there is no cap on non-economic damages in general personal injury cases, but there is a cap on non-economic damages in medical malpractice cases. (Percy Law Group, PC 2022)

III.   A BACKGROUND ON TORT REFORM

Tort reform is ever changing, as its basis rests on the changing of laws. But its history is important to understand in order to comprehend its position today. Tort reform goes back as early as 1910, and since then, there have been a couple substantive reforms. This brief overview will cover two of the reforms pertaining to medical malpractice; worker's compensation and comparative negligence. (White 1987, 1265) Towards the beginning of tort law reform, plaintiffs were favored; but, more recent trends have shifted the benefits towards defendants.

A. Worker's Compensation

Back in 1910, New York State passed the state's first worker's compensation statute. This statute shed light on the hardworking individuals undertaking dangerous jobs in the industrial economy. Railroads were an example of one of those booming industries. Railroads were the first mode of transportation of such efficiency and speed, and required intensive labor. When workers were involved in wrecks and injured, this affected more than just the workers–it included passengers, operators, and fellow employees.

With current laws in place, as well as the frequency of these accidents, they seemed to be inevitable. The workers themselves were actually least likely to receive any compensation for their injuries. The only way in which they would be compensated was if they presented proof of their employer's negligence, and only if the worker himself had not been negligent in his own job. The worker could not recover if the injury was caused by a fellow employee, which was unfortunate, given that this was the most common mode of injury. With this, the incentive to work these dangerous jobs was decreased, and to keep the demand high, oftentimes employers would instate private contracts with employees which assured compensation for them in the event of work-related injuries.

However, there were some significant changes to tort law with the worker's compensation statute. The statutes no longer included fault as a basis of recovery. Previous to

when workers could only receive compensation with proof of negligence, they could now receive compensation for injuries regardless of who had been negligent. The second change, and possibly even more substantial, the statute removed "causation as a prerequisite for liability." It did not matter how a worker had been injured in employment; if a worker was "'within the scope of employment'", they were eligible for recovery. (White 1987, 1272)

In improved worker's compensation, the fault principle stated that liability is not just liability without fault, but also without defenses. This meant that it was not very easy for the employer to escape liability, as the act of being involved in employment was enough[1]. However, this legal doctrine was not accepted by all. In 1914, Jeremiah Smith expressed his opinions in an article in the Harvard Law Review, arguing that the rule of liability adopted in worker's compensation (liability for damage irrespective of fault) contradicted the fundamental common law and the requisites of a tort itself. Smith argued that the fundamental common law includes that there must be fault on the part of the defendant.

A year earlier, two judges adopted arguments similar to Smith's in the *Ives v. South Buffalo Railway* case. Earl Ives was injured during the course of employment, and sued his employer South Buffalo Railway Co. The case was filed in state court, and appealed once. Both judges agreed that the employer should have some responsibility in accidents occurring during employment, in order for the injured employee to be awarded damages. However, the more pressing concern in the Ives court was that worker's compensation took property from employers without "just compensation." Plaintiffs were receiving recoveries and taking money out of employers pockets with no true evidence of negligence. The *Ives* decision regarded this as unconstitutional—"the taking of property from person A and giving it to B"—and that it could not be done at the state or at the federal level.

At the start of worker's compensation legislation, tort law was not defined clearly, and many court decisions were made by precedent, meaning they were decided not based on any statute but by facts and reasoning and reference to earlier case law. Prior to the *Ives* decision, fault for liability was not required, but after this case, the system was reoriented to prevent assets being taken from innocent employers. The bottom line for the change in the fault principle was the injured party having "no means of accountability," and so any fault of the worker was taken into further consideration.

B. Comparative Negligence

Comparative negligence is a tort principle used in court to reduce the amount of damages that a plaintiff can recover in a negligence-based claim. Damages are awarded to the plaintiff based on the degree of fault in a case. Comparative negligence systems first came into the conversation through means of literature in the 1920s and 30s, and started to receive vocal

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[1] This type of reasoning, strict liability, is also seen in product manufacturers. It is difficult to find proof of negligence in cases like these. The *res ipsa loquitor* doctrine, meaning "the thing speaks for itself", had already amounted to the strict liability principle. Also, the manufacturer was "in the best position to minimize the risk of harm and loss due to product related injuries" partly because the manufacturer is responsible for product design and the integrity of actual manufacturing.

support in the 1950s. But the concept of comparative negligence was not actually reflected in law until the 1970s, which is also the time recognized today as when tort reforms took off and each state started to make their own laws. There were responses of annoyance that the tort law system had been reformed again. Some doubts of the system from a law? student note included "'its lack of definiteness, the difficulty of the jury in apportioning damages, the impossibility of enforcement in the courts, the openings for fraud, etc.'" (G. Edward White 1987, 1285)

Comparative negligence was so different from past reforms in the way that it quantified the degree of negligence. Courts began this in 1932 by using the terms "slight," "ordinary," and "gross" in a sense of legal terms to assess damage, and then attempted to make mathematical assessments to the degree of negligence displayed by one party as well as the other (in a scenario such as a workplace environment). However, responses to this approach from opponents of the reform called it absurd, needing no exposition. (G. Edward White 1987, 1295)

C. MICRA

In the 1970s, medical malpractice tort reform began to surface in states, when each state instituted their own damage caps. Concerns about plaintiffs receiving exorbitant jury awards, even after fault was no longer included as a basis of recovery, gave rise to efforts to help the defendant-physicians, enacted into California law as the 1975 "Medical Injury Compensation Reform Act" (MICRA). This act aimed to lower malpractice insurance premiums for healthcare providers by decreasing their potential tort liability. By lowering the malpractice premium cost for healthcare providers, insurance coverage became accessible to them.

The constitutionality of MICRA was challenged in the 1970s and 80s, but passed as constitutional under rational basis review.[2] It is still mostly in place in California but has undergone updates in 2022. (Wikipedia n.d.) (Institute for Legal Reform n.d.)

IV.   OPPOSING PERSPECTIVES

A. Tort Reform Disincentivizes Improvements in Safety

Opponents of tort reform argue that tort reform does not allow for healthcare to improve safety or assure patients that they are being properly cared for. Hospitals, doctors, and medical malpractice insurance companies can continue questionable practices without consequences. For example, in the case *Condon v. St Alexius Medical Center*, Condon suffered a stroke caused by negligence from the physician-defendant, cutting the main artery supplying blood to her brain. The judge awarded Condon $3.5 million total in damages, $2 million in economic and $1.5 million in non-economic. However, the defendants brought to the court's attention North Dakota's statutory limit of non-economic damages of $500,000.

Condon's attorney argued against the cap, arguing that it discriminated against plaintiffs who were "unable to establish large economic loss—particularly children and stay-at-home parents" (Gallegos 2018, 19). Her attorney argued that this cap indeed benefited physicians the

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[2] The rational basis test is a level of review that determines how a court will approach analyzing the constitutionality of a law. Rational basis is the lowest level and under rational basis, the person challenging must prove that the government has no legitimate state interest in the law, or that there is no reasonable link between the interest of the individual and the challenged law. (FindLaw)

most: "The greater the harm caused by the negligent doctor, the greater the discount" (Gallegos 2018, 20).

The judge denied the defendants' motion to reduce the award, stating that it did not pass the rational basis test as there was no evidence of a cost crisis for medical malpractice insurance in North Dakota (which may have constituted a legitimate state interest). The judge found no convincing reason as to how a $500,000 cap would improve the legislature's goals of increasing healthcare access, improving the quality of care, and maintaining insurance premium prices at a reasonable level.

Under tort reform law, physicians can continue to give negligent care in the case of malpractice, because the law is on their side, and one could even go as far to say that it is cheaper to kill the plaintiff instead of just injure them. Laws in favor of physicians and other healthcare providers limit plaintiffs' ability to receive quality representation. This fear is especially present due to the payment terms under which most malpractice and personal injury attorneys work: a contingency fee basis. A contingency fee means that a lawyer only receives compensation if and when a plaintiff wins a case, and their fees are also a percentage taken from the awards. (Andrus Wagstaff n.d.) Without assurance of good legal support from an attorney, then there is not much hope for those suffering as a result of medical malpractice negligence.

B. Pro-Business Efforts Influence Jury Attitudes

As mentioned above, trends that favor tort law have had a massive shift. From the plaintiff liberation in worker's compensation, to the opposite treatment in comparative negligence; as the economy has grown, interests have shifted to corporations. In 1970-1980, there was a large increase in medical malpractice insurance premiums. Physicians-defendants use this occurrence as a call to action for tort reform. However, this argument persists, whether or not there is actually a 'crisis' at hand of premiums rising, continuing to restrain plaintiffs' ability to fully recover financially in their legal cases.

Defendant lawyers believe that jurors are uninformed of the contents of a corporation. They believe that jurors have "naive and unrealistic expectations of business people, their lack of experience and understanding about corporate affairs, and the American tradition of sympathizing with the underdog all place the corporate defendant at a disadvantage in the courtroom." (Hans 1998, 329) A wealthy corporation and an injured plaintiff are not in the same financial position. Some critics believe that jurors have awarded substantial recovery to plaintiffs simply out of spite for booming enterprises; for their insurance companies have "deep pockets."

However, as a whole, commentators that have overseen the broader conversation of business treatment in courts have actually been benefiting towards business; "societal desires to stimulate the economy [have led] to generous treatment of business corporations in the evolving tort system." Corporates are what are referred to as "repeat players" in civil litigation. They are often involved in legal processes, and they have the knowledge and skills to play to their advantages. As much as Americans like to support the underdog, they are also partial to "cultural values underlying a capitalist economy, such as the Protestant work ethic, personal ambition, and

competition". From a *Business Week* national survey, many are much more confident in the way that major corporations are functioning rather than Congress. (Hans 1998, 332)

In regards to tort reform, these trends do not help plaintiffs. Businesses continue to gain a higher standing from consumers needing services, and insurance premiums rising give them a credible reason to argue so. Plaintiffs' safety in economic and non-economic damages are not assured, and furthermore, constitutionality is in jeopardy.

V.   LEGAL BASES AND RATIONALES

Constitutionality differs based on who is being discriminated against, but the topic has been raised concerning plaintiffs especially. Some plaintiffs believe that non-economic damage caps are unconstitutional. The states with damage caps set them at a value much lower than what plaintiffs who suffered a catastrophic injury should receive. Some plaintiffs believe that they should recover a substantial amount corresponding to the amount of trauma and pain they sustained; due to the fact that some injuries have altered patients' lives forever, and even money cannot bring back a cognitive ability or bodily function.

A.   Non-Economic Damage Caps Discriminate Against Plaintiffs Who Cannot Establish Loss

1.   Nestlehutt v. Atlanta Oculoplastic Surgery

To put this into perspective, the Georgia Supreme Court affirmed a Georgia trial court that had struck down a 2005 cap on non-economic damages in a case put forth by Beth Nestlehutt. Beth Nestlehutt worked in real estate with her husband. Noticing that her clients were moving towards younger agents, she wanted to get some surgical cosmetic work to make herself look younger. She met with Dr. Harvey P. Cole of Atlanta Oculoplastic surgery, and he recommended that she get a full face lift, although she was 71 at the time. (Georgia Watch 2010)

Due to her age and the risks of the surgery, the blood flow in Nestlehutt's face was compromised. Her skin began to fall off and die. Her face was extremely disfigured, and due to her appearance, her career in real estate was also in jeopardy. Her case was first heard by the Georgia trial court, and the verdict was in favor of Nestlehutt. With recovery for past and future medical expenses and Nestlehutt's affected quality of life, the judge awarded $900,000 in non-economic damages. This surpassed the $350,000 cap instituted in 2005.

In the lower court, the cap was ruled unconstitutional. This was because a statute capping a jury's verdict violated the plaintiff's constitutional right to a trial by jury. The decision was appealed by the defendants to the Georgia Supreme Court. In 2009, the Supreme Court agreed with the lower court judge's ruling that the cap was unconstitutional. Originally, the cap instituted in 2005 did not assure patient-plaintiffs their rights and safety, and it was not a priority for the legislation at all. Nestlehutt lost much more than her physical appearance. She was the face of her business, and she lost her way of making money due to her ailment, an economic loss. But beyond that, Nestlehutt lost her identity, self-confidence, and ability to communicate with others; all non-economic losses. By striking down the cap, "the promise of justice for all

and the rights of all Georgians—young and old, rich and poor—to access the courts" was restored. (Georgia Watch 2010)

2. Condon v. Alexius Medical Center

Non-economic damage caps "discriminate against plaintiffs who cannot establish large economic loss." After suffering malpractice and being denied redress, plaintiffs cannot continue with their way of life as it was before, and therefore cannot properly cover any future medical expenses. For example, in *Condon v.s. Alexius Medical Center*; Chenille Condon, a 35 year old woman, suffered a stroke from negligently performed surgery. The physician, Dr. Allen Booth, had cut the main artery supplying blood to Condon's brain, leading to a stroke and paralysis. Condon's brain condition was also expected to deteriorate over time.

The judge awarded $3.5 million total in damages, $2 million in economic and $1.5 million in non-economic. However, Dr. Booth tried to reduce the verdict pursuant of current non-economic damages to North Dakota's statutory cap on non-economic damages, which was $500,000. Condon argued against the cap, arguing that the cap violated the state's constitutional guarantee of equal protection, as it discriminated against citizens who could not establish large economic loss, such as children and stay-at-home moms. She also argued that the cap protected physicians from having to pay rising insurance premiums: "The greater the harm caused by the negligent doctor, the greater the discount." (Gallegos 2018, 19)

Constitutionality is not acknowledged without concerns of it initially raised. Condon believed that she was not rightfully compensated in her case, which is why she brought legal action questioning constitutionality. But, unfortunately for Condon, the North Dakota Supreme Court held that the cap was not unconstitutional and remanded the case back to the district court for a reduction in non-economic damages consistent with the state statute. There was no "fundamental or important substantive interest" to a legitimate government concern. (Gallegos 2018, 20)

3. Gourley vs. Nebraska Methodist Health System

Lastly, in 2003, the Gourley family brought action against the Nebraska Methodist Health System and Nebraska Methodist Hospital (collectively Methodist Hospital). Lisa Gourley, a resident of Nebraska, was receiving prenatal care from Nebraska Methodist Hospital. Lisa was unknowingly suffering from bradycardia, a decrease in heart rate and lack of amniotic fluid. However, the doctors had failed to detect this, resulting in one of her twin boys being born with cerebral palsy and many other health complications.

Lisa and her husband filed a suit against Methodist Hospital. From the suit, the jury awarded the family $5,625,000. However, the Gourleys moved for a new trial, arguing that the court had made an error of entering a direct verdict. The district court reduced the award to $1,250,000, on account of Nebraska's cap on damages. The final decision by the Supreme Court upheld the reduction of the award.

The Gourleys argued that the cap affected fundamental rights. They could not have rights to a proper jury trial, property, and medical care. The Gourleys argued that the cap affects a "suspect class": due to the fact that "plaintiffs with damages awards over the cap are 'saddled with disabilities.'" (Google Scholar 2003) Although Lisa Gourley still had a child that was healthy, her other son was suffering the consequences of negligence. The Gourleys would still have to pay thousands of dollars in treatment for Colin, as well as other concerns. The extent of the negligence should not be the only factor weighing in when awarding damages: the consequences from a lack of necessary damages should have equal, if not more, significance.

VI.   CONCLUSION

Throughout this paper, we have explored the various views of medical malpractice, history and trends of tort reform, and the potential benefits and drawbacks of its measures. It is clear that medical malpractice cases play a crucial role in holding healthcare professionals accountable for their actions and ensuring the quality and safety of patient care. However, the system has been criticized by defendants for its high costs and lengthy legal proceedings; implementing reform that does not support the needs of all involved.

Tort reform initiatives have been proposed as a means to address some of these concerns, aiming to strike a balance between providing fair compensation to injured patients while minimizing the negative impacts on healthcare providers and overall healthcare costs. By implementing caps on non-economic damages, proponents of tort reform argue that these measures could lead to more efficient and equitable resolution of medical malpractice claims.

On the other hand, critics of tort reform caution against potential limitations on patients' rights and access to justice. They stress the importance of preserving the ability of injured patients to seek appropriate compensation and hold negligent healthcare providers accountable, thus maintaining the integrity of the healthcare system.

As we navigate this complex landscape, it is essential to consider the diverse perspectives of stakeholders, including patients, healthcare professionals, legal experts, and policymakers. Striking the right balance between ensuring patient safety, fair compensation, and maintaining the healthcare system's functionality is a challenging task that requires thoughtful deliberation and evidence-based decision-making.

In the end, the pursuit of effective and just solutions for medical malpractice and tort reform requires a collaborative effort, drawing upon the expertise of various fields and a commitment to continuously improve the healthcare system for the benefit of both patients and providers.

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Entrepreneurial Marketing: From Idea to Billion Dollar Valuation by Maya Wen

Abstract

      This paper seeks to find the most effective strategies for startup companies to maximize their success. To do this, I will analyze some of the most successful startups in recent history and determine how their marketing strategies helped them expand their businesses. I will leverage company financial data to demonstrate the impact of various marketing strategies, and case studies to understand the objectives and actions within different marketing campaigns and other publicly available sources. The results of this research will be applicable to any entrepreneur looking to develop a successful marketing strategy for their company.

Introduction

      Every business starts somewhere. Even the most successful businesses, like Amazon, Starbucks, and Apple, were once small struggling startups. How did they become so successful? As a startup, companies first need to make their name renowned to the rest of the world. A company's initial marketing strategy is often key to its success. Once successful, companies can implement different strategies as established players in the space. Through well-planned marketing tactics and strategies, companies can rise to the top of the world, becoming exceptional leaders in their fields.

      In this research paper, I will explore the different strategies many successful companies have used to build their brands and gain recognition. First, I will review the tactics of three of the largest companies in their respective industries: Nike, Patagonia, and Uber. Nike is one of the largest sports and apparel brands, offering a large variety of sportswear and exercise products. Nike is easily identified by their world-famous slogan "Just Do It" and signature swoosh logo. Through leveraging several prominent athletic endorsements, they were able to attract and retain a much broader customer base. Patagonia is also a clothing brand. However, their brand is centered around a core belief in environmental justice. Patagonia is widely recognized for its ethical and sustainable approach to business. Since its founding, Patagonia has stayed true to these values and features them prominently in its marketing and brand growth strategies. The independence and freedom they give to their employees is also a unique, striking feature of their brand. The last brand featured in this paper will be Uber, one of the leading rideshare companies. While the idea of getting into a stranger's car was once a strange and foreign concept, today most people call an Uber without a second thought. Uber's unique way of marketing to both customers and drivers was a defining aspect of its growth and acceptance by the masses.

      These three industrial titans employed valuable marketing tactics to garner brand recognition and success, but their approach is not the only path to growth for new brands. Another avenue to achieve rapid growth is Shark Tank, a show where entrepreneurs can appear and attempt to earn an investment from prominent investors - the "Sharks". While an investment is beneficial, it is not the only way entrepreneurs benefit from appearing on the show. The benefits these founders and their startups receive from the show make it unique from any other

strategy, with evidence of several featured companies' sales skyrocketing after appearing on the show. Even companies that did not get investments, like Ring, were able to become extremely successful after the show aired. Other companies that did get investments, like Scrub Daddy and Bombas, were able to largely increase their profits with the influx of cash and new customers.

Through exploring the marketing strategies and resulting impact of the abovementioned companies, I hope to create an entrepreneurial marketing guide to support the growth of startups across all industries.

Nike

Nike was founded in 1964 by Phil Knight and his former track and field coach, Bill Bowerman (Meyer). Knight had toured a Japanese factory and became fascinated by the speed at which they created shoes. He partnered with them and created Blue Ribbon Sports, the original company name. In 1971, he split from the factory and changed their branding, with a new name and logo - Nike and their renowned swoosh. The company continued to expand after that, endorsing famous athletes such as Michael Jordan, creating a new line of basketball shoes, and creating their signature slogan, "Just Do It." As they grew, they broadened their range of shoes, acquiring several other shoe companies like Cole Haan and Converse. They also diversified their product offerings to include athletic, sports, and lifestyle apparel.

Nike is now one of the most recognized and valuable brands in the world, with a current estimated net worth of $155.36B ("Nike Net Worth"). With a large variety of athleticwear, streetwear, and equipment, Nike has been able to rise to the top of the sports and apparel industry. They increased their reputation with their brand image along with the image of their partners. Nike has strategically leveraged their slogan, logo, and athlete endorsements to grow their brand and dominate the global sportswear industry.

"Just Do It"

Nike knew that to expand their customer base, they had to change their branding strategy. They needed to not only connect with professional athletes but also a wider fitness audience. Their slogan first emerged when Dan Wieden, an advertising executive, heard about an inmate on death row who said "You know, let's do it" (Restrepo) This inspired Wiedan, who tweaked the phrase and made it one of the most well-known slogans in the world. Their slogan is memorable due to its simplicity and shortness. According to NBA feature writer Nick DePaula, the slogan was "approachable and vague enough that anybody could apply it to whatever it was they were trying to aspire to do." Their slogan targets anybody who wants to exercise, and encourages them to "Just Do It."

The Swoosh

Similar to their slogan, Nike's logo is highly recognizable; it's unique and easy enough to be easily identified. It was created by graphic design student Carolyn Davidson and, despite its relative simplicity, took approximately 17 hours to design. In 1971, Phil Knight paid Davidson

$35 for the iconic swoosh (Oliver). They eventually gave her 500 shares of stock, but to believe that the original creation of such an incredible logo cost $35 is incredible. Today, the Swoosh is valued at more than $26 million ("Nike Logo Worth"). Because their logo isn't as complicated as other companies' logos, it is easy for you to imagine Nike when you see the swoosh. This means that seeing the swoosh anywhere will lead you to think of Nike. This implicit association is key in securing new customers.

Athlete Endorsements

Along with smart branding, Nike's success can be attributed to strategic partnerships with world-renowned athletes. Nike has sponsored athletes from countless sports, spending around $1.5 billion on athlete endorsements. One of their most successful endorsements was with basketball legend Michael Jordan. In 1985, Nike and Jordan collaborated on a new line of basketball shoes - Air Jordans. In 2022, the Jordan brand passed $5.1 billion in revenue (Cuofano). Over 10% of Nike's profit comes from the Air Jordans line. This shows how important that partnership with Michael Jordan was for Nike's company. Endorsing a well-known athlete expands a company's consumer base, as supporters of those athletes will now associate them with Nike. Jordan also requested a percentage of all sales on Jordans, indicating that fans can support him and Nike by buying his shoes. Together, Nike's simple yet effective branding and partnerships with global athletes have been key to the company's success.

Patagonia

Patagonia is an outdoor clothing brand rooted in environmental justice and sustainability. In the 1950s, Patagonia founder Yvon Chouinard encountered an issue with the climbing gear he used; the gear was all single-use, forcing climbers to dispose of it at their climb sites (Biron). This was extremely wasteful, as you had to buy new gear each climb, and it also left unnecessary trash in the wilderness. To solve this problem, Chouinard learned blacksmithing and started creating his equipment. In 1957, he opened Chouinard Equipment, where he sold hand-forged, multi-use climbing gear. The more Chouinard climbed, the more problems - and solutions - he discovered. He expanded his business into clothing, selling rugby shirts which helped stop the slings from rubbing against their necks.

Values-Based Branding

As Patagonia continued to expand and grow in notability, Chouinard did not lose sight of his original belief that we should take care of the environment. In the late 2010s, Patagonia discontinued corporate-branded apparel after noticing that it was likely to be thrown away or unused after employees left the company. However, Chouinard continued producing branded clothing exclusively for companies with environmental initiatives. Patagonia's strong beliefs restricted some parts of the company, but Yvon Chouinard strongly believed that they should stick to their mission. During one particular Black Friday sale, Patagonia released an ad that read "Do not buy this jacket" (Patagonia). They did not want anyone to buy their clothing with the

idea that because it was on sale, it was necessary to buy. They only wanted people to buy it if it was truly needed. Furthermore, they had a repair policy in which if your Patagonia items were damaged, customers could return the item and the company would fix it. Instead of having a return policy where they would simply give customers a new one, Patagonia wanted to ensure that no clothing would be wasted. Patagonia creators and CEOs created an organization called "1% for the Planet." In it, they partner with other businesses and environmental organizations Patagonia refuses to part ways with their beliefs, no matter the outcome. However, their unique marketing approach did catch the eye of many environmental advocates (Paige), who were more likely to buy their products if they knew that it was going towards a good cause.

Complementary Product Offerings

Chouinard found initial success with his climbing gear. To grow and scale the business, he decided to diversify and expand his product offerings. Businesses need to recognize and respond to the evolving needs of their customers as they relate to their core competencies. To make the business a 'one-stop-shop' for customers, the release of additional, complementary products tailored to the needs and experiences of customers is vital. This also invites the possibility of broadening your consumer base. Patagonia expanded its suite of products to solve problems that Chouinard saw in his climbing career. If there was a problem with some of the equipment he used, he would remake it, find a better solution, and sell it. Recently, they've included selling duffel bags, snow clothing, and comfortable clothes. Now, there are hundreds of different Patagonia products for sale, including jackets, shoes, backpacks, climbing gear, and hats.

Employee Benefits

A successful company requires both happy customers and employees. Patagonia's employees are afforded many unique and desirable benefits. For example, there is a subsidized daycare facility located in the company's main headquarters building for all employees. This alleviates a financial and practical burden faced by many working parents. Furthermore, Patagonia emphasizes a healthy work-life balance, exemplified by Chouinard's surfing policy stating that "when the surf comes up, you drop work and go surfing" (Anderson). In an interview, Chouinard revealed his workers are given a unique level of autonomy. Their work culture is such that each employee acts as their boss. They are clear on what their main goal is, and it is up to the individual to decide on how and when to accomplish it. Patagonia customers are well aware of the company's positive corporate culture; knowing that employees are treated equitably, customers are more likely to continue to shop - and support - the company.

Uber

"I'll call an Uber." In today's world, the word "Uber" has become synonymous with cab, taxi, or car. While once a foreign word and concept - getting into a complete stranger's car to travel to a destination - Uber is now a mainstream staple in modern-day transportation.

Uber was founded in 2009 after Travis Kalanick and Garrett Camp were unable to find a taxi one snowy evening (Blystone). They noticed that it could be extremely difficult to find a taxi in less urban areas, and you would have to often wait a while to find one. They then came up with a solution: what if you could call a ride through your phone? At first, very few people were willing to trust the idea of getting in a stranger's car. To earn customers' trust, Uber leaned on a professional limo/black car service model to start. It was relatively high-end and led to strong initial success. However, the company wanted more. In 2012, they launched their now more popular section, UberX, a more casual and cheaper version of UberBlack. In 2015, they became one of the most valuable startups in history at $51 billion. As of April 16, 2023, Uber's market capitalization is an impressive $63 billion. Uber was the first ride service of its kind, coming before Lyft and establishing a strong position in the market. Because they were able to start around 3 years before Lyft, they managed to bring their market cap to over 15 times that of Lyft's.

Product Evolution

Ever since Uber was first founded, the company has grown exponentially. The founders quickly recognized the difficulty in gaining people's trust to use their service. They wanted to make a good impression on the public, and they knew that they needed to present themselves as high-end and elite to accomplish this. This led to the initial 'black car' concept; Uber required their drivers to have a certain black car, with the app originally targeted towards a wealthier consumer base (Main). With a desire to grow users, Uber then launched UberX, a lower-tier ride-share option intended for the general public (Knight). UberX provided drivers and riders with more flexibility and accessibility, as the drivers could use whatever car they wanted and the prices were more affordable. Today, UberX is the most popular ride-share service in the market (Kaczmarski).

However, Uber's services did not stop there. They continued to grow, releasing a new product called UberEats, which was focused on picking food up from restaurants and delivering it to customers to homes, apartments, or places of work. Uber noticed the popularity of third-party delivery services like Doordash, felt that it fell within their areas of strength, and managed to release their version in 2014. Uber knew how to adapt to any market changes and capitalize on the latest trends. With their ever-expanding service offerings, Uber's monthly users in the U.S. have increased to over 130 million people. Despite expanding their horizon, Uber has made sure to have their offerings still within their core competency: hiring drivers.

Dual-Target Advertising Strategy

To create the best company possible, Uber needed to ensure that they had good drivers that could attract customers and customers to create demand for new drivers. To attract drivers, Uber offered several incentives over other transportation-based companies. They decided to provide a larger pay than that of taxi companies. They also provided specific packages, such as

hourly wages, even if drivers had no customers (Solomon). This made it a lot easier for drivers to earn money if they worked in less-populated areas. Being paid an hourly wage, in addition to a fare percentage per ride, provides drivers with a more stable, reliable income. Additionally, Uber drivers had control over their working hours (Knight). They get to choose if they want to accept their passengers or not. This autonomy over their schedule led to a better perceived work-life balance and job satisfaction for drivers.

To attract customers, Uber knew that they had to be able to drive consistent demand. To do this, they offered a referral program, giving customers who referred friends to the app various benefits including future in-app discounts (Smoliar). According to a study done by the Harvard Business Review, customers are four times more likely to buy a product if their friend referred them (Minsky and Quesenberry). This is due to a greater established trust in a friend than in a company or advertisement. This understanding helped Uber grow their customer base, while also being a lot cheaper and more widespread than traditional advertising. Uber's digital marketing also proved to be an immediate strength. The app is simple and allows users to easily call a driver in most areas of the United States. It is a lot easier than hailing a cab and cheaper than renting a car. Furthermore, it's also more beneficial to the customers, as they can view their driver's ratings and choose to find a different one if they notice that their driver has a poor rating.

Shark Tank

Shark Tank is one of the most popular entrepreneurial shows on television. With around 10 different judges who have rotated over time, Shark Tank aims to help small startups establish themselves in the business world. While a strong and comprehensive marketing strategy can help propel a startup's growth, a significant financial investment and mass exposure can do the same. On Shark Tank, a panel of 4-5 judges decides whether they want to invest in a business after seeing their pitch. Startup founders who participate in the show can gain advice, investments, and attention from notable investors and viewers alike. But to what degree are the various benefits of Shark Tank helpful in the long run?

Shark Tank Benefits

Shark Tank can provide many direct and indirect financial benefits for participating startups (Barreto). The main benefit is that contestants can earn financial investments from the Sharks. This is extremely helpful, especially if they need some money to increase factory production, elevate their advertising, or generally improve their business. While investments can greatly boost the quality and quantity of products, they are also something to be wary of. Although contestants can get an investment, they need to give something back to the Shark in return. Most judges request a lifetime equity in the company, while others ask to buy the entire company. In addition to financial investments, contestants can also receive expert advice on their companies. All of the Sharks are experienced entrepreneurs in several different fields, making it advantageous to earn investments from certain judges based on their area of expertise. Even if contestants don't receive an investment, they can receive valuable advice that will help change

their startup for the better. Moreover, contestants can receive public attention from the over 6 million viewers who tune in to the show weekly. Even without an investment, founders are allowed to turn viewers into new customers. Indeed, a Shark's investment and endorsement certainly motivate viewers to learn more and possibly purchase the product.

Successful Companies

Scrub Daddy is one of the most successful companies that has competed on Shark Tank. Before their episode aired, Scrub Daddy was earning around $120k in retail sales annually. In 2015, they hit $50 million. In October 2023, their retail sales were at $670 million (Ammons). Although they were able to gain traction before they appeared on the show, their exposure was limited, making it hard to find new customers. Scrub Daddy founder Aaron Krause managed to secure time on the popular retail channel, QVC but the company still had yet to achieve mass-market popularity. Everything changed in 2012 when Krause pitched Scrub Daddy on Shark Tank and landed a deal with Lori Greiner worth $200k for a 20% equity stake. Immediately after the episode aired, they sold nearly 42,000 sponges in just 7 minutes. Scrub Daddy saw an explosion of traffic and sales on their website.

Most entrepreneurs who appear on Shark Tank do not receive an investment, but many of them still experience incredible success with their startups. Ring, originally called Doorbot, did not earn any investments from the Sharks. Ring's founder, Jamie Siminoff, shared that he "was pitching a dream out there." His idea hadn't been fully formulated, and not everything was complete. Because of this, no judges were willing to invest in the startup. Lori, one of the sharks, claimed that there was not enough differentiation in her doorbell for it to be marketed and sold at a higher price point.

Siminoff left the show feeling disappointed but stayed determined. He changed several aspects of his company, hoping to change it in a way that would become more successful. Siminoff refined his product and released it into the world. In 2015, celebrity entrepreneur Richard Branson was fascinated with the idea of the Ring. He invested over $20 million in the company, almost tripling its estimated value of $7 million (Bishop). After continued growth and success, Ring was acquired by Amazon. In 2018, Ring was valued at around $1.5 billion. Jamie Siminoff's original request on Shark Tank was $100k for a 10% stake. Had the Sharks invested in Ring, their share would've been valued at $150M today. Today, their products are sold in over 17,000 retail stores and are used in around 100 countries (Perkins).

Conclusion

Nike, Patagonia, and Uber each had a unique, yet successful, approach to growing their brand and consumer base. Nike chose to use specific brand marketing, centering around their logo, the "Swoosh", and their slogan, "Just Do It". They also leveraged prominent athlete endorsements, an integral part of garnering mass-market appeal. Patagonia engrained its core belief in sustainability into its business and marketing plans. They strictly adhere to their ideals of sustainable and equitable practices. They also knew that they needed to be able to attract new

customers, and they decided to do so through tailored product offerings and a positive corporate culture. Uber, which was a radical idea for its time, increased its customer base through product evolution and the attraction of both customers and drivers.

Although entrepreneurs can follow any of these methods, it could also be beneficial to seek advice, exposure, and financial investments. A prime example of this is Shark Tank. Benefits from the show could be an investment, advice from Sharks, and national attention. Successful companies such as Scrub Daddy have managed to increase their profits by more than 1500% after appearing on the show, receiving an investment, and improving their marketing and distribution strategy with the expert assistance of their advisor. Even if contestants aren't lucky enough to earn an investment, like Ring, they can gain advice and attention from Sharks and viewers, which could potentially lead to other outside investments and public popularity. Ring was subsequently able to improve their product, grow their customer base, and win the attention of Richard Branson and Amazon after their Shark Tank appearance, which helped bring the company's value to $1.5 billion.

These marketing strategies supported these companies' growth paths toward billion-dollar valuations. They were able to rise from small startups to some of the most popular businesses in their respective categories. These strategies can provide a roadmap for marketing success for any startup, however, it also requires a large amount of luck to become so successful. startups need to be able to capitalize on their chances, and establishing a strong marketing plan will help prepare them to do so.

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Heart Health dos and don'ts: Diet, exercise, and other choices By Anushka Nishar

Heart disease and related cardiovascular problems are important issues that can endanger people of all ages. These health conditions typically include heart failure, arrhythmia (irregular heartbeats), heart inflammation, and coronary heart disease. About 695,000 people die of heart disease in the United States every year, which accounts for 1 in every 5 deaths, making it the largest cause of death in the country (NY Department of Health, 2023). In 2020 alone, adverse cardiovascular conditions leading to heart failure cost the U.S. healthcare system $43.6 billion (Urbich et al., 2020). Heart disease can eventually lead to heart failure, which occurs when the heart muscle is unable to pump enough blood into the body to satisfy the need for oxygen, glucose, carbon dioxide removal, and other essential functions. These adverse cardiovascular events often begin as inflammation that affects the blood vessels, the lining of the valves, and the tissue surrounding the heart. This is influenced by many factors, including diet, exercise, disease, stress, alcohol, smoking habits, and drugs. This paper will therefore explore these factors in more detail to better understand the causes of heart problems and how they can be prevented.

Diet plays an important role in the development or prevention of adverse cardiovascular issues. For example, omega-3 fatty acids are a group of three fatty acids that are essential to human health: alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). ALAs are found in plant oils, while EPAs and DHAs are usually found in cold-water fatty fish (National Institutes of Health, 2023). Omega-3 fatty acids have multiple positive effects on heart health. They prevent arrhythmias, decrease circulating blood triglycerides (a type of lipid), lower blood pressure, and slow plaque buildup in arteries. While omega-3 fatty acids positively affect heart health, other fats can be detrimental to cardiovascular health.

Saturated fats are one such group of unhealthy fats and can cause higher levels of low-density lipoproteins (LDL) in the blood. The LDL to high-density lipoprotein (HDL) ratio strongly relates to the quantity of cholesterol in blood because LDL brings cholesterol from the liver into the blood while HDL brings cholesterol from the blood back to the liver. Therefore, as LDL rises relative to HDL, so does the amount of cholesterol in the blood, which raises the risk of strokes and heart disease. This occurs because cholesterol causes atherosclerosis in which arteries stiffen due to the formation of fatty deposits called plaques that obstruct blood flow and increase the risk of blood clots as they grow (Johns Hopkins Medicine, 2023). Resulting blood clots can cause heart attacks or strokes. The main foods that contain high levels of saturated fats are mammal meat, animal fat (e.g., butter and lard), cheese, and many processed foods.

Although it is important to lower saturated fat intake, trans fats are a group of fats that should be entirely eliminated from the diet due to how harmful they are to the heart and health in general. Trans fats have many of the same adverse consequences as saturated fats, such as raising LDL, which corresponds to plaques forming in arteries, and increasing the risk of heart attacks and strokes (Pipoyan et al., 2021). However, they can have these effects from consuming much smaller quantities than saturated fats. Trans fats are mostly found as an additive in highly

processed foods, but fortunately, their use has been heavily restricted in most developed countries.

Even though salt is an essential nutrient, avoiding foods high in sodium is also important to maintaining heart health since excessive sodium intake can lead to chronic high blood pressure (hypertension) (Stathos, 2023). Chronic high blood pressure can contribute to heart disease, stroke, and kidney disease as well as other health issues. Foods high in sodium include processed foods, cured meats such as sausage and bacon, and canned vegetables with added salt.

A diet rich in fruits and vegetables improves heart health, partly by balancing the effects of excess sodium, lowering blood pressure, improving cholesterol, and balancing blood glucose levels. For example, many fruits and vegetables contain potassium, which balances the effects of sodium on blood pressure by increasing the amount of sodium that is excreted in urine (Kim et al., 2024). These same fruits and vegetables are also low-calorie, nutrient-rich foods that are very healthy for the heart. Some leafy greens (e.g., spinach, cabbage) and whole grains (e.g., plain oatmeal, brown rice, whole-grain bread) are particularly healthy for the heart because they contain large amounts of fiber. Fiber is vitally important because it helps to balance and improve blood cholesterol and glucose levels as well as blood pressure, which lowers the risk of strokes, heart disease, obesity, and type 2 diabetes (Anderson et al., 2009). Consuming these foods on a regular basis can build a strong foundation of not only heart health but also overall health. Conversely, refined grains should generally be avoided as they contain much lower nutritional value in comparison to whole grain foods both in their fiber and micronutrient content. Refined grains also cause a higher spike in blood glucose levels, which can cause adverse health effects related to insulin sensitivity and the formation of diabetes.

Another important aspect of a healthy diet is proper hydration. Staying hydrated can reduce blood pressure, diluting the sodium in the blood and allowing more to be excreted in urine, which reduces strain on the heart. Researchers at the National Institutes of Health found that staying hydrated was associated with a lower risk of heart failure (NIH, 2022). In this study, they analyzed 11,814 participants of the ages 45-66 over 25 years of which 1,366 developed heart failure. The researchers found that participants with serum sodium levels in midlife starting at 143 milliequivalents per liter (mEq/L) had a higher risk of heart failure and that this increased by 5% for every additional 1 mEq/L of serum sodium levels. Based on these results, they concluded that a sufficient daily water intake to stay healthy is 6-8 cups (1.5-2.1 liters) for women and 8-12 cups (2-3 liters) for men. This research shows that staying properly hydrated helps to lower serum sodium levels and therefore reduce the risk of high blood pressure.

Another fluid that many people consume daily is coffee, which contains caffeine. The FDA claims that healthy adults can safely consume 4-5 cups of coffee per day, and research over the past decades has only found mixed conclusions regarding the long-term effects of regular caffeine use on the heart (Reyes et al., 2018).

Conversely, smoking is very harmful to the heart. The chemicals consumed from smoking cause plaque buildup in arteries (NIH, 2022). Current and former smokers have roughly double the risk of heart failure of people who have never smoked (MNT, 2022). People who

smoke even a few cigarettes a day have around double the risk of dying from cardiovascular disease compared to those who have never smoked. Harmful chemicals in cigarette smoke thicken the blood which can lead to thrombosis in which clots block blood vessels, limiting the natural flow of blood. The most common types of thrombosis are acute venous and arterial thrombosis, which respectively occur in veins and arteries. The relationship between smoking and venous thrombosis remains unclear, but smoking has been clearly shown to greatly increase the risk of arterial thrombosis. Other cardiovascular conditions that are caused by smoking are coronary heart disease (blockages in the arteries that supply blood to the heart), hypertension (high blood pressure), heart attacks, strokes (blockage of blood flow to the brain or rupture of blood vessels in the brain), aneurysms (a bulge or weakness in arteries), and peripheral artery disease (narrowing of the vessels that carry blood from the heart to the legs). Many of these conditions are caused or contributed to by atherosclerosis.

Excessive alcohol intake is also very harmful to overall heart health. It can raise the risk of high blood pressure and obesity, and eventually lead to heart failure or strokes. Alcohol consumption can also contribute to obesity because it contains 7 kilocalories per gram (twice as much as carbohydrates and almost as much as fat). Obesity itself is a serious issue that not only causes substantial damage to the heart but also to the overall body. Drinking large amounts of alcohol directly links to high blood pressure, which leads to cardiovascular diseases (increases the chances of a stroke or heart attack). Chronic intake of alcohol can also cause a cardiac disease called alcoholic cardiomyopathy (ACM). Over time, the toxicity from alcohol causes the left ventricle of the heart to stretch, which makes the heart pump less effectively and eventually leads to heart failure. In addition, alcohol is a depressant drug, meaning that it slows the nervous system, which also indirectly reduces heart rate. Subsequently, alcohol poisoning can cause the heart to stop entirely, which often leads to death. Many people believe that a small amount of red wine can be beneficial to the heart because it contains resveratrol (a compound found in red grapes), which has been thought to improve cardiovascular health. However, more recent research found that the amount of resveratrol in red wine is insufficient to have these effects and that the risks of drinking overwhelmingly outweigh the benefits.

It is also very important for people to moderate their stress levels. Stress has a negative impact on immune and physical health. According to the University of Rochester Medical Center (2024), high stress correlates with the incidence of heart disease. The body releases the hormone cortisol when stressed, which if consistently released can harm the heart. High levels of cortisol can increase blood cholesterol, triglycerides, and glucose, as well as blood pressure. All of these factors greatly contribute to heart disease as previously discussed. Even chronic mild stress has a great impact on the body because it worsens blood flow to the heart, which reduces the amount of blood and oxygen it can obtain. Long-term stress also raises the risk of blood clots in arteries, which can cause strokes and heart attacks. To deal with stress, many people resort to unhealthy behaviors such as drinking alcohol and smoking. However, it is important to remember that there are other options like meditation, taking breaks from social media, eating well-balanced meals, and participating in enjoyable activities like hobbies and spending time with friends and family.

Being physically active is a major factor in having a healthy, functioning heart. It has direct links to strengthening the heart muscle, weight loss, and keeping arteries clean and healthy. It also lowers blood pressure, lessens the risk of diabetes, and reduces heart inflammation. According to the American Heart Association, aerobic and resistance training are most helpful for strengthening the heart. Aerobic exercises include jogging, swimming, and biking, while resistance training includes weightlifting and calisthenics. Exercising also allows muscles to more effectively extract oxygen from blood so that the heart does not need to pump blood to the rest of the body with as much effort. This decreases the force on arteries and thus lowers blood pressure. Exercise also burns excess calories, which allows people to maintain a healthy weight or lose excess weight. Being overweight or obese has many direct harmful effects on the heart. In addition to those already discussed above, obesity can cause two more unique harms: adipokines and fatty tissue infiltration. Adipokines are a type of molecule released from fatty tissue that increases heart rate and can cause expansion of blood volume, which raises the amount of blood the heart must pump. The heart can then have difficulty pumping enough blood to the body, raising the demand of cardiac output (the amount of blood pumped per minute). Adipokines also cause endothelial damage (a type of coronary artery disease), which impairs the functioning of the lining of blood vessels. Obesity can also cause fatty tissue infiltration into the heart. This slows the heart's movement, causing arrhythmia and other heart problems. Fatty tissue infiltration also causes LVH (left ventricular hypertrophy), which is the thickening of the wall of the heart's main pumping chamber (Ashraf et al., 2013). Overall, obesity leads to coronary artery disease, heart failure, and arrhythmia, which is why it is important to exercise regularly to maintain a healthy weight.

According to Pinckard et al. (2019), exercise can improve metabolic and cardiovascular health by lowering body weight, improving glucose homeostasis, balancing blood pressure, and lowering HDL levels. Furthermore, exercise helps improve the cardiovascular health of lean and overweight individuals. In a year-long study involving non-obese participants, a 16-20% rise in energy was found through different exercises, and there was a 22.3% reduction in body fat (Fontana et al., 2007). There was also a decrease in LDL and total cholesterol. Walking approximately 12 miles per week for 7-9 months helped overweight individuals maintain their weight and improve cardiorespiratory fitness (Duscha et al., 2005). These findings suggest that exercise plays a significant role in reducing the risk of cardiovascular disease for individuals who are lean, obese, or afflicted with type 2 diabetes. Exercise is also extremely important for people who already have heart issues. For example, a study of patients with heart failure showed that aerobic exercise at 60-70% of the maximum heart rate 3-5 times per week improved cardiac health over 3 years (Flynn et al., 2009).

Despite having good health habits, various diseases can cause damaging acute inflammation of the heart, including endocarditis (inflammation in the inner lining of the heart chambers and valves), myocarditis (inflammation of the heart tissue, myocardium) and pericarditis (swelling of the pericardium, the outer lining of the heart). These can be treated by

medication or surgery, depending on their cause as they can result from bacterial infections, autoimmune diseases, certain medications, and toxic reactions to drugs. Endocarditis mainly occurs in older people due to bacterial buildup around valves in the heart. These clumps of bacteria can eventually break free into the bloodstream, which can block the flow of blood and spread infections to other organs. This is normally treated with antibiotics. Alternatively, myocarditis and pericarditis are most common in middle-aged adults. The former can be caused by medications, particularly those for diabetes, that expose the myocardium to elevated glucose and insulin levels. It must be treated with rest, anti-inflammatory medication, and changes in lifestyle to prevent reoccurrence. Lastly, pericarditis can be caused by a variety of viral or bacterial infections, autoimmune diseases such as lupus or rheumatoid arthritis, as well as due to immune responses after heart damage such as surgery or heart attack. Because it has many different potential causes, the treatment varies.

   Certain medications can also harm the heart. For those with existing heart problems, nonsteroidal anti-inflammatory drugs (NSAIDs, such as ibuprofen) can be dangerous as they increase arterial blood pressure which can increase the risk of heart attack. Even in people without existing heart problems, more and more research shows that NSAIDs can increase the risk of harmful cardiovascular events. According to Christian Ruff from Harvard Health (2019), even though NSAIDs reduce inflammation, regular use can have long-term effects on the heart. For patients with heart disease, it is recommended to find an alternative pain reducer such as acetaminophen. However, if the patient must take NSAIDs, Ruff recommends the nonselective NSAID naproxen or the COX-2 selective NSAID celecoxib, as these are the safest for patients with heart disease. To limit potential side effects, Ruff advises that people take the lowest effective NSAID dose for the shortest possible duration of time. Conversely, beta blockers can alleviate heart problems as they improve blood flow and irregular heartbeat, and thus lower the risk of future heart attacks. Although aspirin is a common medication for pain or fever, it can also be taken regularly by people with heart problems because it helps to prevent blood clots that may result from plaque formation and would thus lead to heart attacks or strokes (Ruff, 2019).

   Preventing heart problems requires cultivating good habits and the discipline to maintain them. This most importantly includes having a healthy diet, engaging in regular exercise, and avoiding tobacco and excessive alcohol. It is challenging for many people to maintain healthy habits due to insufficient time and an inflexible schedule, so it can be helpful to create meal plans and exercise routines in advance to get organized and stay motivated. This can also ensure that stress is managed in healthy ways instead of turning to activities like drinking alcohol or eating unhealthy food. Certain medications can also harm the heart and should therefore be used with care. Following these guidelines can greatly reduce the risk of heart inflammation and subsequent more severe issues, which is essential to maintaining overall health.

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Recent Diagnostic Techniques and Potential Therapeutic Implications towards Acute Myeloid and Chronic Neutrophilic Leukemia By Issac Lee

Abstract

Leukemia is characterized by the uncontrolled proliferation of abnormal white blood cells within bone marrow, leading to immaturities within blood cells. In acute myeloid leukemia (AML) and chronic neutrophilic leukemia (CNL), genetic mutations induced by either foreign or natural processes lead to the development of leukemia. Although leukemia is a diagnosable disease, the diverse subtypes and a complex, multi-step diagnosis makes identifying expedient, accurate diagnosis methods a top priority. With specific methods being attributed as the only means of diagnosing leukemia, and the importance of proper subtype classification in patient prognosis, the lack of research regarding novel diagnostic approaches remains a concern due to the important role leukemia classification plays in the prognosis of the patient. Currently, three diagnosis methods can be regarded as prevalent to the modern diagnosis of leukemia: epigenetics, molecular genetics, and cytogenetics. Each of these current methods are capable of identifying specific subtypes of leukemia. Furthermore, developing more detailed diagnosis criteria will provide better prognostic stratification. This review will cover various diagnosis methods regarding acute myeloid leukemia and chronic neutrophilic leukemia. Further inquiry in the area of diagnostics could reveal novel patterns within the diagnosis of Leukemia, furthering the ability to treat patients more specifically which can increase the prognosis of the patient.

Introduction

Leukemia is a group of malignancies in the hematological, or blood, cells of the body, typically originating in the bone marrow. Every year about 178,520 people are diagnosed with leukemia, with around 4.8-5% of these cases being diagnosed in children. (*Blood Cancer Statistics*, n.d.) Over countless decades since its discovery, leukemia has remained a large concern in the field of public medicine. Due to the complexity and diversity of its many subtypes, leukemia requires an accurate patient diagnosis with targeted treatment plans. The modern diagnostic approaches integrate newer technology such as cytogenetics, molecular genetics, and epigenetics and has allowed for a comprehensive identification of subtypes. These methods have, overall, contributed to the improvement of the overall prognosis of patients with leukemia due to their contributions in creating new treatment methods that can be applied to patients. Given their critical role in treatment approach and patient outcome, modern techniques play crucial roles in the diagnostics of leukemia and it is a necessity to understand as well as to improve upon possible limitations of these modern techniques. Research to further analyze and explore novel diagnostic tools and approaches serves to improve patient diagnosis and ultimately survival.

While modern diagnostic specialties and their respective tools have contributed to significant advances within the world of medicine, a more holistic, comprehensive approach integrating each discipline is currently lacking. An integrated approach affords researchers and

clinicians a more thorough analysis of genetic, epigenetic, and proteomic biomarkers, opening new possibilities for disease classification and patient stratification. The valuable insight provided by such integration would better inform diagnosis and treatment plans, ultimately improving patient care and prognosis.

In this review, we will highlight both the individual disciplines and their interdisciplinary use. Through an understanding of the benefits, complexities, and potential drawbacks of an integrated diagnosis system, we envision an improved era of precision medicine, whereby patients receive a more accurate diagnosis, targeted treatment plans, and ultimately leading to increased survival with fewer treatment side effects.

2. Cytogenetics

Cytogenetics is the study of chromosomal structures and abnormalities. While decades old, it still plays a pivotal role in the diagnostic approach to leukemia. Many discoveries made through cytogenetics, such as the aberrations t(9;22) and t(15;17), have been instrumental. These breakthroughs have allowed further subclassification of leukemia into distinct molecular subtypes. (Takahashi et al., 2011)

2.1 The Principles of Cytogenetics

Cytogenetics analysis, also known as karyotyping, requires meticulous examination of chromosomal aberrations that underlie the subtypes of leukemia. The technique analyzes the collection of metaphase chromosomes in dividing cells. The chromosomes are stained, arranged, and visualized. These data are analyzed to visualize to identify any structural changes, particularly deletions, duplications, and rearrangements. Notably, the constant recurring discoveries of chromosomal abnormalities found through karyotyping has been pivotal in classifying the different subtypes of leukemia. Additionally, greater than 3 aberrations detected by karyotyping identifies a risk of leukemia. (Mrózek, 2008) Despite this however, it must be taken into consideration that a large change in genetics (5 MB) must occur for cytogenetic methods to detect changes. (*Demystifying the Lab: Cytogenetics*, 2021)

To improve its accuracy in diagnosis and risk stratification, cytogenetics has integrated more modern technologies such as fluorescence in situ hybridization (FISH). The FISH process involves hybridizing fluorescently-labeled DNA probes onto target sequences of DNA. It is effective at identifying subtle chromosomal abnormalities that can be missed by the traditional karyotyping method and has been used to identify the t(15; 17) translocation or the RARA genes. (Shakoori, 2017)

More advanced cytogenetic methods such as array comparative genomic hybridization (aCGH) directly compare cytogenetic analysis to reference DNA samples for diagnosis. These comparisons highlight differences in hybridization intensities, which identifies copy number changes in regions of DNA. Copy number changes are phenomenons where the genome sequence is constantly repeated in a different way. This method will not be discussed in this review paper, as this method has been extensively reviewed. (Ahn et al., 2015)

2.2 Chromosomal Aberrations Across the Subtypes of Leukemia

Using cytogenetics, chromosomal aberrations can be identified in patient samples to inform disease subtypes. The two subtypes of leukemia addressed in this paper are acute myeloid leukemia (AML) and chronic neutrophilic leukemia (CNL).

The AML subtype has been one of many to be identified by cytogenetics. Specific chromosomal alterations, such as translocation of t(8;21)(q22;q22), t(15;17), t(8;21)inv(16), t(16;16) have been identified in more than 50% of patients with AML. Notably, the t(8;21)(q22;q22) translocation has prognostic implications, as this alteration is associated with improved survival (Reikvam et al., 2011).

Chromosomal translocations, however, are not the only identifiable factors revealed by cytogenetics. Fluorescence-based polymer-chain reaction (PCR) has also allowed for the identification of genetic alterations in AML, such as NPM1 (33%), FLT3-ITD (18%), and CEBPA (19%); each percentage indicating the likelihood of being found within AML. (Chauhan et al., 2013) The percentage of patients who possess these identifiable genes are much lower than alterations discovered by karyotyping, however the application of fluorescence-based PCR alongside karyotyping has increased prognostic stratification of patients. Furthermore, FISH has been used to identify the AML-M2 mutation which occurs within the t(8;21)(q22;q22) translocation (Suto et al., 2015).

CNL is also identifiable through cytogenetics. The (8;22)(q11;q11) translocation is a key biomarker found in the majority of CNL patients. Furthermore, the ability to identify the formation of fusion genes such as PCM1-JAK2 has made FISH the primary method for diagnosing CNL. Presence of these fusion genes indicate a poor prognosis.

2.3 Prognostic Significance of Cytogenetic Findings

With this paper's focus on diagnosis, it is also worth noting the importance of these diagnostic tests on patient prognosis and treatment options. This section will focus on the influence of cytogenetic analysis on prognosis for AML and CNL patients.

In AML, patients with a translocation of RUNX1-RUNX1T1 t(8;21) are given a favorable risk. In contrast to such favorable prognostics, karyotypes with multiple chromosomal abnormalities are associated with poor outcomes and typically require patients to undergo risky and aggressive treatment regimes. In general, the usage of cytogenetics alone is ineffective in establishing a reliable prognostic outcome and requires assistance from other methods that allow for a more refined view (Reikvam et al., 2011). Certain molecular markers such as NPM1 with standard cytogenetics provide a favorable prognosis. However, FLT3-ITD with the absence of NPM1 provides a less than favorable prognosis for the patient. (Juliusson et al., 2020)

2.4 Challenges and Future Prospects of Cytogenetics

Cytogenetics techniques have made significant contributions to identifying the genomic landscape of leukemia. However, many challenges lay ahead. The dynamic nature of cancer and the field studying it demands constant innovation to address the growing challenges. However, these limitations and challenges also provide opportunity to capitalize on prospects for the future through continual improvement.

While cytogenetic analysis provides remarkable insights into diagnosing the different subtypes of leukemia, it faces challenges identifying more complex features on the genomic landscape of leukemia. Some key genetic and chromosomal alterations are missed, revealing the need for more sensitive detection methods and innovations. For example, a traditional method such as karyotyping is accurate but possesses limitations as it can only be as fast as the growing cells. If it was necessary to analyze slow growing or underdeveloped leukemia cells, karyotyping would not be an efficient approach for diagnosis.

Cytogenetics also poses a high possibility for error in data analysis as there is simply too much information to analyze effectively within a timely manner. Differences in lab practices may also pose challenges to the accuracy of cytogenetic analysis. The most crucial measure to overcome this is standardization of data, ensuring that all data is reliable. However this is not always a possibility due to extensive amounts of data that is constantly collected.

Despite these current challenges, the future of Leukemia diagnosis regarding cytogenetics is bright. With next generation technology, such as FISH and fluorescence PCR, paving the way to a new generation of cytogenetics, continued improvement in capabilities cytogenetics remains promising.More recent techniques such as single nucleotide polymorphism (SNP) analysis allows for genome wide analysis. This technique allows greater sensitivity for more subtle genomic abnormalities. The integration of cytogenetic data with new generation methods proves effective, providing a much more holistic understanding of leukemia. Furthermore, technological advancements would also assist in the diagnostic capabilities of cytogenetics as well as the ability to compare data to other methods.

2.5 Ethical Considerations of Cytogenetics and Leukemia Diagnostics

The field of cytogenetics has substantially improved our understanding of leukemia and opened up the opportunity for accurate disease prognosis. It is, however, important to acknowledge the ethical considerations surrounding the context of cytogenetic analysis and its implications for patients, researchers, and clinicians.

For ethical purposes, a patient must be well informed about the purpose, outcomes, and limitations that follow the usage of cytogenetic procedures. Acquiring informed patient consent prior to any procedure(s) ensures patient understanding regarding research access to their genetic information. If targetable alterations are identified, available treatment options will be discussed with the patient, and they will be able to make an informed decision based on the information provided. Furthermore, when tumor samples are being utilized for research purposes beyond clinical care, patient material is de-identified to maintain confidentiality. The availability and use of patient material is paramount to continued advancements in the field. Cytogenetic data from

these sources informs possible hereditary, or familial, as well as epidemiological implications of disease. For example, cytogenetic findings could identify the increased familial risk of leukemia amongst family members. Provided patient consent and ethical disclosure is strictly adhered to, this may result in preventative measures which increase survivorship.

2.6 Conclusion: Challenges and Future Prospects for Cytogenetics

Cytogenetic analysis through identifiable aberrations such as t(8;21)(q22;q22) and t(8;21)(q11;q11), allow for diagnosis to be made along with accurate prognosis. Certain translocations in tandem with identified aberrations may lead to (un)favorable prognosis and modifications to treatment plans. The success rate of accurate diagnosis and prognosis with Cytogenetics was studied to be 70-75% within adults, while for children it increased upwards to 85%. Such accuracy provides valuable insight onto the majority of patients and highlights the significance of cytogenetics in the field of leukemia diagnostics (Mrózek et al., 2009).

Even with reliable results, cytogenetics must still be used with caution. More intricate translocations and aberrations cannot be identified by cytogenetics, which presents a risk to relying on cytogenetic data alone for diagnosis. For this reason, it is recommended that cytogenetic approaches be coupled with other methods to allow for a more comprehensive assessment of genomic alterations, translocations, and aberrations.

3.0 Molecular Genetics

Molecular genetics is a branch of genetics that delves into the molecular structure and function of DNA and begins at the recognition of genetic information found within DNA. The technique deciphers the sequences found in the bases of DNA. Within molecular genetics, techniques such as PCR and next-generation sequencing (NGS) are commonly applied. PCR is used to amplify specific DNA material, whereas NGS can determine the precise nucleotides contained by the DNA. Molecular genetics allows for the identification of genetic aberrations, or mutations, underlying a person's cancer.

Molecular genetics has opened a new realm of precision medicine and has revolutionized our understanding of leukekmia's complex etiology. Some mutations in genes such as *NPM1*, *TET2*, and *PML-RARA* are known to cause leukemia, inviting development of targeted treatments against these aberrant proteins. (Lagunas-Rangel et al., 2017)

These new generation technologies allow for high-throughput testing of many patient samples simultaneously, in addition to increased sensitivity of detection at a lower cost. This makes the identification of genetic alterations more probable and practical. Molecular genetics testing can later be combined with data from cytogenetics, further refining the classification of leukemia. This section will cover the principles of molecular genetics and its contribution to the field of diagnostics for leukemia.

3.1 Principles of Molecular Genetics and Common Gene Mutations

Advances in molecular genetics have mapped out the genetic landscape of leukemia much further than initially thought possible. This mapping allowed for identification of common genetic mutations in leukemia. These common mutations have improved the disease classification and contribute to the improved prognostic indicators. In this section, three of the most common genetic mutations found in leukemia will be discussed: *NPM1, FLT3, and CSF3R*.

Genetic mutations to the nucleophosmin 1 (NPM1) protein are frequently observed in AML. Mutations to *NPM1* are usually identified in patients with a normal karyotype. This common mutation is linked to a favorable prognosis, especially if the mutation is isolated. As a result, this mutation gives specific implications about the treatment approach to be taken.

FMS-like tyrosine kinase 3 (FLT3) is a mutation in leukemia which is one of the most prevalent mutations within AML. Two different types of *FLT3* mutations have been identified: *FLT3-ITD* and *FLT3-TKD*. *FLT3-ITD* is an internal tandem duplication which is typically accompanied by a worse prognosis. Leukemias with this mutation are oftentimes more aggressive, resulting in higher rates of patient relapse and lower rates of survival. Conversely, *FLT3-TKD* is often found in patients with a more favorable prognosis. *FLT3-ITD* is stated to be much more aggressive, and is often related to higher relapse rates, and a lower survival rate. (Kiyoi et al., 2020)

Colony-stimulating factor 3 receptor (*CSF3R*) mutations are common in CNL. This mutation causes aberrant activation of the CSF3R receptor, resulting in uncontrolled growth of neutrophilic cells. This contributes to the high levels of neutrophils commonly seen within CNL cases. (Kelemen, 2022) Further information can be found in (Dwivedi & Greis, 2017).

3.2 Next-Generation Sequencing and Clinical Applications

NGS has revolutionized the ability of scientists to capture and identify rare, previously unknown genetic mutations in leukemia. This has significantly expanded our understanding of the genomic landscape of this disease. NGS has also been crucial in identifying therapeutically targetable mutations, particularly those for which treatment methods may already exist. The implication of NGS is a shift in DNA sequencing which goes from traditional sequencing methods to one that allows the simultaneous analysis of multiple DNA fragments. NGS has cut down the time, cost, and manpower needed to analyze DNA and even allowed for more extensive analysis than before. Adopting NGS has increased the ability to discover uncommon mutations.

3.3 Challenges and Future Prospects of Molecular Genetics

With the introduction of molecular genetics, cancer research has made remarkable advancements towards understanding and treating leukemia. As we look to the future of leukemia diagnostics, molecular genetic tools and techniques offer a good prospect towards the challenges. The ability to map out the entire genomic landscape and identify multiple different mutations is invaluable towards the discovery and treatment of rare disease subtypes. However, this widened understanding of disease is not without its limitations. The extent to

which novel genetic mutations can be validated and then therapeutically targeted remains challenging. If a novel, rare mutation is discovered, much additional research and funding is required before being clinically actionable. As a result, no matter how good the diagnosis may be, it is challenged heavily by the treatment method applied. In addition, discerning the most relevant mutation for disease etiology is another significant limitation. As molecular genetic approaches capture numerous, if not all, present mutations in a sample, the challenge is to identify the main driver mutation(s) of disease, those that result in disease onset and/or progression, rather than ancillary passenger mutations. Identifying and validating driver mutation(s) requires extensive time and resources. As a result, many patients may not initially or directly benefit from their impact on improved diagnostics or therapies.

4.0 Epigenetics

A more recent field of study is that of epigenetics. Epigenetics is, in essence, the study of gene regulation and function; specifically, epigenetics describes heritable differences in an observed phenotype or behavior despite no changes in DNA sequence. (Dupont et al., 2009) Epigenetic modifications are utilized in cells to regulate gene expression patterns on a per cell basis. These mechanisms allow different cell types to produce different proteins while having the same DNA **(Figure 1)**. However, epigenetic mechanisms can be dysregulated and research has focused on identifying aberrant epigenetic modification events that can result in leukemia formation or progression. Indeed, diagnostic tools capitalizing on this area of biology identify epigenetic changes that occur during the onset and progression of diseases such as leukemia. (Al Aboud et al., 2023) Knowledge of the aberrant epigenomic landscape present in leukemia also invites potential use of epigenetic-based anti-cancer therapies, as well as additional insight into leukemia's development progression, and heritability.

4.1 Epigenetic Aberrations in Leukemias
4.1.1 DNA Methylation

One type of epigenetic modification is DNA methylation. (Al Aboud et al., 2023) Typically this involves the addition of methyl groups to cytosine residue(s) within a particular section of DNA containing CpG dinucleotides (i.e., cytosine and guanine nucleotides linked together by a singular phosphate group). Methylation of cytosines in CpG dinucleotides is important because these regions regulate gene transcription. In general, DNA methylation results in gene inactivity or silencing. Aberrant DNA methylation at gene sites typically responsible for *suppressing* tumorigenic activity can thus contribute to the progression of disease. Indeed, certain patterns of DNA methylation in AML have been found to inform prognosis. Aberrant methylation of the gene *CDKN2B* is one such alteration that has been identified and related back to a specific prognosis. With an overall survival rate of 40% across all ages, the prognosis is relatively favorable for patients with this specific methylation pattern. (Chim et al., 2006)

4.1.2 Histone Modifications

Another type of epigenetic modification involved in gene regulation histone modifications (**Figure 1**). In each of our cells, DNA is tightly wrapped around proteins called histones. Modifications of these proteins will either make the DNA more or less accessible for transcription, thereby influencing gene expression patterns. Generally, histone modifications may include acetylation (and its reverse de-acetylation), methylation, phosphorylation, or ubiquitination. Dysregulation of histone marks has been identified in multiple cancers, including leukemia. (Audia & Campbell, 2016) As the epigenetic field is relatively new, our understanding and utilization of this phenomenon for clinical purposes is still developing. Similar to molecular genetic tools, validation of identified epigenetic targets is required before informing patient prognostication. Fortunately, several epigenetic-based drugs, such as histone deacetylases (HDAC) inhibitors, are already clinically approved to treat other diseases. (Kim & Bae, 2011)Regulators have been used clinically, especially histone deacetylases (HDAC) inhibitors, targeted therapy could become available.

Heterochromatin

Euchromatin

Histone acetylation, nucleosomes packed loosely

DNA and Histone methylation, nucleosomes tightly packed
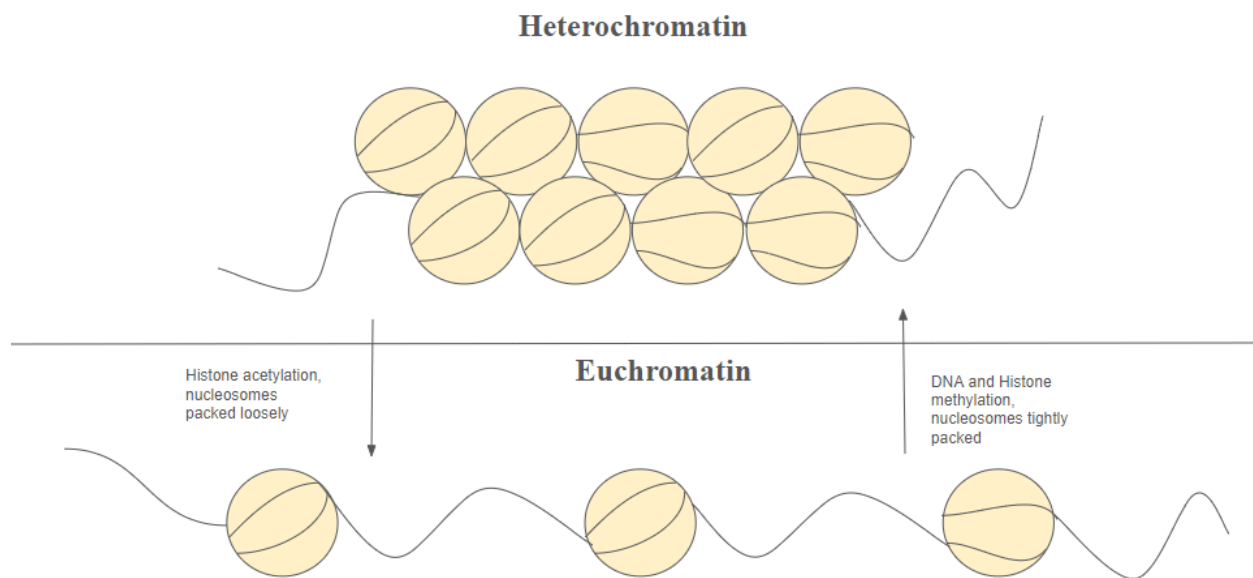
Figure 1: Epigenetic regulation of transcription
Epigenetic regulation influences the chromatin accessibility, allowing alternative expression of proteins in various cells. In a closed chromatin state, called heterochromatin, transcription is limited. These states are usually influenced by DNA methylation. In contrast, in euchromatin, chromatin is accessible. This is generally influenced by lack of DNA methylation and histone modifications.

4.1.3 Non-Coding RNA Dysregulation

A third and final method of epigenetic regulation involves non-coding RNA (ncRNAs). ncRNAs are typically sequences of transcribed DNA that do not get translated into functional proteins. Instead, these sequence fragments become long non-coding RNAs (lncRNA), among

others. Similar to other methods of gene regulation, disruption in these processes can adversely affect the activity of tumor-suppressor or tumor-promoting genes. For example, a specific lncRNA, called HOTAIR, has been identified in AML. (Hao & Shao, 2015)With much research focusing on these pathways, new ncRNAs will likely be identified in the near future, increasing our understanding of leukemia development and providing novel therapeutic targets.

4.2 Challenges and Future Prospects of Epigenetics
Epigenetics is a promising field for leukemia diagnostics. With improvements in navigating and managing the vast amounts of data provided by these methods, along with standardization practices, the potential for methods exploiting epigenetic aberrations such as methylation and ncRNAs is vast. However, with these novel approaches also come specific obstacles that must be overcome for clinical adoption.

For one, there is currently no validation to assess the accuracy of epigenetics. Similar to molecular genetics, targets need to be validated to distinguish driver from passenger targets. Understanding the variations in the activity of lncRNAs and validating data regarding their ties to leukemia will allow for better diagnosis in the future. Although it may not help current patients right now, down the line it's going to help after data has been validated and sorted in a way that can clinically be applied. Furthermore, with multiple different methods validating specific indicators for cancer, the targeted methods can be produced in a manner that becomes clinically applicable. For one, there is currently no validation to assess the accuracy of epigenetics. Similar to molecular genetics, targets need to be validated to distinguish driver from passenger targets.

5.0 Conclusion
Convergence of the fields of cytogenetics, molecular genetics, and epigenetics opens up a realm where the biology of leukemia is much more comprehensively understood. It is of major importance that these methods get integrated together to provide a more holistic view into disease initiation and progression. This will allow more advanced patient risk stratification. By integrating or coupling these diagnostic approaches, the overall effectiveness of diagnostics will likely improve by diminishing challenges faced by each approach individually. Furthermore, it will provide a more holistic overview of a patient's tumor, allowing for more precise prognostic indicators and therapeutic opportunities.

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The Looming Epidemic of Hypertension in South East Asian Countries By Christine Wong

Hypertension also referred to as the "silent killer" is a medical condition characterized by elevated blood pressure in the arteries. Some people with high blood pressure may not feel symptoms, however, the only way to confirm is to get your blood pressure checked. Hypertension is common but can lead to serious consequences including cardiovascular diseases such as heart attack, stroke, and heart failure if left untreated (WHO, 2023).

Globally, hypertension is one of the major causes of premature death. An estimated 1.28 billion adults aged 30–79 years worldwide have hypertension, most (two-thirds) coming from low- and middle-income countries. Even worse, it is estimated that 46% of adults with hypertension are unaware that they currently have the condition (WHO, 2023).

The trend of global prevalence for hypertension has been dramatically increasing for the past two decades in Southeast Asian countries. In Southeast Asia, which consists of Myanmar, Thailand, Laos, Cambodia, and Vietnam the prevalence of Hypertension is 25%. Slightly higher than the global prevalence at 22% (Udaya, 2023). About one-third of SEA adults have currently been diagnosed with hypertension, and an estimated 1.5 million deaths are associated with hypertension annually (WHO, 2018)

Furthermore, given the lower socioeconomic conditions of the Southeast Asian region, Meta-Analysis found that prevalence among urban areas for men was 31% and for women was 31%. In rural areas, the prevalence for men was 22% and for women was 21%. The high reports of hypertension in the region could be due to epidemiological transition in disease pattern from communicable to noncommunicable diseases (Dinesh et al., 2014). This increase in the number of people affected could be caused by aging, population growth, and the presence of behavioral risk factors which may include an unhealthy diet, alcohol, lack of physical activity, and exposure to persistent stress (CDC, n.d.). Other economically developed or developing countries show similar trends. In the USA, diet adherence and body weight management are only 18% and 39%, respectively, among hypertensive patients. Poor body weight management (53.2%) and poor physical exercise (69%) were also reported among hypertensive patients in Ethiopia (Irwan AM et al., 2022).

In the past decades, substantial socioeconomic and demographic changes have occurred in the region resulting in the transition from rural to urban lifestyle. Therefore, possibly leading to reasons behind the higher prevalence of hypertension in the urban areas (Dinesh et al., 2014).

Food intake in Southeast Asian countries are closely affected by the culture. The food is often cooked salty, oily, and with coconut milk. Things that should be reduced in self-care management, and successful intervention of hypertension. Another inhibiting factor is the financial status of the individual and family. Insufficient response of health-care systems in low-income/middle-income countries in many SEA nations left the burden of medical cost to the patients, including the patient with chronic diseases such as hypertension who need lifelong treatment. The cost of medication was a major reason for non-compliance in self-care management.
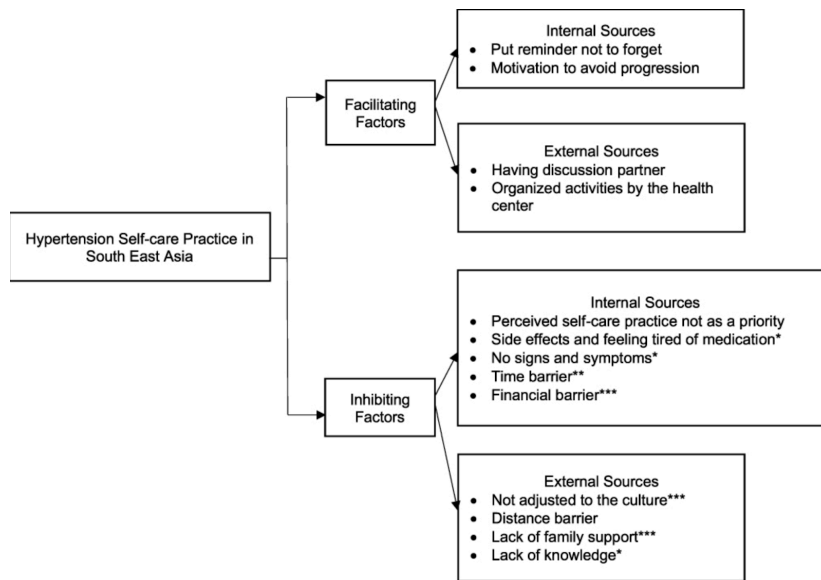
Figure 1. The framework of hypertension self-care practices inhibiting and facilitating factors in South East Asia. (Irwan AM et al., 2022).

Figure 1 shows the facilitating and inhibiting factors contributing to Hypertension Self Care Practice in Southeast Asia. Factors are linked to internal and external sources including financial barriers and lack of knowledge.

If we better understand the particular issues affecting hypertensive individuals, it will allow us to better address the needs of particular patients in their environments and contexts. Personalized approaches that consider both personal attributes and external circumstances in self-management of hypertensive populations were found to be important in this scoping review and should be rigorously studied in future research. (Irwan AM et al., 2022).

Ultimately, it is important that hospitals and health care agencies consider issues of access and cost for hypertension treatment which is prevalent among the adult populations of Southeast Asia and often requires lifelong treatment.

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The Downfall of Sports in Pakistan: A Tale of Missed Opportunities By Muhammad Sheikh

Pakistan, a country full of zeal and enthusiasm, is well known for its sporting prowess. Pakistani sportsmen are well-known in the annals of sports history, having made their mark on everything from the hockey grounds in Karachi to the cricket pitches in Lahore. But in recent times, the glitter of Pakistani sports has faded, to be replaced with a feeling of decline and stagnation. This downfall has been caused by a wide range of circumstances, which presents a depressing picture of missed opportunities and unfulfilled potential.

Infrastructure and Financial Woes

The degrading infrastructure of Pakistan is the root of its sporting woes. Aspiring athletes are hampered in their development and evolution by deteriorating stadiums, run-down training centers, and a dearth of basic amenities. These facilities, which are frequently dilapidated, don't offer the right atmosphere for athletes to develop to the best of their abilities.

The financial limitations that Pakistani sports face make matters worse. Sports organizations are finding it difficult to make ends meet due to a lack of support from the government and commercial sponsors. This underfunding has made it difficult to find competent trainers, host competitions, and provide necessary equipment, which has led to a vicious cycle of underdevelopment and stagnation.

Administrative Turmoil and Corruption

There is a great deal of unrest and corruption in Pakistani sports administration. Sports organizations have been beset by allegations of financial irregularities, nepotism, and favoritism, which has cast question on the fairness of the athletic process. The public's faith has been damaged by these scandals, which have also taken funds away from infrastructure and athlete development, impeding Pakistani sports' ability to grow.

Lack of Grassroots Development

There aren't many gifted athletes rising through the ranks as a result of the absence of a strong grassroots development program. Future sports stars are no longer being produced in the same quantity due to the concentration on elite sports and the lack of attention paid to spotting and developing talent at the school and community levels. This phenomenon is known as the talent drain.

Social and Cultural Barriers

Pakistani sports have declined significantly due in large part to societal and cultural obstacles. Because women are discouraged from participating in athletics because they believe it is a male domain, there is a smaller pool of ability from which future athletes can be selected. The

absence of mentors and networks of support for female athletes has also made it more difficult for them to participate in sports.

The Way Forward: Rekindling the Passion

There is yet hope for a comeback for Pakistani sports in spite of the obstacles. A comprehensive effort from all parties involved—the government, sporting organizations, commercial sponsors, and the general public—is needed to reignite the passion for sports.

When it comes to providing the infrastructure and financial support required for sports growth, the government must take the lead. This involves making investments in the building and upkeep of contemporary sports complexes, training centers, and stadiums. The government should also enact laws that encourage students to participate in sports at the community and school levels, spotting and developing talent early on.

Sports bodies have a responsibility to be open and accountable, to make sure that money is spent wisely and that athletes are chosen on the basis of merit. They should also actively pursue collaborations and sponsorships with the commercial sector in order to increase the funding available for sports development.

Through financial support, equipment, and experience, private sponsors can play a critical role in bolstering Pakistani sports. By planning competitions, supporting athletes, and launching media campaigns, they can also aid in encouraging people to participate in sports.

By encouraging their kids to play sports, rooting for their local teams, and going to athletic events, the general public may help Pakistani sports make a comeback. Additionally, they can increase understanding of the value of sports in fostering social cohesiveness, mental health, and physical fitness.

The revival of Pakistani sports will not happen overnight. The development of sporting skill necessitates a sustained commitment from all parties involved in addressing the underlying problems. With cooperation, we can rekindle Pakistan's love of sports and see the rise of future national heroes who will once more make the country proud.

Nutrition and Cancer By Samuel Lin

Introduction

Eat your vegetables! Everyone is taught this simple phrase from the beginning of their childhood to even adulthood. Rather than eating junk food, people have been taught since the beginning of time to eat their vegetables. The reason is simple: vegetables provide a lot of valuable nutrients for the body and are low in calories [1]. With the rise of junk foods and fast foods, diets have become ever so important in this day and age. The appeal of junk food and fast food is that they are accessible and taste good. However, there are many drawbacks to eating such foods. They are high in calories and fat and barely provide enough nutrients for the body [2]. These are devastating foods that people continue to indulge in everyday. Thus disease has become more widespread in people who have poor diets because the food that satisfies them in terms of taste is poisonous and damages their body from the inside.

Cancer is a disease that has a variety of different types. From blood cancer all the way to breast cancer, it is a disease that is endless in its different forms. Yet while there are many different types of cancer, they all have the same thing in common: they revolve around uncontrolled cell division. Cell division is normal in the human body but when problems arise such as wrong cell signaling then these cells can start to uncontrollably divide even though they don't need to and thus cancer arises. These cancer cells then continue to rapidly divide in the body, forming tumors and competing with normal cells over resources including nutrients which are needed by normal cells to function. Eventually, there are so many cancer cells in the body that the normal cells die off because they don't have enough resources and this results in death [3].

However, while cancer may seem like a very inevitable and scary disease, there are many ways to decrease the risks of developing cancer. The importance of lifestyle choices becomes ever so important in the prevention of cancer. Simple lifestyle choices such as getting regular screenings, having a healthy diet, exercising daily, not smoking, etc., all play a significant role in making sure that cells in the body are functioning properly and no abnormalities form. As mentioned, eating vegetables is important because it provides healthy nutrients for the body, but having a healthy diet in total, and not just eating vegetables has an utmost importance in maintaining a healthy lifestyle [4].

This article serves the purpose of showing how having a balanced diet can play a strong role in the prevention of cancer. This is not to say that simply having a healthy diet will ultimately prevent cancer , but rather by eating healthy, people can help maintain the body in a healthy manner to better protect it against possible diseases.

Understanding Cancer

As previously discussed, cancer is uncontrolled cell division. But let's get a little bit of a deeper dive at what exactly is occurring and how it is starting. Cell division and cell signaling are major factors that can influence the production of cells in the body and determine whether or not

the cell should divide. In cell division there are numerous checkpoints some of which help make sure that all the DNA components have been copied correctly and others might check if there is an adequate amount of MPF(maturation-promoting factor), the main factor that will allow the cell to start the division process [5].

On the other hand cell signaling sends signals out to cells and will direct the cell to either divide or remain undivided. If the body needs more cells for any reason then signaling will take place and communicate for cell division. However, it is obvious to see what can go wrong. When signals are miscommunicated or sent improperly, then cells can start to divide uncontrollably and/or do not respond to signals that are meant to stop the cell cycle. A typical example is when cell signaling goes wrong and proto-oncogenes can get activated and turn into oncogenes. For a quick summary, proto-oncogenes are inactive but still help in regulating cell division by allowing the passing of the checkpoints. However, when mutated into oncogenes, these genes can produce an elevated amount of proteins that encourage cell division in the cell resulting in an increased number of cells [6].

Overtime, these cells will start to lump together and form a tumor which can be either benign or malignant. Benign tumors are stationary and stay in one place while malignant tumors spread throughout the body. Cancer cells can undergo a process called metastasis where they detach from the primary tumor and spread throughout the body to other locations where they can create another tumor. Malignant tumors are more serious due to this reason and harder to treat because if not detected early, then cancer cells can spread throughout the whole body. Also to note that in some cases benign tumors can turn into malignant tumors so it is always wise to get a lump checked out because it may possibly be signs of cancer [7].

Now, we will get into the specifics of the nutrition aspect of this. After getting a better understanding of what exactly cancer is, this portion will now talk about how certain foods can increase the likelihood of developing cancer and how they do so. There are some types of foods that will now be discussed, which can possibly promote the risk of cancer.

1. Processed Foods/Preservatives:
   a. Processed foods such as red meat products such as bacon, ham, hot dogs, etc. have chemicals called nitrates and nitrites. These chemicals can become N-nitroso chemicals that can damage cells that line our bowel. Preservatives also have the same dangers. Preservatives, which are found in frozen and canned foods, have the ability to turn into carcinogens (cancer-causing agents) because they contain nitrites and nitrates. If they mix with gastric acids then they can turn into cancer-causing agents and thus lead to cancer. Therefore it is important to have a diet low in processed foods and foods that have preservatives [8].
2. Alcohol: (can increase liver cancer)
   a. There are multiple ways that alcohol is able to increase the risk of developing cancer. One way is damage to cells. The human body can turn alcohol into a chemical called acetaldehyde, and this chemical damages our cells and stops them

from repairing the damage. Alcohol can also bring changes to hormones. Alcohol can increase levels of hormones such as estrogen and insulin and these increased hormone levels can lead to more chemical messengers and chances of cell signaling going wrong. This can thus increase the chance of cancer development. Thirdly, alcohol can bring changes to cells in the mouth and throat. Alcohol can possibly make the cells in such body parts more likely to absorb harmful chemicals that may lead to cancer. Therefore, it is important to not drink a lot of alcohol as there can be a possible correlation to cancer development [9].

3. Fried Foods:
    a. Fried foods are really delicious ranging from french fries to fried chicken. However, while these foods taste good and fulfilling to eat, they have very negative consequences on the body. Foods that are cooked in high heat are shown to have higher levels of advanced glycation endproducts (AGES). These AGES have been shown to be associated with increased oxidative stress and pro-inflammatory effects. These effects lead to higher chances of cancer development as DNA in cells can be damaged in a more likely manner and thus progress to cancer. It is also important to note that the characteristics of oil/fat exposed to higher temperatures may also be a risk factor. Deep frying changes the chemical structure of oils through oxidation which leads to increased trans fatty acids. These toxic compounds are incorporated in fried foods and metabolized in the gut after being eaten. These compounds, especially acrylamide have been found to be carcinogenic in studies as this compound can damage DNA and induce apoptosis [10].

Cancer Prevention Through Nutrition

This portion of the review will focus on many different types of food that are very helpful in the prevention of cancer. Some specific foods might correlate with specific types of cancers and so it is recommended that people have a variety of different healthy foods in their diet.

Blueberries

Blueberries are simple fruits that buyers can get at the grocery store at any time of the year. The special property of the blueberry is its antioxidant properties. These special antioxidants are anthocyanosides and resveratrol. Anthocyanosides are potent antioxidants that have anticancer properties. They contribute in scavenging activity, stimulation of phase II detoxifying enzymes, and reduced cell proliferation and inflammation. Resveratrol is an antioxidant that is helpful in prohibiting progression of cancer stages. It not only acts as a chemo-preventative agent, but also has chemotherapeutic properties such as anti-inflammation. Research has also shown that blueberries have the ability to help in radiation treatment. They improve the effects of the treatment by making the cancer cells more sensitive to the radiation. It

has also been found that blueberries reduced abnormal cell growth when conducting an experiment on mice giving them a different variety of diets [11].

Mushrooms

Mushrooms are another superfood that have the power of preventing cancer. Just like blueberries, mushrooms provide the special property of antioxidants. These antioxidants are very useful in cancer prevention because the body relies on them to prevent cell abnormality or even cell metastasis. Mushrooms also have a soluble fiber, called beta-glucan, that can boost the immune system. Boosting the immune system can help the body have stronger natural killer cells that will be able to fight off the cancer cells in the body. Studies have shown that eating mushrooms was associated with a lower risk of total cancer but studies have also shown a significant decrease in the risk of developing breast cancer more specifically [12].

Pulses

Pulses are edible seeds such as beans, peas, and lentils. Their endosperms are rich in protein and carbohydrate. Studies have shown that pulses have bioactive compounds that help prevent risk factors for diseases such as diabetes, metabolic syndrome, inflammation, and cancer. Pulses have been found to have the potential to reduce the risk of cancer development and its progression, which may have implications of eliminating malignant cells. DNA damage from free radicals leads to errors in DNA replication during cell cycle, which is essentially how cancer starts, but the bioactive ingredients such as phenolic compounds have antioxidant activity that can scavenge such free radicals. The seed coats of the pulses are rich in these phenolic compounds and so pulses offer outstanding benefits to the human body [13].

Broccoli

Broccoli is infamous for the fact that children hate this vegetable. However, experiments reveal that broccoli and other cruciferous vegetables such as cauliflower and cabbage have anticarcinogenic properties that help prevent cancer. In broccoli, there is a high amount of a phytochemical called sulforaphane. Sulforaphane is a cancer-fighting plant compound that is associated with reduced risk of prostate, breast, colon, and oral cancer. CSC, cancer stem cells, are very dangerous and important in the originating of cancer. These cells have the ability for self-renewal and differentiation capabilities which is the reason why many patients get cancer again even after they have gone through treatment. However, sulforaphane is a compound that might be a preventive measure due to its anti-CSC properties. These compounds can possibly prevent, block, or even revert tumor initiation processes [14].

Walnuts

Walnuts and all nuts have cancer-preventing properties. It is important to note that nuts are different from one another in that each offers a special nutrient or compound that can help in cancer prevention. But specifically with walnuts, they have a substance called pedunculagin,

which the body metabolizes into urolithins. Urolithins are special compounds that bind to estrogen receptors and may play a role in preventing breast cancer while also serving as antioxidants. Studies have shown the possibility of estrogen receptor binding activity that may have cancer suppression abilities. In other studies, walnuts have also been shown to reduce prostate cancer growth. A diet rich in walnuts leads to increased suppression of insulin-like growth factor 1(IGF-1), which is associated with prostate and breast cancer [15].

Tomatoes

Tomatoes are best served when cooked. Tomatoes have a substance called lycopene, which is a carotenoid that can fight cancer, that makes the tomatoes look red. Due to its fatty nature, more lycopene is released when tomatoes are cooked rather than eaten raw. Possible evidence has shown that tomatoes can lead to reduced risk of prostate cancer. Other evidence might suggest potential benefits for lung, esophagus, stomach, colorectal, pancreas, breast, and cervix cancers. Lycopene has been seen to stop cancer cells from growing in laboratory tests as well as prevent chemically-induced carcinogenesis. Thus it is possible that lycopene may promote anti-tumour activity [16].

Garlic

While it may make people's eyes water and breath stinky, garlic is rich in antioxidants that help get off free radicals in the body that can contribute to heart disease, cancer, and Alzheimer's. Most of the positive effects of eating garlic come from organosulfur compounds (OSCs), which originate from allicin. Alliinases are part of the defense system of the plant and are released when the plant is damaged. The OSCs from garlic have been shown to reduce the expression and activation of multiple cell-growth stimulatory proteins. OSCs are also believed to affect cellular redox systems. The activation of cysteinyl S-conjugates in OSCs leads to reactive persulfide or sulfane sulfur progenitors. Research reveals that S-allylcysteine from garlic suppresses the growth of human prostate cancer and the allicin can induce apoptosis (programmed cell death) in a variety of cancer cells. Thus garlic has cancer-preventive properties that make it a superfood to add to diets [17].

Nutrition During Cancer Treatment

Looking at the cancer patient aspect, when people already have cancer there are nutritional challenges that they must face. There are many sorts of treatments that help to deal with cancer such as immunotherapy, chemotherapy, surgery, radiation, stem cell transplant, etc. There are some common side effects from going through these treatments that all contribute to the total nutrition challenges. These side effects include loss of appetite, dry mouth, changing food taste, trouble swallowing, or feeling full after a small amount of food. All of these symptoms pose challenges when planning a diet for cancer patients. There are certain restrictions and limits and thus treatments for cancer patients make it more restrictive on what sort of food they should eat. However, when it comes to proper nutrition for these patients, there are always

common essential points to consider. This includes having foods that are high in calories, protein, vitamins, and minerals. Below are common symptoms that are caused by cancer or cancer treatment and ways to deal with them [18].

1. Loss of appetite

    Having a loss of appetite may lead to anorexia. To deal with anorexia, cancer patients are recommended to have a diet high in protein and calories. These include foods such as beans, chicken, fish, meat, yogurt, and eggs. There are also many different ways to get protein such as having liquid food rather than solid food. These can include blenderized drinks, milkshakes, smoothies, juices, or soup. Another key element is for cancer patients to eat when they are hungry. While they may have a loss of appetite, patients can still feel hungry at times. It is critical to eat during these times because it is when their appetites will be at their peak. Exercising can also play a role in helping patients to use more energy and thus feel more hungry later on and thus allow them to have a larger meal.

2. Nausea

    When feeling nauseous, it is advised that patients eat foods that are appealing and not just favorite foods. It should be foods that smell and look good rather than whatever it is that others are eating or a patient's favorite food. It may also be better for patients who feel more nauseous to eat lighter foods to make them easier to digest. These can include dry foods, soft foods, easy-on-stomach foods, or liquid foods. These can include crackers, bread sticks, toast, yogurt, soup, white toast, etc. It is better to have regular food throughout the day because having an empty stomach can make the nausea even worse but it is also important to eat foods that are light on the stomach.

3. Vomiting

    For patients who are experiencing vomiting phases, they should not eat or drink as long as they feel they are about to vomit. It may also be better to eat multiple small meals throughout the day rather than having a few large meals. This way the vomiting won't get rid of all the food that patients eat at once. It is better to eat a small amount throughout the day so that the vomiting won't get rid of the nutrients from the food that you eat often. It is recommended to take liquid foods rather than eating solids. These can include strained soups such as vegetable soup or clear chicken soup as well as drinking other foods such as a milkshake.

4. Dry Mouth

    Patients who have dry mouths should eat foods that are easy to swallow. This way the mouth will not have to move as much and affect the dry areas. A nice way to make foods easier to swallow is firstly eating liquid food rather than solid food. This can include soups or milkshakes, smoothies or juice. However, other alternatives can include adding sauces to your food to make it more moist and

thus easier to swallow. Another element to making it easier to eat for patients who have dry mouths is to eat foods that make their mouths produce more saliva. Such foods can include candy or gum. These types of foods can moisten the mouth and more saliva is being produced. It is also recommended not to eat foods that are spicy or sour because they can worsen the dry mouth situation.

5. Taste Change

    Taste change can be a more tricky symptom to deal with in nutrition because some patients might respond differently compared to others. However, some key takeaways are to avoid eating red meat, rather replace it with eating poultry, fish, eggs, or cheese because their flavors aren't lost that easily compared to red meat. Another way to deal with taste change is to add more spices or sauces to foods. The marination can add more flavor and make it easier for the patient to enjoy the food. Some patients may have a metal taste in their mouth and to deal with this they can eat with plastic utensils and chew gum or take mints to avoid the taste of metal.

6. Trouble Swallowing

    For patients who are having a hard time swallowing the elements are similar to those of having a dry mouth. Patients should have a diet that is rich in protein and calories. They should also eat lighter foods that are easier to swallow. These can include milkshakes, scrambled eggs, oatmeal, or cooked cereals. Also, people can moisten food by adding sauces or gravy to their food to make it more moist. Foods to avoid are hot, spicy, sour, and crunchy foods since these are harder to swallow and they can cause more pain.

Depending on certain symptoms some patients might require specific diets compared to other patients. It all depends on what kind of symptoms the patient has and how to make a diet plan that fits those accommodations. This section advises on certain symptoms patients have and generalizes what sort of diet is recommended for such patients.

The Role of Specific Nutrients

As previously listed some superfoods help in cancer prevention but it is also important to look at some of the nutrients that are important in lowering the risk of several types of cancer, and the foods that are rich in these nutrients. A nutrient the reader should already be familiarized with is called antioxidant and this is just one sort of nutrient that is important in cancer prevention.

Nutrients/Foods Associated with Cancer and Cancer Prevention:

Glucose: Junk food is bad because it contains a lot of refined sugars. Refined sugars are low in nutrients and provide a high amount of energy. Other forms can be refined wheat flour products, which have less fiber and vitamins B and E. These two carbohydrates make up a large

portion of people's diets. Studies have shown a correlation between an increased risk of cancer and high glycemic load. High glycemic load is a measurement of the blood sugar response of the body to a standardized amount of carbohydrate in a food. Such foods contribute to hyperinsulinemia, which is a dysregulation of glucose metabolism, and therefore they should be avoided. While these nutrients are not helpful in cancer prevention, it is still important to recommend that people avoid these types of foods. Examples of such foods are candy, cookies, ice cream, soda, white bread, cereals, waffles, etc [19].

Fiber: Fiber is a carbohydrate that is useful for regulating blood sugar and keeping hunger in check. While fiber doesn't have a direct correlation with increased cancer risks, low-fiber diets typically mean less plant food intake. Vegetables and fruits provide an adequate amount of fiber so a lack of fiber means a lack in such plants. The lack of such plants can have negative implications on the body and thus increase the chance of getting cancer. It is recommended that people eat about five daily servings of vegetables to reduce cancer risk so having more vegetables in your diet is necessary. Some examples of high-fiber foods include apples, potatoes, avocados, berries, whole grains, etc [20].

Omega 3:6 Ratio Imbalance: Omega 3 fats such as alpha-linolenic acid, EPA, and DHA have been proven in studies to protect from cancer while on the flip side, omega 6 fats such as linoleic acid and arachidonic acid are cancer-promoting fats. Studies have then shown that there is a positive association between a higher ratio of omega-3 to omega-6 fats and a reduced risk of breast cancer. Having more omega-3 fats has a strong implication for cancer prevention and thus is encouraged to be added to the diet. The body is not able to naturally produce omega-3 fatty acids so the body needs to get these fatty acids from a food source. Omega-3 is an immunonutrient and is helpful in cell signaling, it also helps in inflammation and has anti-inflammatory and antinociceptive (painkiller) effects. Inflammation can become harmful to the body because immune cells that fight pathogens release reactive oxygen species, which can damage the DNA of normal cells. Omega-3 thus helps in the reduced amounts of inflammation in the body. Foods that are rich in Omega-3 include fish(salmon, mackerel, tuna, sardines), plant oils (flaxseed oil, soybean oil, canola oil), and nuts and seeds(flaxseed, chia seeds, walnuts) [21].

Selenium: Selenium is a mineral that has anti-cancer properties. Studies have shown the major functions of selenium which include:
1. Selenium is present in the active site of enzymes that catalyze oxidation-reduction reactions and these reactions may encourage cancerous cells to undergo apoptosis.
2. Selenium improves the immune system's ability to respond to infections.
3. Selenium causes the formation of natural killer cells, which fight cancer cells.
4. P450 enzymes in the liver may be induced by selenium, leading to the detoxification of some carcinogenic molecules.
5. Selenium inhibits prostaglandins that cause inflammation.
6. Selenium can decrease the rate of tumor growth.

Thus selenium minerals are very helpful in cancer prevention. Foods that include this mineral are seafood, organ meats (liver, heart, etc.), Brazil nuts, cereals, grains, dairy products, etc [22].

Folic Acid: Folic acid is a vegetable vitamin that has a crucial role in DNA methylation and DNA synthesis. If there is not enough folic acid, the body uses available uracil to substitute thymidine in DNA, which leads to DNA strand breakage. DNA breakage can lead to cancer development as this leads to a mutation. Folic acids are vital nutrients that can help make sure that DNA is copied correctly so cell division can go according to plan. Some foods rich in folic acid include spinach, broccoli, peanuts, asparagus, brussels sprouts, beans, liver, etc [23].

Dietary Strategies for Different types of Cancer

The next part of this article will include different types of dietary strategies for different types of cancer. This section will not be able to cover all the different types of cancers but will attempt to address the more common and general ones. Different cancers require different treatments and with different treatments come different side effects. With all of these precautions in place, dietitians must make sure that the patient has the proper food to eat, which will accommodate all these obstacles.

Common types of cancer and diets include:

Breast Cancer: An important thing that cancer patients must do is stay hydrated. Patients should be drinking at least 2 to 3 liters of water every day. Many side effects from treatment such as vomiting, diarrhea, and loss of appetite can contribute to dehydration. Hydration is necessary for the body because it helps regulate body temperature, blood pressure, and electrolyte balance. Water is also important for organs to filter out wastes and toxins and therefore water is necessary to make sure that the body is properly functioning. Fruits and vegetables are important during breast cancer treatment. Around 5 servings a day is good because fruits and vegetables have antioxidants and anti-estrogen properties which can help patients in their fight against cancer. Vegetables, especially those of the cruciferous family such as broccoli, cabbage, and Brussels sprouts are recommended. Whole grains are also important, with a recommended intake of around 25 to 30 grams of fiber daily. High fiber intakes have been shown to have a positive effect by altering the hormonal actions of breast cancer and other hormone-dependent cancers. Whole grains include those of oats, brown rice, nuts, or legumes. Lean meat and soy are also beneficial because they are good sources of protein. This can include poultry, fish, lentils, and beans. Soy food can be such as tofu, soymilk, or edamame [24].

Skin Cancer: For those with skin cancer it is important to have a well-rounded diet. Staying hydrated is key to having a positive functioning body. For skin cancer important nutrients include those of Vitamin E, lycopene, Omega-3 fatty acids, and zinc. Vitamin E helps protect cells from free radicals and UV light while also improving the skin's overall condition. Vitamin E foods include almonds, peanuts, beet greens, collard greens, spinach, red bell pepper, and sunflower seeds. Lycopene helps to protect the skin from the sun. Foods that are rich in lycopene are red and pink foods such as watermelon, grapefruit, tomatoes, and blood oranges.

Omega-3 fatty acids are good for reducing inflammation while inhibiting the growth of skin cancers. Foods rich in omega-3 fatty acids include walnuts, flaxseed, and fish. Zinc is an immunity booster that helps the body fight against cancer and foods including red meat, poultry, baked beans, and nuts are good sources. These are some important nutrients that are good for the skin when dealing with skin cancer and are recommended to be incorporated into diets [25].

Lung Cancer: Once again, staying hydrated is important. Make sure that the patient is drinking a lot of water. A recommended meal plan for lung cancer patients is to eat small frequent meals throughout the day. This will help the body get enough calories, protein, and nutrients to tolerate treatment. Protein is good for the body because it helps repair cells and tissues. Foods rich in protein are lean meats, eggs, low-fat dairy products, beans, and soy foods. Next are whole grain foods which are a good source of carbohydrate and fiber which keeps energy levels up. These foods include oatmeal, whole-wheat bread, brown rice, and pasta. Vegetables are a must. Fruits and vegetables provide important antioxidants and these can be whatever the patient chooses to have. Just try to have at least 5 servings of whole fruits and vegetables daily [26].

Prostate Cancer: An important note is to keep drinking water to stay hydrated and keep bodily functions properly maintained. During prostate cancer, the treatment may affect appetite, eating habits, and weight. Some men should avoid weight loss by getting enough calories daily while others who are overweight should lose some weight in moderation. Important essential nutrients the body needs are protein, carbohydrates, fiber, vitamins, and minerals. Lean protein is good for the body and includes eggs, lentils, chicken, and beef. Plant-based foods help with a lot of nutrients and minerals and these include fruits, vegetables, and whole grains. As previously mentioned, similar foods can be eaten in this situation. Low-fat dairy products include those of yogurt and hard cheese. Patients must avoid eating processed foods and undercooked red meats because these can contribute to the recurrence of the disease [27].

Colon/Rectal Cancer: Again, it is important to be drinking water. If you have colon/rectal cancer, then a dietary fiber intake is advised. Fiber-rich foods help with constipation side effects of treatment. These can be foods such as whole-wheat bread, brown rice, legumes, or lentils. These are good sources of protein, fiber, vitamin B, and vitamin E. Patients should also have a nutritious diet eating healthy foods like vegetables, whole grains, and nuts, and consume protein in moderation such as fish and poultry [28].

Leukemia: Patients should drink water throughout the day to have a healthy body. For patients who have leukemia, it is advised to have a good breakfast. Starting the day with a good breakfast can help to make the rest of the day easier to manage. A good breakfast includes porridge, beans/egg on toast, or a breakfast smoothie. Another important aspect of food is carbohydrates. Carbs should be around a third of the meals that patients eat. Carbohydrates are found in foods such as wholewheat pasta, brown rice, whole-grain bread, or potatoes. Vegetables and fruits are also advised to eat. 5 servings a day, vegetables are packed with vitamins, and minerals, and are a good source of fiber. Protein is also important for the body for proper growth and repair and includes beans, lentils, fish, meat, and eggs. Another crucial aspect of food that is

vital for energy is iron. Iron is found in foods such as beans, nuts, dried fruit, whole grains, and dark-green leafy vegetables [29].

Recipes and Meal Plans

This portion (pun intended!) will cover multiple recipes and meal plans for cancer patients. There are a variety of meal plans and this section will try to detail how each of those foods is good and how exactly to make these foods.

Meal Plan:

Breakfast

Mango Lassi- This is an easy-to-make smoothie that is easy to drink and digest and can help with nausea. The Mango Lassi requires around 10 minutes to make and requires ingredients of 2 cups of chopped mango, ½ cup whole-milk yogurt, ½ cup coconut milk or whole milk, 1 teaspoon lime juice, 1 teaspoon honey, a pinch of cardamom, and 6 ice cubes. After getting all of these ingredients, put them all into a blender and pulse until smooth. This light breakfast has 260 calories, 15g of fat, 3g of fiber, 5g of protein, 12g of saturated fat, 35mg of sodium, and 28g of sugar [30].

Banana Bread Muffin- This is a simple muffin made out of banana bread. This is light on the stomach but requires a bit more steps to create. Total cooking time will require 35 minutes. Gather ingredients of 1 stick of butter, ¾ cup brown sugar, ½ cup plain Greek yogurt, 2 eggs, 1 teaspoon vanilla, 2 cups flour, 1 teaspoon baking powder, ¼ teaspoon baking soda, ½ teaspoon cinnamon, ¼ teaspoon ground ginger, ½ teaspoon salt, and ½ cup mashed overripe banana. To create the muffins, first, preheat the oven to 350 Fahrenheit degrees (180 Celsius degrees) and line a 12-cup muffin tin with muffin cups or parchment paper. Then in a large bowl, cream butter with brown sugar, yogurt, eggs, and vanilla, and whisk in banana. Then in another bowl, whisk flour, baking powder, baking soda, cinnamon, ginger, and salt. After that, mix the wet and dry ingredients in a large bowl until combined. Then put the batter in a muffin tray and bake it in the oven until golden (around 20 to 25 minutes). This meal has 210 calories, 9g of fat, 1g of fiber, 4g of protein, 180mg of sodium, and 14g of sugar [30].

Breakfast Egg Cups- These egg cups are a delicious treat and are a great low-fiber alternative to muffins and other breakfast foods. The total time to cook this meal is 25 minutes. Ingredients required are cooking spray, 1 small russet potato (peeled and diced), 8 eggs, ½ cup cottage cheese, 2 ounces cheddar cheese (grated), 1 small bell pepper (chopped), and 2 tablespoons of ketchup. To create this meal, first preheat the oven to 350 Fahrenheit degrees (180 Celsius degrees) and grease a muffin tray. Then place the potato in a microwave, cover, and microwave for 5 min and let it sit for 5 minutes. In a large bowl beat the eggs, add cottage cheese, cheddar, bell pepper, ketchup, and cooked potato. Then put the mixture into the muffin tray. Finally, bake until the tops are golden and this should take around 15 to 18 minutes. This

meal has 160 calories, 240mg of cholesterol, 7g of fat, 1g of fiber, 13g of protein, 260mg of sodium, and 5g of sugar [30].

Salad and Soup

Crunchy Chicken Salad- This is a delicious salad option to eat either during lunch or dinner. However, this is not a good meal for those on a Low Microbial Diet. Ingredients required are 2 cups cubed jicama, 2 tablespoons light mayonnaise, and 8 oz (240g) cooked chicken breast or turkey breast (cubed). 1 red bell pepper (cut into quarters), 4 cups salad greens, salt and pepper, 1 tablespoon freshly squeezed lime juice, and ½ tablespoon crushed dried tarragon or dried thyme leaves. To create this meal, first, preheat the boiler, line the baking sheet with foil, and place bell pepper on the foil. Broil 6-8 inches away from the heat until the pepper skin is blackened (about 12 minutes required). Then let it cool slightly and remove the skin. Then in a large bowl, toss the pepper, chicken, and jicama. In a smaller bowl, stir mayonnaise, lime juice, tarragon, salt, and pepper. Then pour this over the chicken mixtures. Cover and refrigerate for at least 2 hours and then it is ready to serve. This meal has 143 calories, 5g of fat, 18g of protein, 4g of fiber, and 105mg of sodium [31].

Hot and Sour Soup: A delicious and thick soup from Chinese cuisine. Ingredients required are 1 cup sliced fresh mushrooms or 4 dried black Chinese mushrooms, 1 can fat-free reduced-sodium chicken or vegetable broth, 1 tablespoon minced ginger root, 2 scallions (chopped), 1 cup finely chopped bok choy cabbage, ½ can bamboo shoots, 1-2 tablespoons hot pepper oil or sauce, ½ cut extra firm tofu, 1 tablespoon cornstarch dissolved in ¼ cup cold water, 1 tablespoon rice wine vinegar, 1 tablespoon lite soy sauce, and 1 egg white. If using the dried mushrooms first soak in water for around 15 minutes, remove stems, and slice. In a large saucepan bring the broth to boil. Reduce heat to simmer and add ginger, scallions, cabbage, and bamboo shoots, Cook for 3 minutes, add pepper oil, vinegar, soy sauce, tofu, and mushrooms, and simmer for 3 more minutes. Set broth over medium heat and slowly pour in cornstarch mixture while stirring, until soup thickens, Then add egg white while stirring to form long strands, and add reserved ingredients. This meal has 108 calories, 3g of total fat, 11g of protein, 2g of fiber, and 624mg of sodium [31].

Main Course Meals

Egg, Spinach, and Bacon Sandwich- Similar to a BLT(bacon lettuce tomato sandwich) but has egg and spinach rather than tomato and lettuce. This is an okay meal for those on a Low Microbial Diet. Ingredients required are vegetable oils spray, ¼ cup skim milk, 4 one-ounce slices low-fat cheese, 8 fresh spinach leaves, 4 eggs, 1 tablespoon imitation bacon bits, ⅛ tablespoon black pepper, and 2 six-inch white or whole-wheat pita rounds, split crosswise. To make this meal, first spray a medium skillet with vegetable oil. In a small bowl, stir together eggs, milk, bacon bits, and peppers. Then place the skillet over medium heat, add the egg mixture, and cook without stirring until the mixture begins to set on the bottom and around the

edges. Then use a large spoon or spatula to lift and fold partially cooked eggs so the uncooked portion flows on the bottom. Then continue cooking for 2-3 minutes until the eggs are cooked throughout. Line each pita pockets with spinach and 1 slice of cheese and spoon warm egg mixtures into pita pockets. This meal has 185 calories, 5g of fat, 16g of protein, 15mg of cholesterol, and 701mg of sodium [31].

Grill Ginger Tuna: An excellent choice of fish that will have omega-3 benefits. Ingredients required are 1 pound of fresh tuna (boneless and skinless), 1 tablespoon canola oil, 1 tablespoon grated peeled fresh ginger, 1 small jalapeno chile (minced), ¼ tablespoon salt, fresh ground black pepper, and 1 tablespoon freshly squeezed lime juice. To make this meal, first prepare a BBQ grill to medium-high. Cut the tuna into 16 equal cubes and place them in a bowl. Add canola oil and toss fish to coat. Add ginger, jalapeno, salt, pepper, and lime juice. Then toss and mix well. Divide tuna cubes evenly among skewers and grill for 4 to 5 minutes, turning frequently using tongs. The fish is done when it is slightly cooked and no longer pink on the inside. The meal has 134 calories, 2g of total fat, 27g of protein, 0g of dietary fiber, and 187mg of sodium [31].

Bean Surprise- A bean surprise which is a meal based on beans. Ingredients are 15 oz (450g) black beans, 1 tablespoon olive oil, 2 tablespoons yellow mustard, 4 large wheat tortilla shells, 1 tablespoon cumin, 2 tablespoons low sodium soy sauce, and 4 oz (120g) shredded mozzarella cheese. To make this meal first rinse the black beans and rinse away the liquid around the canned beans. Combine black beans, cumin, olive oil, low-sodium soy sauce, and yellow mustard in a pan on medium heat. Then stir beans and other ingredients together while heating. Then mash the beans slightly to make the mixture a little sticky. Divide the mixture into 4 portions and place each portion onto half a large tortilla shell. Then sprinkle 1 oz (30g) of shredded cheese onto the beans on each tortilla. After that, place 1 teaspoon of olive oil and spread around to coat a flat skillet and heat the skillet to medium heat. Fold the tortilla in half and press down to stick together to create a half-circle shape. Then place a tortilla on the skillet, heat each side, and heat until the cheese melts and the tortilla is brown. This meal has 225 calories, 11g of protein, 6g of fat, and 9g of fiber [31].

Lifestyle and Behavior

Cancer can occur for many different reasons, so it is hard to pinpoint exactly what factor caused cancer growth in a patient. However, some distinct lifestyles and behaviors can significantly influence the growth of cancer. Diet is one of the major factors, however, this segment will focus on other factors beyond the scope of diet that can help in cancer prevention and recovery. Exercise and stress management are just a few examples of how one can better themselves in cancer prevention and recovery.

Lifestyle Factors [32]:

Smoking: It is no surprise that smoking is one of the biggest factors among lifestyle choices that induce cancer. Tobacco has many carcinogenic chemicals and by smoking this substance all those chemicals enter the lungs and the body systems. Scientific studies have shown the science of how tobacco smoke can induce activation of NF-κB, which is a major component that can cause inflammation in the body and cause cancer by damaging DNA. Damaged DNA eventually leads to cancer as cells can start to multiply without control. Smoking can lead to many different types of cancer, but its main contribution is lung cancer. Smoking is a direct way to put these chemicals into the lungs leading to damaged lung cells, which can then lead to cancer. Thus living a life of no smoking would be the best option. However, not everyone can quit smoking immediately because it is a form of addiction and therefore therapy or a healthier substitution to smoking is advised.

Alcohol: Studies have shown that alcohol consumption can become a risk factor for cancer of the upper aerodigestive tract as well as cancer of the liver, pancreas, mouth, and breast. While not fully understood, current studies believe that ethanol which is found in alcoholic drinks plays a role in cancer development. Thus while not being a carcinogen, ethanol can be considered a co-carcinogen. While ethanol doesn't induce cancer alone, it can amplify the carcinogenic effects of other chemicals. When ethanol is metabolized, acetaldehyde and free radicals are generated. Free radicals are dangerous to the body as they can bind to DNA and proteins and ultimately damage DNA. Other chemicals from alcohol induce the production of cytochrome P-4502E1, which is also associated with the production of free radicals. Alcohol can play a role in cancer growth, however, data shows that the incidence of cancer caused by alcohol consumption is considerably lower compared to other factors like smoking. Thus this is not to say to not stop drinking alcohol, but rather to drink alcohol in moderation.

Sun Exposure: Too much sun exposure can also be damaging to the human body and especially to the skin. The sun releases ultraviolet (UV) radiation which is a type of energy that can cause skin cancer. The main two types of UV rays are UVB and UVA. The UVB ray reaches the outer layer of the skin and causes problems such as sunburns. UVA on the other hand reaches deeper into the inner layer of the skin and is responsible for aging the skin, but doesn't account for problems such as sunburn. Studies have shown that UV induces unique types of p53 mutations in skin cancers at a high frequency. P53 is responsible for tumor suppression and by mutating it there is less control of cell division. Too much UV radiation can damage DNA in skin cells and enough DNA damage over time can cause cells to grow out of control which can then cause skin cancer. To avoid sun exposure, stay indoors more and less outside. When outside make sure to wear sunscreen at the recommended amount and time and also wear other accessories to block sunlight such as hats or sunglasses.

Stress: Chronic stress has been shown to induce tumorigenesis and promote cancer development. Stress can activate the HPA axis, and the SNS, and cause immune disorders and inflammatory responses. Excessive levels of stress hormones promote carcinogenesis by inducing DNA damage accumulation, increasing p53 degradation, and other pathways. These hormones can also prevent immune cells from effectively controlling cancer cells by increasing

inflammation and suppressing immunity. They can also act on tumor and stromal cells in the tumor microenvironment to promote tumor growth, invasion, and metastasis. It is important to reduce the amount of stress that one has on their body. To manage such amounts of stress it is recommended to get away from one's root cause of stress, get therapy, or pursue a new passion/hobby to reduce stress hormone production.

Obesity: Obesity is another major factor that contributes to higher chances of getting cancer. Obesity is an established predisposing factor for many malignancies, specifically breast and colorectal cancer. Excess fat in the body involves altered fatty acid metabolism, extracellular matrix remodeling, secretion of adipokines and anabolic and sex hormones, immune dysregulation, and chronic inflammation. Evidence also indicates that obesity may also increase the risk of recurrence in early-stage cancer. This means that as a cancer patient, one must be careful of their diet to make sure that they aren't eating more than the daily recommended amount and gain excess fat as this can lead to recurrence of cancer. To keep a safe weight one should make sure to follow a healthy diet and not overeat. It is also important to include healthy exercise to help keep their body healthy and also not overweight.

Exercise: Exercising offers many health benefits and is essential to having a healthy body. By regularly exercising, one can help their body and brain perform better, feel less fatigue, lessen depression and anxiety, possibly sleep better, improve physical ability, improve muscle strength and bone health, strengthen their immune system, increase appetite, and help maintain a healthy weight. Physical activity is very important for both those who have cancer or don't . Physical activity helps to keep the body balanced and evidence even shows a higher chance of no recurrence of cancer in those who exercise regularly. Whether it be walking outside more often or running a whole marathon, exercising regularly is important and should be done by everyone.

Conclusion

And with that our summarized and simplified version of the connection between Nutrition and Cancer comes to a conclusion. Making healthy choices is important for the body and eating in an unhealthy manner can lead to negative consequences. Eating junk food and fatty foods and consuming alcohol are just some of the bad choices that can potentially lead to you developing cancer in your body. While it may be impossible to entirely avoid these foods all the time, it should be warned that people should eat these types of foods in moderation. Cancer can develop from these foods as there are harmful carcinogens that can lead to cancer. Whether you are a cancer patient or not, having a healthy diet is one of the few steps to leading a healthy life. Along with having a healthy diet many other aspects of the body are as equally important to be taking care of. Mental health and physical exercise and avoidance of the sun are just some of the examples mentioned previously and should be implemented into one's life to be living healthier. Eating healthy fruits and vegetables doesn't always guarantee that you won't get cancer, but it is important to keep in mind that eating such foods greatly reduces the likelihood of developing cancer. Eat foods that are healthy and there are many recipes that can be found online, or you can

create your own recipe. Don't eat your way to death but rather eat your way to a healthier life and so I encourage everyone to eat healthy and live a healthy lifestyle to reduce the chances of getting cancer, but cancer is afterall a very scary and possibly life-threatening disease.

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Exploring How Anticancer Peptides Perform and Fight Leukemia By Beatrice Barbieri

Abstract

Every year in the United States, more than 60,000 people get a leukemia diagnosis and about 23,000 people die annually from it (Leukemia and Lymphoma Society). Leukemia is the sixth-leading cause of cancer deaths among men. The current and traditional treatments that medicine is currently using are often unsatisfactory and offer limited hope. The outcomes of these cures clearly highlight the need for new advanced therapies for leukemia like anticancer peptides. Anticancer peptides are wonders in the world of cancer research. These types of peptides are special proteins that have the power to target and fight against cancer cells; they come from three different types of peptides: naturally occurring or derived from a known protein, cell penetrating peptides and tumor targeting peptides. In this article we will discuss how anticancer peptides work and how they impact leukemia treatments. These types of treatments are very promising, many new therapies are currently being used to treat cancer. Among these new methods, chemotherapy based on peptides has been of great interest due to the unique advantages of peptides, such as a low molecular weight, the ability to specifically target tumor cells, and low toxicity in normal tissues.

Leukemia: Disease Overview, Current Treatments, and Limitations

The cells that make up the corpuscular part of the blood (red blood cells, white blood cells and platelets) originate from immature cells, also called stem cells. These cells are produced by the bone marrow, a gelatinous tissue contained within the spongy part of the flat bones in the adult and long ones in children (Agenzia Zoe). In people affected by leukemia, there is an uncontrolled proliferation of these stem cells, called leukemia cells or blasts, which interfere with the growth and development of normal blood cells. Leukemias are commonly divided into acute and chronic, based on the speed of progression of the disease. In acute leukemia, the number of tumor cells increases rapidly and the onset of symptoms is early, while in chronic leukemia the malignant cells tend to proliferate more slowly, although they accumulate in greater quantities. Over time, however, even the chronic forms can, in a variable percentage of cases, become aggressive. Another important distinction concerns the cells from which the tumor originates. If the disease arises from the lymphoid cells of the bone marrow (from which white blood cells called lymphocytes develop) it is called lymphoid leukemia, if instead the starting cell is of the myeloid type (from which different red blood cells, platelets and white blood cells develop from lymphocytes) is called myeloid leukemia. Therefore, the most common types of leukemia are four: acute lymphoblastic leukemia (ALL); chronic lymphocytic leukemia (CLL); acute myeloid leukemia (AML); chronic myeloid leukemia (CML). There are also other rarer types of leukemia, such as hairy cell leukemia.

Therapy Options

Treatment depends on the type of leukemia, its stage, and whether the disease is in the

acute or chronic phase (Agenzia Zoe). Age at the time of diagnosis is also important. The treatment of leukemia often makes use of the use of multiple therapies in combination or in sequence, with the aim of offering patients remission of the disease and in some forms also definitive recovery, or in any case the best possible quality of life. Chemotherapy includes one or more drugs administered by mouth or intravenously; if leukemic cells are present in the cerebrospinal fluid, chemotherapy drugs can also be administered by means of a needle inserted through two lumbar vertebrae. Chronic myeloid leukemia was the first tumor form for which a molecularly targeted drug, called imatinib, was developed, which inhibits the protein produced by the BCR-ABL fusion gene. Subsequently, many other targeted therapies active in leukemia have been developed. Then there are therapies that stimulate the immune system to recognize and destroy leukemia cells. In some leukemias, for example, interferon alpha is used to slow the growth of tumor cells, or monoclonal antibodies that target leukemia cells, favoring their destruction by the immune system.

CAR-T peptide-based cells treatments

An innovative therapeutic approach for the treatment of certain leukemias that do not respond to conventional treatments is immunotherapy with CAR-T peptide-based cells (Agenzia Zoe). CAR-T peptide-based cells are the patient's own T lymphocytes which are genetically modified so as to be equipped with the CAR molecule (chimeric antigen receptor). Thanks to this molecule, once they are reintroduced into the patient, the CAR-T peptide-based cells specifically and with great efficiency recognize the tumor cells to be killed.

In some cases, hematopoietic stem cell transplantation is used to replace diseased cells, destroyed with high doses of chemo or radiotherapy, with healthy cells from a compatible donor. Often the donor is a sibling or family member, but it can also be a stranger who has cells compatible with those of the patient. In some cases this approach manages to definitively cure the disease, especially in younger patients, and can be used for forms that no longer respond to chemotherapy. Radiotherapy and surgery, however, have a marginal role in the treatment of leukemia.

Anticancer Peptides: Mechanisms and Utilization in Leukemia Treatment

Of the existing treatment strategies for cancer, anticancer peptides have been proposed as an effective modality that is expected to overcome the limitations of traditional treatment schemes (Chinnadurai et al. ScienceDirect). Antimicrobial peptides that exhibit anticancer activity are called anticancer peptides (ACPs). ACPs are small, cationic peptides that contain 5–50 amino acids. ACPs possess a variety of structures; e.g., Tritrpticin and Indolicidin have extended linear structures, whereas other ACPs possess α-helices in their secondary structure (e.g., LL-37, BMAP-27, BMAP-28, Cercopin A, etc.) or fold into β-sheets (e.g., Defensins, Lactoferrin, etc.). Compared to normal cells, cancer cells exhibit a number of diverse properties, including the presence of a negative charge on their cell membranes, high membrane fluidity, and microvilli on their cell walls. ACPs can interact with the negatively charged cell membrane

of cancer cells via electrostatic interactions and subsequently lead to necrosis i.e., selective killing of the cancer cells. ACPs can also exert anticancer activity by other well-known mechanisms, including induction of apoptosis (i.e., lysis of mitochondrial membranes), inhibition of the angiogenesis pathway, or recruitment and engagement of immune cells to kill the cancer cells (Figure 2). In addition, ACPs can promote pore formation and even activate essential proteins that eventually lead to the lysis of the cancer cells summarizing the functional mechanisms of ACPs activity. The major advantage of ACPs is their low tendency to promote the development of drug resistance, unlike conventional chemotherapeutic agents. Moreover, some ACPs can even be utilized for the intracellular delivery of cancer drugs, which further improves the drug permeation and therapeutic effects. Currently, a number of naturally occurring and synthetic peptides are undergoing clinical trials as anticancer therapies. However, compared to natural peptides, synthetic ACPs have higher stability and sensitivity.
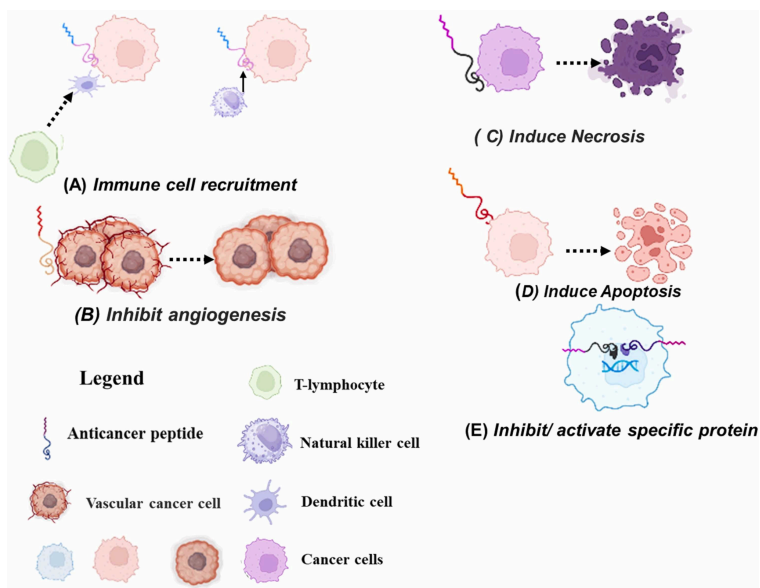
Figure 1. This figure presents the role of ACPs in the treatment of cancer, with a focus on their specific mechanisms of action and the challenges of this treatment pathway. This figure is reproduced with permission under the Creative Commons License 4.0.

Most of the effective natural peptides have α-helical structure with cationic properties; however, some of the other natural ACPs have different folds patterns and may be anionic in nature (Chinnadurai et al. Biomedicine & Pharmacotherapy), (Leukemia and Lymphoma Society). For example, natural peptide extracted from Lentinus squarrosulus mushrooms can kill human lung cancer cells via apoptosis. ACP isolated from Bombina orientalis has antiproliferative activity. This review presents the role of ACPs in the treatment of cancer, with a focus on their specific mechanisms of action and the challenges of this treatment pathway. Anticancer peptides can bind to and activate immune cells such as natural killer cells (NK), and

the activated immune cells can kill cancer cells. ACPs also stimulate dendritic cells to present cancer antigens that bind to receptors on T lymphocytes, which ultimately stimulates an immune response against cancer cells. (Figure 2) ACPs can inhibit angiogenesis by causing the death of vascular endothelial cells that line blood vessels or prevent the growth of new blood vessels by blocking the action of the VEGF. ACPs can induce necrosis in cancer cells by disrupting the cell membrane, damaging DNA, and affecting cell signaling pathways in cancer cells. ACPs can induce apoptosis in cancer cells by disrupting the mitochondrial membrane of cancer cells (figure 2). ACPs can activate (or inhibit) specific proteins that prevent (or promote) the progression of cancer. Anti-cancer peptides (ACPs) specifically target cancer cells and act at different stages, such as initiation, promotion, and progression. ACPs have tremendous potential over chemotherapeutic agents, such as higher specificity, more substantial tumor penetration, lower side effects, and easier modifications. Several mechanisms for the antitumor property of anti-cancer peptides have been recognized, which are discussed below in detail. Figure 1 shows the mechanism of action of a few ACPs. Anti-tumor peptides (ACPs) bring hope to the world of cancer research. In fact, researchers are currently exploring new peptides coming from different sources: natural proteins, synthetic, animal or bacterial peptides. ACPs are chains of amino acids that have been shown to exclusively target cancer cells without necessarily having to target healthy cells.
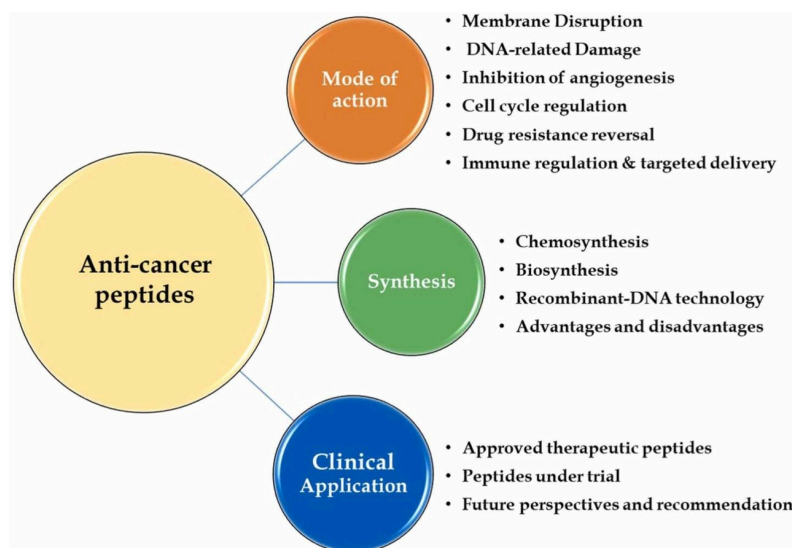
Figure 2. This figure presents an updated overview of different anticancer peptides, their mechanisms of action and current production strategies employed for their manufacture. This figure is reproduced with permission under the Creative Commons License 4.0.

In 2013, Duke University conducted a new clinical trial for patients with hematological cancer (Duke University). The purpose of this study was to determine the safety and effectiveness of administering Wilms tumor gene 1 (WT1) cancer peptides. Cancer peptides are short pieces of protein that are made in a laboratory to be like the peptides that can be found in cancer. These peptides are intended to be given as a "vaccine" to activate the immune cells in a person to attack his/her cancer. These peptides are mixed with an oily substance called Montanide ISA-51 and a white cell growth factor called Granulocyte-macrophage colony-stimulating factor (GM-CSF), which may help make the immune response stronger. Two subgroups with 2 dose cohorts of up to 6 patients each will be enrolled in this exploratory study in order to attempt to obtain immunologic and clinical data on patients with a variety of hematologic malignancies and amongst those in remission and early relapse. The 2 subgroups of patients will be treated with different schemas depending upon whether they are undergoing or have undergone autologous or allogeneic stem cell transplantation. In conclusion, for this type of therapy there is more work that needs to be conducted, but there is much hope for improving treatments and patient outcomes.

Conclusion

The article sheds light on the current leukemia treatments and how anticancer peptides are starting to lead the road to new therapies in the cancer field. Since every year in the United States the death and diagnosis rate for leukemia are still very high it is important to continue researching and exploring new therapies that can help people survive. Treatments are lacking and the ones in circulation right now are not efficient as they should be. This article leads to novel ideas, innovation for treatments and exposes new material to be analyzed. There's more research that needs to be done but this is paving the way for finding a cure.

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How 3D Printing Has Changed the Landscape of Prosthetic Devices by Atri Shankar

When I was younger, I was in awe of 3D printers after seeing the first versions of commercial products at family trips to a local makerfaire. But I always questioned what these machines could really mean for the world, thinking. "They're so expensive now, but in the future could they become something that could help everybody someday?"

Today, I am excited to say that this is the case. This is especially true for those in need of artificial limbs. 3D printing and rapid prototyping technology has not only transformed mechanical prosthetics to be widely manufacturable and accessible, but has also allowed for a significant improvement in the development and testing of prosthetic devices.

Affordability and Cost-Effectiveness

3D printing has allowed for increased accessibility, affordability and cost-effectiveness of prosthetic devices. According to the World Health Organization, an estimated 35–40 million people globally require prosthetics and orthotics services (Chadwell et al. 1). It is clear that prosthetics are in extremely high demand, but that need is not completely fulfilled.

In low-income countries, there are only a few big cities capable of providing reasonable healthcare conditions, and travel to these cities from rural areas is usually complicated, expensive, and long (Cuellar et al. 1). Local prosthetic workshops are limited and hard to manage due largely to the high price of these devices, often costing thousands, if not tens of thousands, of dollars.

But recently, 3D printers have decreased dramatically in price, and more people have access to printers than ever before. In the last few years, quality printers have become available for $200-$300, with some extra-budget options going down to $100. This newly lowered price encourages communities to provide 3D-printed prosthetic limbs to amputees facing financial constraints.

One such community that serves to help people is e-NABLE. Funded by global donations and comprised of a network of over 10,000 people, makers involved in the e-NABLE network manufacture prosthetic arms and hands; due to the cost-effectiveness of 3D printing, a typical prosthetic arm is priced as low as $30-50, and designs for each hand are publicly available for anyone to print. In many e-NABLE chapters across the world, these arms are made with no cost to the patient ("Enabling the Future").

Processes to make affordable 3D printed prosthetics are happening worldwide, such as an automated production line developed by scientists at the Israel Institute of Technology in March 2021 ("Global 3D Printed"). With these types of systems, corporations investing in the development of these prosthetics will contribute to a significant rise in market share and investments. In 2020 for example, the market was valued at $91.163 million and its compound annual growth rate is expected to be 31.50% over the forecast period to reach a total market size of $619.961 million by 2027 ("Global 3D Printed"). As these numbers indicate, the market will likely skyrocket and expand as rapid prototyping and manufacturing evolve. Costs will continue

to go down and more prosthetic labs and workstations will open across the world to continue to serve those who need limbs.

Material Flexibility and Patient Centric Design

3D printing has not only changed the accessibility of prosthetics, but has surpassed traditional manufacturing technologies in its ability to print using wide ranges of materials and creating complex shapes otherwise impossible. Before 3D printing technology, prosthetics were being made using techniques such as injection molding and vacuum forming for plastics and complex cutting, rolling, and welding techniques for metals. But these processes all take significant time, resources and people to start, operate and maintain, as each material needs a specific chain of machines to use.

However, 3D printing can bypass these complex systems through multiple methods such as fused deposition modeling (FDM), selective laser sintering (SLS) and stereolithography (SLA) that each can work with ranges of materials. Plastic, a safe and cheap material, is widely used in the form of PLA, polylactic acid. Other materials such as acrylonitrile butadiene styrene (ABS), polyethylene terephthalate glycol (PETG), thermoplastic polyurethane (TPU) and even carbon fiber-infused plastics can also be utilized with FDM technology, which melts the filament (a roll of material in string-like form) into a liquid and puts layer over layer of material that naturally dries to take the desired shape. Resins are used as part of the SLA process, which uses a laser to cure a vat of resin in layers, creating complex yet detailed and smooth geometries. TPU and other soft materials can be used to make prosthetics more soft and pliable for certain uses.

Researchers at Northumbria University studying the design of 3D printed upper limb prosthetic sockets have found that a selection of advanced materials, such as thermoplastics, mixed materials, and resins, is important to determine the best material based on the needed mechanical properties, biocompatibility, and resistance to wear and tear (Xu and Qin 6). The versatility of 3D printing technology enables prototyping and manufacturing with many different materials that best suit the end user.

Additionally, 3D printing creates support structures to hold overhangs in place, allowing for more complex shapes that no other manufacturing method can create as quickly and for models to be easily scaled up or down to fit a certain patient. This customization is integral to the comfort and functionality of a prosthetic.

As a report from the Journal of NeuroEngineering and Rehabilitation highlights, "Allowing for personalization of the outside of the prosthetic will help prevent non-use of the device. Adding customizable options to the aesthetics of prosthetics can be valuable in making the person feel like it is their own" (Chadwell et al. 2). Unlike previous manufacturing technology, 3D printing can create unique geometries and curvatures that can add to the aesthetic of a device and make someone feel more connected with their device.

Recent Advancements in Prosthetics

The advent of 3D printing will push research on prosthetics and biomechanics to a new level, as rapid prototyping technology will allow for smaller lead times in projects and faster testing of prosthetic parts and mechanisms. This may prove particularly helpful for prosthetic arms. There are multiple types of prosthetic arms: passive, myoelectric, hybrid and body powered. Passive prosthetics do not have any motion and serve as a cosmetic to replace a limb. Myoelectric limbs use electroencephalograms (EEGs) to detect electrical signals from the brain and convert these signals into movement in an arm powered by motors. A hybrid arm uses a mix of mechanical movement from the elbow and electric systems to actuate joints and fingers. Body powered prosthetics utilize the motion of a wrist or elbow to actuate joints, typically with cords connected to the controlling joint to create tension. They serve as highly functional replacements that can be lightweight, waterproof, and have natural feedback through resistance in the clamping mechanism (Philipson 3).

3D printing allows for the development of all of these arms, especially body-powered limbs. Even with no engineering experience or communication with prosthetics corporations or other external groups, anyone can print and assemble these cost-effective devices. But more importantly, large organizations, research groups, and companies can utilize 3D printing as a rapid prototyping technology (RPT). RPT offers many advantages when fabricating and manufacturing custom prosthetic devices, allowing for more design possibilities/freedom, more functional mechanisms, greater cost efficiency, shorter lead times, and an overall better end product. This is especially important for areas of the arms and legs that have more complex curvature and would require significant time to fabricate with traditional manufacturing methods (Barrios-Muriel et al. 2).

Rapid prototyping can create parts and assemblies extremely quickly, both dramatically reducing lead time on devices and improving testing capabilities of certain mechanisms or parts. A design can go through many more iterations and feedback, especially when no third party manufacturer/printer is involved; prototyping can become completely independent and domestic.

Additionally, joint function is vital to the function of an entire prosthetic device, and the fitting of sockets and joints can be expedited and controlled more effectively through the use of 3D printing. Rapid prototyping, FDM, SLA and SLS technology facilitate the creation of non-assembly linkages and sockets, which can fabricate a mechanism in one piece without any extra assembly or construction necessary. Precise detailing and a multitude of manufacturing methods were previously used to achieve this same feat, but with 3D printing, all of these small tasks can be completed in one fell swoop (Xu and Qin 6).

Conclusions

3D printing has changed every facet of prosthetic technology, providing endless customization solutions, and making rapid advancements in functionality, all while addressing the cost barriers that keep many from living more fulfilling lives. As technology continues to evolve, the integration of 3D printing into prosthetic devices holds promise for further innovations and improvements in the lives of individuals with limb differences. While challenges

persist, ongoing research and collaborative efforts hold the key to unlocking the full potential of 3D printing in the field of prosthetics.

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Harnessing AI: Revolutionizing Cancer Care and Research By Maria Shuboderova[1], Darnell K. Adrian Williams[2]

Abstract

Introduction/Background

Following heart disease, cancer is the second leading cause of death, with approximately 609,820 deaths predicted to occur in the United States in 2023. With this in mind, identifying more sophisticated and efficient methods of diagnosing cancer is crucial. This paper discusses the promising role of artificial intelligence in the field of cancer, focusing on convolutional neural networks and other deep learning models.

Methods

We conduct a literature review, in which peer-reviewed articles in BioMed Central, Pubmed, Google Scholar, Nature, Science Direct, and National Cancer Institute (NCI) databases are analyzed, focusing on publications between 2016 and 2023. Through the use of the developed inclusion and exclusion criteria, the articles utilized in this paper are narrowed down to 101 articles. Articles are only selected if published within the last seven years and contain important keywords, such as "artificial intelligence", "cancer", and "machine learning".

Results

AI models have proven effective in the early diagnosis of many cancers through imaging and pathology, including lung, breast, gastric, and prostate cancer. Indeed, deep learning models such as convolutional neural networks have proven to be highly accurate in their validation test sets, in which several reached high accuracies comparable to expert physicians.

Discussion/Future Work

As cancer continues to have a grave impact on individuals worldwide, it is crucial to develop more efficient methods for cancer diagnoses. In the near future, we must work towards addressing the challenges standing in between implementing AI into clinical practice. These challenges include resolving both legal and ethical concerns, biases, availability of training datasets, and interpretability.

Conclusion

The high accuracy of several artificial intelligence models in recent studies demonstrate their potential to aid physicians. The articles selected in this review discuss the achievements, challenges, and future of such algorithms within the field of cancer.

Keywords

Cancer, Artificial intelligence, Machine learning, Deep learning, Neural Networks, Cancer imaging, Cancer pathology, Literature review, Oncology

Introduction

Cancer Rates

        Following heart disease, cancer is the leading cause of death, with an estimated 609,820 cancer deaths and 1,958,310 new cancer cases predicted to occur in the United States during 2023. To put it in perspective, this estimate is equivalent to 5,370 new cancer cases arising each day (1). Moreover, statistics in 2020 indicate that cancer was the cause of approximately 17.8% of all deaths in the United States, with both cancer and heart disease accounting for half of the overall deaths reported (2). Furthermore, survival rates are highest "for cancers of the thyroid (98%), prostate (97%), testis (95%) and for melanoma (94%), and lowest for cancers of the pancreas (12%), liver and esophagus (21%)" (1).

        In addition, breast cancer rates have been gradually "increasing by 0.5% each year since the mid-2000's" (1); meanwhile lung cancer is the leading cause of all cancer deaths in 2020, with a staggering 1.8 million deaths worldwide (3). Though reported colorectal cancer (CRC) rates have been "declining by 1.4-1.5% per year since 2012", such cases are mainly driven by reports in older age groups, whereas adults under the age of 50 have witnessed an increase of almost 2% (1). When looking ahead in time, global cancer rates are not predicted to decline if the rates reported in 2020 continue to remain constant. Unfortunately, the estimated 19.2 million new cancer cases in 2020 are expected to increase by 47% in 2040 to 28.4 million (3).

Cancer Diagnosis

        Cancer goes through a prolonged, complex path from initial symptoms to cancer grading and staging. When a patient presents with a certain set of symptoms, the physician will obtain information regarding the patient's medical history and risk factors that may assist in pointing toward the risk of cancer or other diseases. These observations may result in the order of lab tests, scans, or other procedures to determine the extent of the abnormality and confirm the presence of malignancy (4). Lab tests usually involve the examination of bodily fluids, such as blood tests, urine samples, or tissue biopsies, though ordered lab tests differ for every patient based on their symptoms and history. One of the most common lab tests ordered for cancer patients is the complete blood count, which measures the number of red blood cells, white blood cells, hemoglobin, hematocrit, and platelets (5). On the other hand, imaging tests such as CT, MRI, or nuclear scans allow physicians to locate the malignancy and the best site for a potential biopsy (4).

        To confirm the presence of cancer, the physician may order a biopsy, in which the most accessible abnormal area is extracted as a sample and sent to a pathologist. Under a microscopic slide, the pathologist can stage, grade, and provide the diagnostic details. Tumor grading describes the tumor's microscopic appearance, in which tumors have normal-appearing cells and are thus referred to as well-differentiated. On the other hand, high-grade tumors have peculiar-structured cells and are described as poorly differentiated. Poorly differentiated tumors

are usually more aggressive, have a worse prognosis, and tend to grow and spread at a faster rate (4, 6).

On the other hand, staging describes the tumor's gross appearance, such as its invasion, tumor size, and anatomic extent. The TNM system is a classification system of three categories for carcinoma and helps define the overall stage of the tumor. The T category refers to the size and spread of the primary tumor, the N category determines the potential extent of cancer spread in the regional lymph nodes, and the M category determines the distant metastasis, or whether the cancer is present in distant areas throughout the body. The TNM system allows cancer to be categorized into stages I-IV, in which stage IV is the most extreme. Moreover, staging is a crucial prerequisite in determining the most appropriate treatment (6, 7).

That said, detecting malignancies is a difficult task in which various characteristics may contribute to diagnostic errors so much so that a staggering 15% account for error rates in cancer tissue diagnosis (8). Several factors that may contribute to the challenges faced in diagnosing cancers include dense tissues masking underlying lesions in mammograms, suboptimal image quality, or inaccurate interpretations of subtle imaging patterns (9). That said, artificial intelligence (AI) has proven to be an assistant to physicians in the field of oncology, allowing for more specific and quick identifications of malignancy. With this in mind, integrating AI into the oncological workplace will assist physicians with more speedy diagnoses and fewer inaccurate results, thus helping reduce the high physician burnout rates observed thus far. Subsequently, such results will benefit patients due to the reduction of time in determining a diagnosis and fewer diagnostic errors, thus reducing medical costs.

As a result of difficulties in diagnosis and with cancer being a prevalent cause of death and plaguing millions of individuals worldwide, the pressure experienced by physicians in oncology is frequent. Shanafelt et al. reported an average of 57.6 hours devoted to professional activities and the treatment of 52 outpatients per week when surveying 1490 oncologists in the US (10). In another study, Banerjee et al. collected 595 surveys from 40 European countries to measure burnout in the oncological field for professionals under 40 years of age. Out of all the participants, 71% were burnt out, with characteristics relating to emotional exhaustion, feelings of cynicism, and a loss of purpose and meaning in work becoming significantly related to an unstable work/life balance (11).

AI-assisted diagnoses have been shown to save time for physicians and allow for more accurate diagnoses, as seen through their high area under the receiving operating characteristic (ROC) curves (AUCs). ROC curves, visualized by a graph, demonstrate "the performance of a binary diagnostic classification method", by connecting coordinates through the x-axis, indicating the specificity, and the y-axis, representing the sensitivity obtained from the test result. Sensitivity refers to the amount of individuals who have a certain disease and are tested positive, while specificity indicates the amount of individuals who do not have said disease and are tested negative. On the other hand, the AUC of a system measures its accuracy based on the closeness of the ROC curve to the upper left corner of the graph (12).

The potential of AI assisting in quick malignancy detection was demonstrated by Zhao et al., who trained, validated, and tested an AI model based on a deep neural network (DNN) with 12,222 cases of 99mTc-MDP bone scintigraphy (BS) images. Its ability to detect bone metastasis was evaluated in a competition with three nuclear physicians with at least five years of experience with a new dataset. The AI model, with an AUC of 0.955 for prostate cancer, 0.988 for breast cancer, 0.957 for lung cancer, and 0.971 for other cancers, required 11.3 seconds to evaluate 400 cases. On the other hand, it took 116, 140, and 153 minutes, respectively, for the three physicians to interpret the same dataset with an accuracy of 89.00%, thus allowing AI to save up to 98.99% of time dedicated to the interpretation of images. Moreover, the model demonstrated a remarkable capability in the recognition of small lesions and an overall accuracy of 93.5% ([13]). It is important to note, however, that the potential of AI continues to have several limiting factors, and the jobs of physicians are more complex.

Artificial Intelligence

"Artificial Intelligence" was first termed by John McCarthy et al. in a proposal for the Dartmouth Summer Research Project in 1956 ([14]). Before John McCarthy, however, Claude E. Shannon was one of the first to propose the implementation of a computer in chess in 1945. Additionally, Shannon listed several other uses of such computers in a similar direction, such as orchestrating a melody, adapting capabilities of logical deduction, and constructing strategic decisions in simplified military operations ([15]). Over the next 50 years, discoveries of AI's capabilities have grown exponentially and have led to a series of advancements, of which the most noteworthy one has been chess.

The involvement of AI in chess was the first time its remarkable characteristics became known to the general public, with the most notable one being Stockfish, developed by Tord Romstad, Marco Costalba, and Joona Kiiski in 2008. Moreover, it has been marked as one of the strongest CPU chess engines of its time and won numerous competitions surrounding similar chess engines ([16]). Along with chess, AI's popularity in other fields grew exponentially, a trend that continues to this day ([17]).

Simply put, AI utilizes computational methods to mimic human intelligence. Machine Learning (ML) algorithms fall into the subset of AI and are divided into three main classes: supervised, unsupervised, and reinforcement learning ([18],[19]). Figure 1, initially found in Chiu et al.'s article, illustrates such types of ML algorithms ([20]). Supervised learning algorithms require annotated, labeled datasets with inputs and desired outputs. When encountered with new datasets, the algorithm utilizes previously learned information from its labeled training dataset to notice familiar patterns ([20]). Unsupervised learning, however, does not require annotated datasets and can be trained with unlabeled data, allowing the model to independently separate the data into clusters and associations ([18]). Though more accurate than unsupervised learning algorithms, annotating datasets for training supervised learning models is time-consuming and labor-intensive. An approach to combine the advantageous sides of the two algorithms results in semi-supervised learning ([20]).

Several hybrid approaches, such as transfer learning, are employed to compensate for a challenge encountered when training algorithms. Transfer learning involves utilizing learned parameters from pre-trained models to perform another task, saving computational costs and reducing the requirement for training datasets ([21]). Lastly, reinforcement learning is a framework trained through trial-and-error, as it interacts with its environment or dataset and learns through reward functions or penalties ([18],[19],[20]).
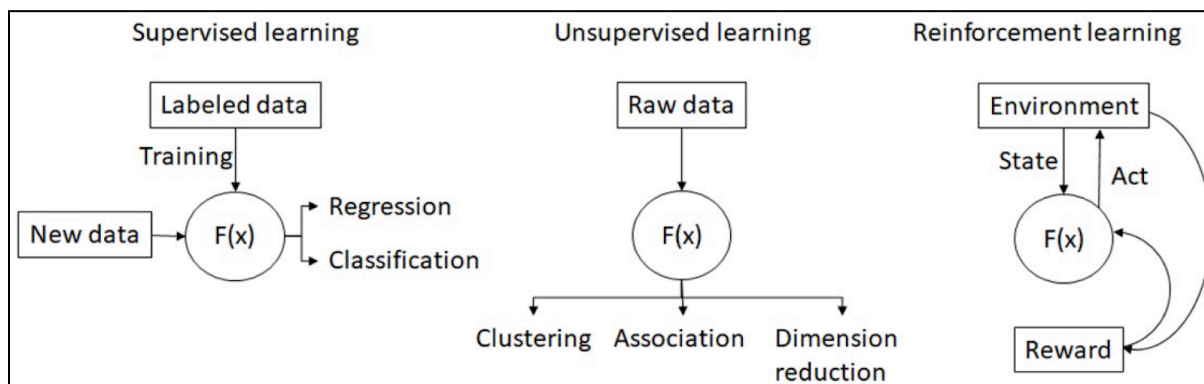
Figure 1: The three types of learning methods commonly used in ML algorithms; supervised learning, unsupervised learning, and reinforcement learning. Though different algorithms are able to combine the best of the ML models into one, such as semi-supervised learning, the three presented above indicate the most general categories used. The following figure comes from the open-access 2022 article by Chiu et al. ([20]), distributed under the Creative Commons Attribution license (https://creativecommons.org/licenses/by/4.0/).

Artificial Neural Networks (ANNs) fall into the subset of ML, utilizing complex computational layers to mimic connections occurring between neurons in the human brain. ANNs travel in one direction, starting with an input layer, which acts as a receiver of information, a hidden layer that reiterates the information, and an output layer that provides the prediction ([22]). ANNs consist of millions of "neurons" separated into successive layers. Within each layer, every neuron is interconnected to all the neurons in the layer above and below it, through which it can receive and send information down the succeeding layers until it reaches the final output layer ([23]).

Deep Learning (DL) is an extension of ANNs that contains several hidden layers and generally requires vast volumes of training data, which may become a limiting factor. That said, DL algorithms are known for making inferences and identifying complex patterns that would otherwise be too complicated for typical ML algorithms ([24]). Within DL algorithms fall in convolutional neural networks (CNNs), which are more complex networks specializing in image-based datasets. All in all, AI encompasses various, complex subsets with unique functions, as demonstrated in Figure 2, initially found in Gastounioti et al.'s 2022 article ([25]).
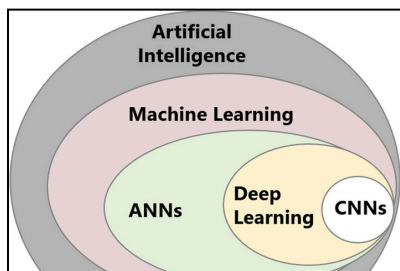
Figure 2: Different types of algorithms within the umbrella term of AI. The following figure comes from the open-access 2022 article by Gastounioti et al. (25), distributed under the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/).

In recent years, AI has taken significant steps in entering the field of medicine, especially in the field of oncology, where it has proven its capabilities in the diagnosis and detection of malignancies. One of the most notable advances of AI in cancer was the Cancer Metastases in Lymph Nodes Challenge 2016 (CAMELYON16) conducted by Ehteshami Bejnordi et al., where 32 algorithms were developed and further assessed on their ability to detect metastasis in axillary lymph node slides. Furthermore, the study included 11 pathologists who interpreted 129 images under a simulation exercise with a time constraint designed to mimic pathological workflow. In contrast to the top-performing algorithm that achieved an AUC of 0.994, the 11 pathologists had a mean AUC of 0.810. Moreover, the 10 top-performing algorithms achieved a higher mean AUC of 0.885 in detecting micrometastases, while the highest-performing pathologist scored an AUC of 0.808 (26).

As cancer cases and deaths continue to be present globally, the necessity for more sophisticated and efficient methods of assisting physicians in oncology continues. The capabilities of AI algorithms may benefit physicians and patients alike, assisting in the detection and diagnosis of malignancies that may have been otherwise unnoticed. This review discusses the effectiveness of AI in cancer, major studies contributing to these advancements, its challenges, and the future it could hold in the field of oncology.

Methods

The objective of the review is to examine the current state-of-the-art of AI in the field of cancer and analyze the challenges it faces in its respective fields. Hence, a literature review is conducted with the aim of finding recent articles on the topic of interest.

Sources

The databases utilized to search for articles are credible, peer-reviewed, scholarly sources. Such articles are extracted from the BioMed Central, Pubmed, Google Scholar, Nature, Science Direct, and National Cancer Institute (NCI) databases for studies concerning the integration of AI in the field of oncology, with the review concluding on August 28, 2023. Utilizing keywords pertaining to the purpose of the literature review allows for a more effective search of studies relevant to the subject at hand. Such keywords include "artificial intelligence", "deep learning", "machine learning", "convolutional neural network", "cancer", "diagnosis", "oncology", "neural network", " pathology", and "cancer imaging".

Inclusion and Exclusion Criteria

The developed inclusion criteria consists of articles written in English, published from 2016 to the present day, relating to cancers and AI, coming from a credible source, and peer-reviewed. On the other hand, articles containing no relation to both cancer and AI, not written in English, published before 2016, not peer-reviewed, and do not come from a credible source belong to the exclusion criteria. Moreover, articles involving non-malignant diseases are excluded. Through the following keywords, as well as the articles fitting into the inclusion criteria, 101 articles were extracted and further utilized in this review. Of these, the role of AI is tested for the purpose of several clinical procedures and different types of cancers in mind, such as breast, gastric, or lung cancer. Moreover, a majority of papers included consist of clinical trials and reviews.

Results

AI algorithms within cancer have been utilized, researched, and improved to aid physicians and patients alike. Advances towards its implementation into the oncological setting have been in the works since 2018 when the Food and Drug Administration (FDA) began approving AI medical algorithms in cancer care with a fast-track approval plan ([27]). Though utilized in assisting physicians with many tasks in the process of diagnosing cancer, a 2022 study by Luchini et al. indicates that 54.9% out of 71 FDA-approved AI-based devices account for cancer radiology, followed by "pathology (19.7%), radiation oncology (8.5%), gastroenterology (8.5%), clinical oncology (7.0%) and gynecology 1 (1.4%)" ([28]). With its rising development in this field, physicians have high hopes for its capabilities and its subsequent, hopefully positive, effects on performance, especially for physicians with less expertise ([29]). Most notably, however, AI has been praised for its ability to learn and analyze images at a faster pace and thus saving time for physicians. For instance, Zhao et al. demonstrated how the use of a DNN trained on BS images with an accuracy of 93.38% was able to decrease image interpretation time by 99.88% when compared to three nuclear physicians ([13]). In another study led by Wu et al., the developed Cystoscopy Artificial Intelligence Diagnostic System, or CAIDS for short, utilized 69,204 cystoscopic images from six hospitals for its training, internal validation, and external validation datasets. With an accuracy of 0.977 and a sensitivity, specificity, and negative predictive value exceeding 0.975, CAIDS required 12 seconds to evaluate 260 images. In contrast, the shortest time, which was achieved by an expert urologist, was 35 minutes ([30]).

In most clinical trials, ML algorithms are developed using training datasets extracted from public or private datasets, refined through validation datasets, and further evaluated through a test set ([31]). It is critical to note the difference between internal and external tests in determining an algorithm's performance and accuracy. Essentially, internal tests are conducted by the developers of the AI, while external tests are conducted by a separate, independent institution. To reduce bias, however, a majority of algorithms are tested using datasets from different institutions, thus producing accurate results rather than overestimating their capabilities ([32], [33]).

Within oncology, AI has not only been evaluated on its performance in detecting, diagnosing, and classifying cancer but has also been utilized in identifying precancerous areas. This ability was tested within cervical cancer in a 2019 study covered by the NCI, where the developed algorithm was able to identify precancer from images of a cervix at an AUC of 0.91, exceeding that of a human expert review, which achieved a score of 0.69 (34).

With multiple algorithms accessible for use, a question regarding which is the most efficient and accurate arises. Nonetheless, such inquiry must take into account the specific cancer type to which the algorithm is being applied. When developing an AI algorithm for the early detection of thyroid cancer, for instance, Olatunji et al. evaluated the performances of support vector machine (SVM), random forest (RF), ANN, and Naïve Bayes (NB) techniques. Out of the four AI architectures, RF achieved the highest accuracy of 90.91%, followed by the ANN (88.64%), SVM (84.09%), and finally NB (81.82%) (35). In another study evaluating the performance of five ML algorithms (XGBoost, RF, SVM, NB, and logistic regression) for the diagnosis of ovarian cancers, Akazawa and Hashimoto discovered that XGBoost and RF held the highest accuracies, with AUCs of 0.80 and 0.78, respectively (36).

Convolutional Neural Networks (CNNs)

Several fields within oncology began adopting new technology within their respective workplace, the most notable being whole slide images (WSIs), which provide high-resolution digital images and easier methods of obtaining diagnostic results. Nonetheless, WSI brings about a subsequent issue of being too tedious to fully visually analyze (37, 38). Thus the use of AI comes into play, and although ML methods are being utilized in this practice, CNNs have led the way in the integration of AI in cancer.

Through layers of convoluted filters, such architectures can detect relevant image features similarly to a human brain and deliver an output of "one or more probabilities or class labels" (39). In other words, a primary reason for the popularity of CNNs in this field is due to their efficiency in learning directly from images, and though they require more computing power, they can derive imaging patterns from the provided data (31). With this in mind, the overall use of CNNs in WSIs has become an increased focus in recent studies, as it allows for a simpler method of diagnosis for pathologists as well (40). The potential of such algorithms has been highlighted in several cases, where utilizing them allowed for accurate results, saved more time during training, required little to no annotations, and was more efficient. In a January 2022 competition involving Bulten et al., "1,010 teams consisting of 1,290 developers from 65 countries" participated in the Prostate Cancer Grade Assessment (PANDA) challenge, in which the participants submitted at least one algorithm trained on the same 10,616 biopsy images. Within the winning and top-scoring teams, a common characteristic observed was that developers chose extracted patches of images from the WSI provided and fed them into a CNN (41).

CNNs have been popularized for being "complex mathematical algorithms" and have been applied in, but not limited to, histopathology, radiology, and endoscopies (42). Moreover, such neural networks have been trained for numerous objectives within cancer to assist

oncologists in a myriad of cancer types. A study by Xu et al. demonstrated the nature of such algorithms, in which a CNN architecture was trained and tested with 1260 2D images extracted from 63 optical tomographic images to diagnose breast cancer. The algorithm yielded a high performance within its test set, with a 90.2% accuracy rate, 0.80 specificity, and 0.95 sensitivity (43). Through a training data set of 5403 esophagogastroduodenoscopy (EGD) images indicating pharyngeal cancer, Tamashiro et al. developed a deep convolutional neural network (DCNN) architecture capable of identifying 40 out of 40 lesions in 28 seconds during its validation set of 1912 images. In addition, the model was able to identify three lesions under 10mm in size (44).

Nonetheless, AI-based systems present drawbacks in which certain characteristics, invasion type, and image quality cause false positive and negative interpretations. For instance, Horie et al. trained a CNN with 8428 images from 384 patients on esophageal lesions confirmed to be esophageal squamous cell carcinoma (ESCC) or adenocarcinoma. After its training, the CNN took 27 seconds to analyze, interpret, and distinguish between advanced and superficial cancer from an independent testing dataset of 1118 images. Overall, it achieved an accuracy of 99% and 92% in differentiating between superficial and advanced cancers, respectively. Of all the false positives interpreted by the algorithm, 50% accounted for shadows within the images, whereas half of the false-negative images were caused by difficult conditions (45). Sandback et al. constructed a CNN algorithm based on hematoxylin and eosin (H&E), or stains used to view tissue slides at the cellular level, WSIs for "tissue detection, classification, and slide-level analysis" from breast cancer biopsies. In the internal testing dataset of 2252 slides obtained from 1090 patients, the algorithm achieved an AUC of 0.998, with 98.27% specificity and 99.02% sensitivity. Whereas in an external validation test set of 841 H&E slides, the CNN had an AUC of 0.990, a 93.57% specificity, and 95.51% sensitivity (46).

That said, deep learning models require vast quantities of computational power, in which manually annotating data, such as CT scans, is laborious and time-consuming (24). Thus, rather than utilizing public or private datasets alone for training and establishing parameters for algorithms, researchers opt for transfer learning even with CNNs. Not only does this method appeal to individuals without expertise in training algorithms from scratch, but it also combats the long-standing concern of DL algorithms requiring extensive training data (21, 47). For instance, Hiroya Ueyama et al. programmed a CNN computer‑aided diagnosis system from ResNet-50, a 50-layered CNN architecture previously trained from an ImageNet database of over 14 million images. After being further trained on 5574 ME‑NBI images and evaluated with a testing dataset consisting of 2300 images, the CNN achieved a staggering AUC of 0.99 with a 98.7% accuracy (48). In another study, Esteva et al. utilized transfer learning on a pre-trained GoogleNet Inception v3 CNN architecture and further trained it with their own developed dataset of 127,463 dermatologist-labeled biopsy images for image-based diagnostic tasks for skin cancer. When compared to 21 board-certified dermatologists, the algorithm matched their performance in "keratinocyte carcinoma classification, melanoma classification and melanoma classification using dermoscopy" (49). Likewise, Tandel et al. demonstrated the high

performance of transfer learning on CNN-based systems, where such an algorithm outperformed 6 different ML approaches in a 2020 study regarding brain tumor classifications ([50](#)).

With several approaches to developing an AI algorithm, one may question which method is most efficient, requires the least computational power, and produces the most accurate results. A trial by Zhu et al. explored this concern, utilizing three distinct computational methods for testing CNN architectures for identifying and differentiating breast cancer molecular subtypes from dynamic contrast-enhanced magnetic resonance imaging. Three computational methods for training the CNN included learning from scratch, transfer learning, and deep feature extraction, in which a distinct network acts as an extractor of distinct features received from the dataset. Out of the three, the learning method for reaching the highest AUC was the off-the-shelf deep feature approach, with its highest score being 0.65, followed by transfer learning, with the best performance standing at 0.60, and finally training from scratch, where its best performance demonstrated a score of 0.58 ([51](#)).

Another type of neural network famously known for its processing and prediction of sequential data is a recurrent neural network (RNN). A factor setting this algorithm apart from its other ANN counterparts is its ability to analyze data over different time points by storing previously obtained inputs and further learning from earlier steps ([37](#), [17](#)). Such networks have been utilized in predicting lung carcinoma subtypes by Kanavati et al., in which a DL-based model composed of an RNN and a CNN analyzed small transbronchial lung biopsy (TBLB) H&E slides. Through a training set of 579 WSIs, the RNN and CNN architecture achieved an overall AUC score of 0.993 ([38](#)).

Lung Cancer

In lung cancer, where image-based data dominates a majority of diseases analyzed by physicians, a secondary, accurate assistant becomes a necessity ([20](#)). Thus, AI algorithms have been widely employed in lung cancer, where previously established architectures such as Google's inception v3 was utilized in differentiating normal or tumorous tissues from histopathology slides at high accuracies (AUC of 0.99) ([52](#)). Moreover, ML architectures have proven to be a useful second opinion, as demonstrated by a study reviewed by the NCI, which trained an algorithm using over 1600 histopathology lung cancer slides found on The Cancer Genome Atlas (TCGA). Overall, the program was able to classify 45/54 images misclassified by the three pathologists involved in the study and differentiate normal lung tissue from the two most common forms of lung cancer, adenocarcinomas and squamous cell carcinomas ([53](#)).

Through the extraction of 1373 annotated cross-sectional lung CT images for training and validation, Coudray et al. developed a CNN and evaluated it in a test with three board-certified radiologists. When measuring the same test set of 244 CT images as one of the human radiologists, the algorithm attained an Intraclass Correlation Coefficient score of 0.959. That said, the CNN nonetheless presented a drawback, as it overestimated the lesion size by 2.97% in comparison to the radiologists, with the presence of a certain cancer invasion type being the most responsible for under and overestimations ([54](#)). Due to the complexities of the subtypes falling

into the umbrella of lung cancers, different characteristics may require different treatment routes. For instance, squamous and non-squamous non-small cell lung cancer (NSCLC) requires altering treatments, thus creating a necessity for proper classifications. With the use of the Inception v3 architecture, Le Page et al. utilized a training dataset of 132 histopathological HES slides with an equal number of images representing squamous and non-squamous NSCLC lesions. In the training, validation, and test evaluations, the Inception v3 architecture received AUC scores of 0.99, 0.87, and 0.85, respectively ([55](55)).

Though the capabilities and performance of DLs go beyond those of their ML counterparts, they nonetheless introduce a limiting factor, where vast amounts of usually annotated data are required ([56](56)). Hence in several cases, researchers opted out of using mass, manually annotated datasets. For instance, an early 2022 study by Xie et al. trained a weakly supervised deep learning model based on lung cytological whole-slide images for assisting cytopathologists in differentiating between malignant and benign cases. Thus, the weakly supervised DL algorithm combatted the labor-intensive work of image annotations found in typical supervised DL algorithms and only required labels for the training and validation datasets ([57](57)).

Prostate cancer

With prostate adenocarcinoma being the most prevalent cancer seen in men, utilizing AI as a tool will assist physicians in a timely, more accurate diagnosis. Pantanowitz et al. developed an algorithm based on multilayered CNNs for image classification and tasks in analyzing WSIs of core needle biopsies (CNBs). After being trained on 1,357,480 labeled image patches, the internal test indicated an AUC for cancer detection of 0.997 and a score of 0.991 on an external validation test conducted at the University of Pittsburgh Medical Center (UPMC) ([58](58)).

One of the most widespread machine-learning algorithms developed for detecting prostatic adenocarcinoma is Paige Prostate Alpha, which categorizes the inputted whole slide image as "suspicious" or "not suspicious" from detected lesions ([59](59)). Raciti et al. evaluated the performance of Paige Prostate Alpha in the clinical setting with three board-certified pathologists when analyzing CNBs. Overall, pathologists achieved a faster performance with the algorithm than without, decreasing the time spent on each cancerous WSI slide by 13 seconds and increasing sensitivity from 74% ± 11% to 90% ± 4%. Additionally, the average sensitivity of smaller cancerous areas under 0.6 substantially increased from 46% to 96% when using Paige Prostate Alpha ([60](60)).

Gastric Cancer

Within gastric cancer, AI has proven to be advantageous in exceeding diagnostic time as well as assisting oncologists in noticing areas of malignancies that would have otherwise been missed. For instance, EGDs, an imaging source used within the cancer type, experience a setback where detection is difficult due to the subtle differences that can be assisted through the use of CNNs ([61](61)). A 2021 study by Niikura et al. trained an AI for diagnosing gastric cancer through

gastrointestinal endoscopies using a dataset extracted from 500 patients, of which 51 consisted of invasive gastric cancer and 49 early gastric cancer. In total, the white-light upper gastrointestinal endoscopy images extracted from the patients resulted in 23,892 images. Compared to expert endoscopists, the AI achieved a higher per-image rate of diagnosing gastric cancer by 13.1% ([62]). In another case, Tang et al. trained a DCNN for the purpose of detecting specifically early gastric cancer, which operated by extracting features from the image and further detecting the lesion's location. Not only did the system present high AUCs within its four validation test datasets, with the scores ranging between 0.887–0.940, it also demonstrated a high diagnostic accuracy of 95.3% compared to expert and trainee endoscopists (87.3% and 73.6%, respectively). Most notably, though, the DCCN demonstrated how the trainees' performance became comparable to that of expert endoscopists with the assistance of the algorithm ([63]).

The high diagnostic accuracy of AI architectures in gastric cancer, especially with non-experts, was also noted by Li et al. in 2019, who trained an Inception-v3 CNN with a dataset extracted from magnifying endoscopy with narrow band imaging (M-NBI). When testing its abilities in diagnosing early gastric cancers compared to human endoscopists, however, results indicated no significant difference in the accuracy and specificity of CNN and the expert's performance. Instead, the CNN's sensitivity was higher than that of experts, while its sensitivity, accuracy, and specificity were higher than non-experts ([64]). Furthermore, another study by Luo et al. involving the use of an AI diagnostic system for upper gastrointestinal cancers demonstrated a much superior performance when compared to non-expert endoscopists ([65]). Another alternative method to the use of CNNs within the field of gastric cancer was noted by Liu et al., in which the fusion of GoogleNet and AlexNet models allowed for a higher sensitivity and specificity of 97.60% and 99.49%, respectively ([66]).

All in all, such algorithms have the potential to assist physicians in the oncological setting when diagnosing gastric cancer, as demonstrated by Song et al., who applied their CNN architecture with AUCs of 0.990 and 0.996 within two test datasets in a real-world scenario. The CNN, when utilized by 12 junior pathologists with a time constraint, allowed for a higher diagnostic accuracy ([67]). Likewise, Jiang et al. indicated an increase in clinician performance in predicting peritoneal recurrence based on CT images with the integration of the AI model. One of the participating physicians, for instance, experienced a rise in sensitivity during the training, internal validation, and external validation cohorts from 0.692 to 0.915, 0.596 to 0.938, and 0.615 to 0.944, respectively ([68]). In contrast, Ikenoyama et al. demonstrated that although their developed CNN algorithm had a shorter diagnosis time (45.5 ± 1.8 seconds compared to 173.0 ± 66.0 minutes in analyzing 2940 endoscopy images) and a higher sensitivity (80% and 53.4%) compared to endoscopists, it nonetheless had a lower specificity ([69]).

It is evident that many studies utilize DL methods, more specifically CNNs, for evaluating the abilities of AI and what effect it may have on the performance of physicians when implemented into the field. For instance, Fan et al. constructed a Multilayer perceptron (MLP), otherwise known as an ANN, as well as Logistic Regression, K-Nearest Neighbor, Decision Tree, Random Forest, and eXtreme gradient boosting classifying models through the same

testing and validation datasets. As a result, the prediction of gastric cancer performed by the ANN proved to have a higher accuracy than the five classifying models ([70](#)).

Colorectal Cancer

Along with understanding which oncological field contains most of the 71 FDA-approved AI-associated devices, Luchini et al. identified that 7.0% of them account for CRC ([28](#)). Indeed, several advances within this cancer type are in progress. For instance, a 2023 study by Buk Cardoso et al. evaluated the extent to which three ML algorithms, RF, XGBoost, and NB, were able to predict CRC patient survival "from hospital-based cancer registry data in low and middle-income countries". Achieving an AUC score of 0.882 in training and 0.858 in testing, the XGBoost architecture performed at the highest accuracy of 78%, followed by Random Forest and Naive Bayes ([71](#)). In addition to utilizing AI-based algorithms in predicting survival rates, the importance of detecting CRC from colonoscopy images was taken into account by Zhou et al., who utilized a staggering 464,105 colonoscopy images in training CRCNet, a DL-based architecture. To address several non-malignant diseases responsible for complicating CRC diagnosis, researchers included such diseases as their control group. Overall, CRCNet achieved high performance in test datasets from Tianjin Cancer Hospital, Tianjin First Central Hospital, and Tianjin General Hospital, with an AUC of 0.930, 0.961, and 0.989, respectively ([72](#)). Moreover, the use of AI-based architectures in assisting physicians, especially with time, was noted by Lu et al., in which the time taken for a pathologist to detect colorectal tumor budding decreased from 13±5 seconds to 0.03±0.01 seconds with the use of the developed Faster R-CNN model ([73](#)).

Nonetheless, the involvement of AI in CRC experiences a major drawback, where a majority of training data is extracted from a singular institution, thus lacking in providing generalized results in a field of heterogeneous characteristics presented in this cancer type ([74](#)). Fortunately, this shortcoming is currently being combated through the use of multiple institutions, providing more generalized, diverse training data. One of the most notable examples of this action was conducted by Wang et al., who further trained an Inception-v3 CNN architecture with a dataset of 14,234 CRC WSIs extracted from 14 independent hospitals and sources located in China, Germany, and the US ([75](#)).

Breast Cancer

While prostate cancer accounts for the most cancer incidences in men, breast cancer, if not including skin cancer, stands as the most significant cause of cancer in women. Thus, accurate and hopefully early diagnoses are vital for decreasing mortality rates ([76](#)). Luckily, developments of AI towards this cancer type are advancing, especially in breast cancer radiology, with the hope of it potentially becoming a secondary interpreter as well as reducing the time spent analyzing the patient's images and the occurrences of false positives ([77](#)). Before its rise in use, however, computer-aided detection (CADe) algorithms, as well as computer-aided diagnosis (CADx) assisted radiologists in interpreting the patient's exams. Developed in the

same manner, both CADe and CADx algorithms are taught through the features indicating what a malignant lesion looks like, and when being faced with data, use such programmed features to locate potential suspicious lesions or evaluate the extent to which a given suspicious area contains them (78). In other words, the algorithms used in the detection and diagnosis learn through the use of pre-programmed features received through the programmer. Nonetheless, the rise of AI, especially DL algorithms, opens the door to cancer diagnosis and detection without the use of preprogrammed features. In cancer imaging, for instance, the use of ANNs, most specifically deep CNNs, was utilized by a majority of winning teams in constructing their algorithm in the previously mentioned CAMELYON16 competitions. Moreover, manually annotated algorithms presented a lower performance relative to their CNN counterparts (26). In general, CNNs provide the most utility within the detection and classification of breast cancer due to their abilities in feature extraction, facilitating easier views of "malignancy in breast masses" (79). Within breast cancer imaging, especially for mammograms, in which the rates of false-positive and false-negative results are substantially high, more advancements towards the improvement of AI algorithms have been proposed as well (80). For instance, Wanders et al., when combining mammographic breast density assessments with an AI cancer detection system, achieved more accurate predictions of interval cancer "after negative screening mammography" (81).

Moreover, DL-based algorithms facilitate more accurate and faster results from physicians in breast cancer, as demonstrated by recent studies. Jiang et al. compared the performance of 19 breast radiologists with ('first read') and without ('second read') the assistance of QuantX, an AI-based breast MRI diagnostics aid. Through the average AUC values developed of the 'first read' and 'second read', the use of QuantX increased the radiologists' accuracies from a score of 0.71 to 0.76 (82). In a later study conducted in 2022, Shoshan et al. trained, validated, and tested an AI model with a cohort of 9919 women, allowing for 13,306 digital breast tomosynthesis examinations. The AI, which is an ensemble of 45 DL and 5 ML classifiers, was not only found to be highly generalizable to unseen sites, but when evaluated in a stimulated workflow, radiologists were able to reduce the worklist by 39.6% (83).

In another case, Lin et al. developed a FasterRCCN algorithm to detect and classify microcalcifications in breast mammography that could assist in providing an early diagnosis of breast cancer. The study utilized a training dataset of 1,964 benign and 1,970 malignant images, as well as a test set of 426 benign and 450 malignant images for the algorithm. Overall, the FasterRCNN algorithm was able to distinguish between malignant and benign breast mammography images at an AUC score of 0.8042 (84). Additionally, a recent, 2023 study conducted by Liao et al. trained and validated EDL-BC, a DCNN-based algorithm to identify early breast cancer from ultrasound images. Regarding its AUCs on its internal test and external validation datasets, the model had a score of 0.956 and 0.907, respectively. Furthermore, the study included six radiologists with over 20 years of experience to evaluate the performance of EDL-BC within the clinical workplace. Without its influence, the average AUC achieved by radiologists was 0.716, but with it, however, the score presented a substantial rise to 0.899 (85).

Discussion

Multimodal

Due to the complex steps taken in diagnosing patients with cancer, it is important to keep in mind that the use of different data modalities is a prevalent factor in the process. Thus, in utilizing multimodal learning, an algorithm is able to accept different types of data as its input and subsequently learn to combine this information, strengthening its overall accuracy as well as assisting physicians in analyzing different types of patient data (86, 87). Such data types may include a multitude of image types, images combined with text, or images integrated with genomic data (88). An advantage to these algorithms is the substitution of additional information from other data modalities if the unimodal data is, by any means, opaque or unclear (89).

Challenges

Aside from the cancer types previously included, studies have applied AI to skin, bladder, head and neck cancers, as well as pancreatic ductal adenocarcinoma (90, 91, 92, 93). The evaluation of AI in oncology is becoming increasingly frequent, especially due to its ability to 'think' similarly to a human brain (94). Their abilities in oncology span from detection to prediction of survival rates, such as for ESCC patients (95). Moreover, neural networks have been proven to learn at a much faster rate than medical professionals, allowing for such algorithms' capabilities to extend to being a "knowledge discovery tool" (96). Even though numerous publications are being put out on the subject of AI in clinical practice, such as breast imaging, very few are currently being implemented into clinical practice (9). Thus, it is critical to address the long-standing issues within AI to develop more accurate algorithms for assisting medical professionals.

Lack of Data

A significant challenge standing in the way of AI becoming integrated into the oncological setting, such as in precision oncology, is the insufficiency of high-quality data (97). Due to many algorithms, especially the ones falling into the subset of DL-based architectures, requiring labeled, robust datasets, the insufficiency thereof brings about subsequently poor performance. In a 2020 review that shed light on the advancements made in deep learning radiogenomics within oncological care, Trivizakis et al. noted that the limited availability of datasets was "the most pronounced limitation for deep learning radiogenomics" (98). Thus, many solutions to this shortcoming can take effect, with the most notable being the adoption of transfer learning and the inclusion of public datasets. Utilizing pre-trained models overcomes challenges concerning the need for high-quality datasets (23, 47).

With training data extracted from a single site, a risk of overfitting occurs in which the algorithm fails in being generally applicable when applied to non-training data, such as external validation cohorts. Keeping in mind the heterogeneous characteristics of cancers found within patients, it is crucial for algorithms to be trained on diverse sets of information and not confined

to a singular institution ([74](#)). Moribata et al. developed a method to combat this drawback by training an automatic segmentation model for bladder cancer magnetic resonance images using multi-vendor scanners from two institutes with a large patient cohort and diverse parameters ([99](#)).

Indeed, many benefits arise with the use of public datasets, with TCGA, for instance, combating the deficiency of information through its compilations of various cancer subtypes and data types ([100](#), [101](#)). In addition, such databases resolve the time-consuming challenge of collecting sufficient images ([102](#)). In a 2023 study involving TCGA's data on patient transcriptome profiles and drug treatments, Sun and Chen constructed a DL-based algorithm capable of predicting cancer patient survival. When distinguishing short-lived and long-lived patients, the algorithm achieved an accuracy of 96% ([103](#)). However, such public datasets present another pitfall in which datasets regarding certain cancers are scarce. For instance, Mahoro and Akhloufi concluded that although DL methods are promising in image analysis, several informative datasets involving breast cancer images are not annotated or publicly available ([104](#)).

Bias

Nonetheless, the call for large datasets is not the only factor that lowers the accuracy of AI. Biases within AI fall into the risk of potentially providing inaccurate results primarily due to training datasets not equally depicting the population as a whole, especially minority groups ([105](#), [106](#)). Thus, when applied to said underrepresented subgroups, such as ethnic minorities or young adults, algorithms fail to give an accurate outcome and may even further aggravate already existing racial disparities ([107](#), [25](#)).

With this in mind, a rising concern regarding the TCGA database is brought about, as a majority of its data is from individuals of European ancestry, while individuals of Asian, African, and Hispanic ancestry are underrepresented ([101](#), [108](#)). Such databases, though diverse in modalities, may fail to generalize towards individuals of minorities. Some solutions have been proposed to combat biases within AI, however. For instance, Bakrania et al. encouraged future studies to "explore in-depth explainability techniques" to overcome such challenges ([109](#)).

Interpretability

In recent times, DL and "relatively less complex models with more user-friendly model representations" are criticized for being a "black box" as their reasonings are viewed as opaque and impossible to interpret ([97](#), [22](#), [19](#)). Where a physician's diagnosis accounts for the most crucial factors in a patient's treatment and path toward recovery, such difficulties refrain AI from being integrated into the oncological practice. Luckily, solutions for increasing explainability have been initiated. For instance, methods such as gradient-based analysis, evaluate pixels within an image to rule out areas responsible for the generated output ([109](#)). Color mapping provides the regions utilized by the AI in creating a conclusion, while class activation maps (CAMs) emphasize the areas of the image that contributed most to the model's decision ([18](#), [110](#)). CAMs

have been shown to be a reliable addition to DL models within oncology such as oral cancer and oral squamous cell carcinoma, where one 2021 study features their addition in classifying "suspicious" or "normal" photographed oral lesions (111).

Ethics

From an ethical standpoint, the sharing of data raises a question regarding the "expectation of confidentiality" within the doctor-patient relationship, hindering the integration of AI in the medical field (112, 113). Thus, if AI was to be implemented in the medical field, its interpretations or decisions must be further evaluated by physicians (114). As noted by Chen et al., the degree to which a physician must supervise and oversee the AI's decision-making, as well as the party responsible in the case of which the DL is incorrect must be established (27). Moreover, in a 2020 review overviewing the use of MLPs and CNNs in detecting early breast cancer, Desai and Shah observed that the reliability of ANN algorithms is questionable, as one study indicated that its accuracy in the detection and diagnosis was lower than that of radiologists (79). Consequently, the prevalence of human physicians in the oncological practice is a necessity, even with the presence of AI.

Concerns on replaceability of physicians and legal liability regarding AI

With the continuous improvements of AI in medical care, a concern regarding whether human practitioners will eventually be replaced comes to light. Nonetheless, the chances of medical professionals being replaced by such algorithms are unlikely, as many current studies indicate a common goal of developing AI to improve efficiency and reduce the time usually needed by physicians to create a diagnosis. Such goals in current studies are supported by the lack of definitive, high-level proof of efficient autonomous AI-enabled machines (115). If such trends continue in the future, physicians will not be entirely replaced by autonomously functioning algorithms, although those who utilize AI will most certainly replace those who do not (116, 117).

Current studies demonstrate the collaborative decision-making nature arising from the introduction of AI, where it provides physicians with an analysis as its output, and the individual subsequently leverages their knowledge for the conclusive decision within the diagnosis. Moreover, the physician validates the given predictions, allowing for human feedback to improve AI's ability to manage more complex cases that were not encountered in its training data (118). Thus, rather than competing, the collaboration between the two parties complements one another, where if one system fails, the other system can potentially notice the mistake (33). Figure 3, extracted from Sezgin's 2023 article, further illustrates such an idea (118).
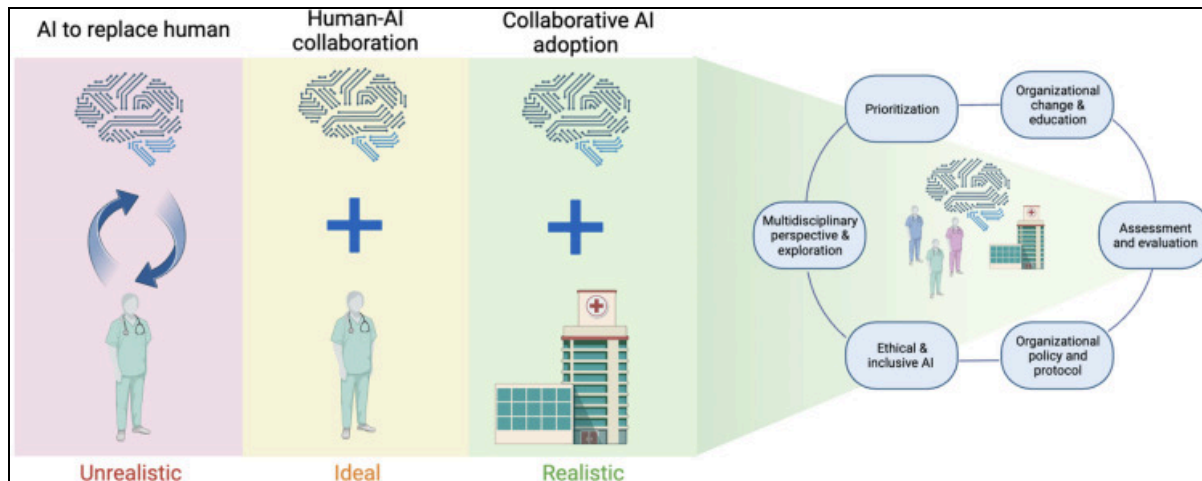
Figure 3: A summary of considerations concerning the integration of AI into clinical practice, demonstrating how the notion of AI replacing human physicians is unrealistic. Meanwhile, the partnership between the two parties is perceived as ideal. The following figure comes from the open-access 2023 article by Sezgin ([118]), distributed under the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/).

Although the effectiveness of AI and physicians working in tandem is positively regarded by many, a legal issue concerning liability remains. For instance, if an AI were to give a false-negative diagnosis of a breast cancer patient, who, in the given scenario, will be liable for the misdiagnosis? Would it perhaps be the mistake of the AI, or would the responsibility fall upon the physician overseeing the analysis of the algorithm? What of the hospital that signed the approval for the adoption of the AI-based model? Might the responsibility and the consequences of the misdiagnosis fall into the hands of the algorithm's developers?

The question of who is liable is rather nuanced, where, at least for the United States and Canada, there are no established legal frameworks overseeing AI in medical care. Due to the new nature of AI, there has been a finite amount of legal precedents concerning liability within this field ([119]). Thus, it is currently difficult to arrive at a definitive answer on the bearer of responsibility in the event of an unjust medical outcome ([120]). The lack of clarity on such a complex situation leaves the public opinion to speculate on the true responsibility. A 2021 survey by Khullar et al. explored this inquiry, where 1007 participants, consisting of both physicians and the general public evaluated whether the physician, the vendor or company licensing the algorithm, the healthcare organization that purchased the algorithm, or the FDA or a governmental entity approving the algorithm is liable in the case of an error. As a result, both the public and physician groups (66.0% vs 57.3%) found physicians to be most liable, with the public being more inclined to choose the physicians. Meanwhile, the physician group was more inclined to regard the company (43.8% vs 32.9%) and the healthcare organization (29.2% vs 22.6%) to be more responsible than the public ([121]).

To a certain extent, it may be reasonable to suggest why the responsibility for an AI's results is primarily placed on physicians, as they bring about the final judgment based on the

patient's data. When examining the current state of liability revolving around medical AI models, Maliha et al. indicate that cases hold physicians accountable for errors occurring due to AI and ML outputs ([122]). If the demand for liability falls on the AI's developer, or its software development company, one may argue that they stand as a third party and it is the hospital and physicians' responsibility to exercise their professional judgment rather than entirely relying on an AI. Nonetheless, Smith & Fotheringham add by noting how the clinician utilizing an algorithm that produces mostly accurate results may experience an "atrophy of vigilance," where one's attention declines when surveilling the AI's recommendations ([123]).

As AI-based algorithms advance into the medical field, especially in cancer care where the early detections of malignancy are of the utmost importance, both hospitals and medical professionals must be trained on the usage of such systems, and thus have ultimate responsibility ([124]).

The future of AI in the field of cancer

It is without a doubt that the abilities of AI will advance exponentially and extend to more medical fields. The studies included in this literature review demonstrated the remarkable ability of AI within a multitude of cancer types and different data modalities. Thus, the upcoming years will most likely witness AI advance and become implemented in such specialties. In a recent 2023 study, Cabral et al. recorded the responses of approximately 1,000 AI and cancer researchers on a web-based survey regarding the future of AI in cancer care. Of these participants, over 73.13% predicted AI would be involved in grading and classifying cancer, and 69.08% expected it to provide more reliable diagnoses within the next 10 years. Regarding the areas of interest which will benefit from the use of AI the most, cancer radiology was chosen by one-third of the participants, followed by pathology and clinical oncology (27.02% and 20.29%, respectively) ([125]).

Nonetheless, its future in healthcare, especially in oncology, is dependent on whether challenges and standards in enforcing greater measures regarding its reliability must be addressed. Future studies revolving around this subject must consequently address ways to overcome current challenges if AI is to be applied in the medical field and gain the confidence of physicians and patients alike. In the upcoming years, the transition to clinical implementation of AI must remain unbiased to any given data and need to overcome the "black box" feature that remains a prominent obstacle in current studies.

More diverse datasets extracted from individuals of diverse ancestries, containing multiple data modalities and cancer subtypes are crucial in developing reliable algorithms capable of providing a definite analysis for all patients. Moreover, the legal and ethical concerns regarding the responsibility of AI need to be addressed, and, as noted by Gowda et al., "Where the law is silent, professional societies can and should step in to fill the void, thereby fostering specialty‑wide uniformity alongside patient safety". For instance, measures providing training for physicians, supporting future research, and constructing AI-specific practice guidelines should be taken by The American Society of Clinical Oncology ([126]).

Within the next ten years, AI will, or become closer to, entering clinical practice. With the rise of such technology, it wouldn't be a surprise if more physicians become trained and informed on how to utilize such algorithms, with knowledge surrounding the use of AI becoming more desired in the medical field. As its development progresses even more, we may see a future consisting of AI-physician collaboration rather than the currently feared replacement of professionals.

Limitations

The literature review, consisting of 101 articles regarding the current state-of-the-art of AI in cancer, does come with several limitations. As discoveries within the field progress and provide new information that was not previously known, the information discussed may become less applicable.

Conclusion

AI, when applied to cancer, demonstrates an accurate, swift performance, comparing or even exceeding that of experts. Though it bears several shortcomings, it is evident that the technology will only improve over time and hopefully become fully integrated into clinical practice, where it may assist physicians and patients alike. By conducting a literature review, this paper discusses the state of the art of AI algorithms in the cancer setting as well as its challenges, achievements, and potential future.

Abbreviations
ANN- Artificial neural network
AUC- Area under the ROC curve
BS- Bone scintigraphy
CADe- computer-aided detection
CADx- computer-aided diagnosis
CAM- class activation map
CAMELYON16- Cancer Metastases in Lymph Nodes Challenge 2016
CNB- Core needle biopsy
CNN- Convolutional neural networks
CRC- Colorectal cancer
DCNN- Deep convolutional neural network
DL- Deep learning
DNN- Deep neural network
EGD- Esophagogastroduodenoscopy
ESCC- Esophageal squamous cell carcinoma
FDA- Food and Drug Administration
H&E- Hematoxylin and eosin
ML- Machine learning

MLP- Multilayer perceptron
NB- Naïve bayes
NCI- National Cancer Institute
NSCLC- Non-small cell lung cancer
RF- Random forest
RNN- Recurrent neural networks
ROC- Receiving operating characteristic
SVM- Support vector machine
TCGA- The Cancer Genome Atlas
WSI- Whole slide imaging

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Chemical Exposure and Worker Health in the Semiconductor Industry By Daelyn Lee

Abstract

      The semiconductor industry, driven by rapid advancements in artificial intelligence (AI) technology, has become integral to electronic devices. However, these technological innovations are causing worker health problems such as chemical exposure, posing serious challenges in terms of safety and health in the semiconductor manufacturing industry. This study analyzed the types and exposure risks of various chemicals used in semiconductor processing. In particular, an in-depth investigation was conducted to examine respiratory problems, skin diseases, carcinogenicity, and reproductive and developmental effects that threaten the health of workers in the semiconductor industry. As a result, it was concluded that there is a need for heightened awareness regarding the long-term health issues faced by workers exposed to these chemicals, necessitating the urgent implementation of effective monitoring and safety measures. For the semiconductor industry to sustain its growth, creating a safe working environment is essential. To achieve this, we must raise occupational health standards globally through international cooperation and establish a systematic management process.

Introduction

      The semiconductor industry is a cornerstone of modern technology, driving the evolution of essential electronic devices in our daily lives, from consumer electronics to emerging technologies like artificial intelligence (AI) and the Internet of Things. Recently, with the rapid growth of the AI market, the demand for advanced semiconductor technology has reached unprecedented levels. It is not an exaggeration to say that sustainable growth in the AI sector is impossible without the robust support of the semiconductor industry.

      The advancement of the semiconductor industry, while promising unparalleled innovation in human life, also brings about multifaceted and complex issues, notably the health risks faced by workers engaged in semiconductor processes. The risks can be inferred by closely examining the cases of several advanced semiconductor countries, including the United States, Japan, Taiwan, and South Korea. These concerns are extending to Singapore, China, and India, which are actively entering the semiconductor industry for technological advancement and economic growth.

      In response, this study aims to investigate the potential risks of chemical exposure during semiconductor manufacturing processes. It seeks to encourage collaboration between the industry, government, and international organizations to promote occupational safety and health. The goal is to contribute to the creation of a secure working environment and the provision of a healthy workplace for those involved in the semiconductor industry.
The following section will delve into specific chemicals used in semiconductor manufacturing and the associated health risks.

Chemicals used in semiconductor process

Semiconductor manufacturing processes use a variety of chemicals, including but not limited to formaldehyde, arsenic, ionizing radiation, and known carcinogens such as trichloroethylene and benzene. As described in Table 1, these chemicals used in processes such as cleaning, etching, and photolithography can pose serious risks to worker health.

Chemical substances	Health Risks
Formaldehyde	Respiratory issues, Skin disorders, Carcinogenicity Reproductive and Developmental effects
Arsenic	Anemia, Headaches, Decreased hemoglobin levels Reddening of the skin, Jaundice, shock Pulmonary edema, Hepatitis
Ionizing radiation	Carcinogens designated by World Health Organisation (WHO) and International Agency for Research on Cancer (IARC)
Hydrochloric acid, hydrofluoric acid, ammonia	Potential carcinogen production
Trichloroethylene	Leukemia, non-Hodgkin's lymphoma, liver cancer kidney cancer, brain cancer, breast cancer
Sulfuric acid (H_2SO_4)	Cancer risks in lungs and larynx
Chromium compounds	Allergic reactions, respiratory difficulties
Benzene	Carcinogenicity, leukemia, drowsiness, dizziness Carcinogens designated by WHO and IARC
Arsine (AsH_3)	Nausea, headaches, anemia, skin reddening, jaundice shock, pulmonary edema, hepatitis
Dimethylacetamide	Infertility, miscarriages, respiratory disorders
Surface Adhesion Agent (HMDS) Dichlorosilane (SiH_2Cl_2) Dichlorosilane (SiH_2Cl_2) Tungsten Hexafluoride (WF_6) Isopropyl Alcohol Phosphine (PH_3) Sodium Hypochlorite (NaOCl)	Various health risks, including respiratory issues nervous system abnormalities, and more
Hydrogen fluoride (HF)	Damage to airways and lungs,Pulmonary edema bronchitis, hemorrhage, necrosis of the pancreas Thyroid dysfunction

Lead and phthalates	Increased risks of miscarriages, birth defects developmental disorders in pregnant workers

Table 1. Hazardous chemicals used in the manufacture of semiconductors

Based on the analysis of Material Safety Data Sheets (MSDS) from 2014 to 2018 provided by two major semiconductor companies in South Korea, one of the advanced countries in the semiconductor industry, the usage of chemicals was examined. In A and B factories, a total of 428 and 432 chemicals were respectively employed. Among these, products containing components classified as carcinogens by the International Agency for Research on Cancer (IARC), such as sulfuric acid, catechol, diboran, and naphthalene, accounted for 11% (47 items) in A factory and 6% (28 items) in B factory. When translated into actual usage by mass, A and B factories used a total of 44,539 tons and 34,115 tons of chemicals, with estimated carcinogenic substance usage of 29% (12,816 tons) and 26% (11,952 tons), respectively.

Chemical	Factory A		Factory B	
	Carcinogen	Non-Carcinogen	Carcinogen	Non-Carcinogen
Number [ea]	47	381	28	404
Mass [ton]	12816	31723	11952	34115

* Carcinogen: Sulfuric acid, catechol, diborane, naphthalene

Table 2. Chemicals Usage
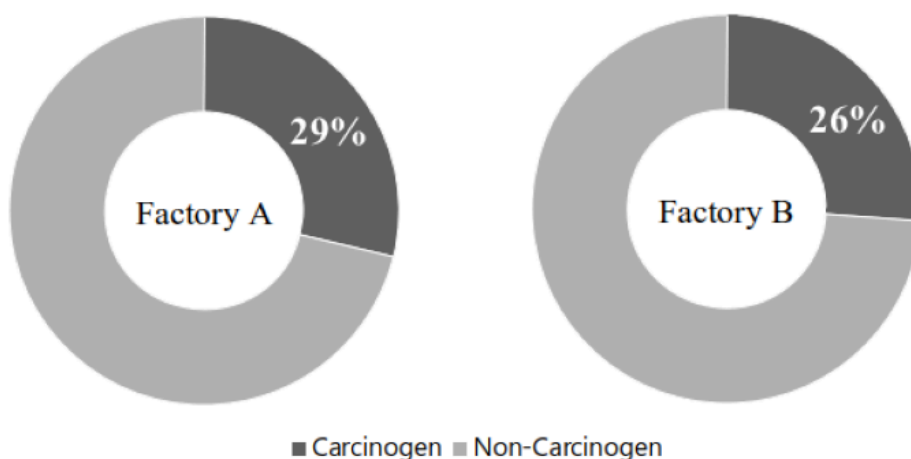
Figure 1. Percentage of chemicals classified as carcinogenic

Furthermore, a survey conducted in 2020 on semiconductor workplaces in South Korea revealed that among the total chemical products, 33% (range: 16~56%) included one or more proprietary ingredients. Only 29% of the chemical components had occupational exposure limits (OEL), and over 60% lacked health, safety, and reactivity ratings from the National Fire Protection Association (NFPA).

Health Risks

Chemical products used in semiconductor manufacturing contain a significant amount of carcinogenic, mutagenic, and reproductive toxic substances. This extensive exposure to hazardous substances poses health risks for workers. Respiratory problems can arise from the smoke emitted by various chemicals such as trichloroethylene and acetone commonly used in the manufacturing process. Skin disorders ranging from mild irritation to severe burns can result from contact with acids and corrosive substances. Furthermore, prolonged exposure to specific chemicals known or suspected to be carcinogenic increases the risk of cancer, and in some cases, semiconductor work has been linked to leukemia and lymphoma. Reproductive and developmental impacts, including deformities and miscarriages, are associated with exposure to lead and phthalates. Let's delve into these details further.

1. Respiratory disorders and organ damage:

Many chemicals used in the semiconductor manufacturing process emit fumes that can cause respiratory problems. Exposure to solvents such as trichloroethylene and acetone can lead to respiratory irritation, coughing, and in severe cases, chronic lung disease. Additionally, surface adhesive (HMDS), dichlorosilane (SiH_2Cl_2), tungsten hexafluoride (WF_6), isopropyl alcohol, phosphine (PH_3), and sodium hypochlorite (NaOCl) cause symptoms such as headache, dizziness, nausea, and respiratory irritation. In particular, exposure to phosphine can cause problems in the nervous, digestive, and respiratory systems, causing symptoms such as vomiting and diarrhea. Methyl chloride, used in cleaning and etching processes, causes dizziness, insomnia, confusion, and vomiting and has toxic effects on the kidneys. Hydrogen fluoride (HF) can cause damage to the airways and lungs after a single exposure, and reported effects include pulmonary edema, bronchitis, hemorrhage, pancreatic necrosis, and thyroid dysfunction.

2. Skin diseases:

Contact with certain chemicals, such as acids or corrosive substances, can cause skin problems ranging from mild irritation to severe burns. Exposure to dichlorosilane, used in the chemical vapor deposition (CVD) process, can irritate the skin and eyes and cause pain, while sodium bisulfite ($NaHSO_3$) can cause allergic reactions and breathing difficulties. Long-term exposure to these substances can cause chronic diseases, adversely affecting the overall well-being of workers.

3. Carcinogenicity:

In the semiconductor manufacturing process, various carcinogenic substances are utilized, and semiconductor workers who are exposed to these substances over the long term reportedly face a 2.3 times higher risk of leukemia and a 3.6 times higher risk of hematologic cancers compared to the general population. Exposure to certain chemicals used in the cleaning process can lead to mutations in the genes of hematopoietic stem cells that produce blood, and stem cells with abnormalities can potentially interfere with the normal production of white blood cells, red blood cells, and platelets, leading to the development of Acute Myeloid Leukemia (AML). Carcinogenic substances such as arsenic are used in ion implantation processes, and in the photo process of drawing circuit patterns on semiconductor wafers, carcinogenic substances like chromium compounds and benzene are employed. Hydrofluoric acid used in the photoresist removal process is a substance with a high probability of inducing lung cancer and laryngeal cancer.

4. Reproductive and developmental effects:

Certain chemicals, including reproductive toxicants such as lead and phthalates, have negative effects on reproductive organs and fetal development, and pregnant workers exposed to these substances may have an increased risk of miscarriage, birth defects, or developmental problems in their children. Substances that can cause reproductive abnormalities such as irregular menstruation, infertility, and miscarriage include hydroquinone and acetone ($(CH_3)2CO$), which are major components of the photo process. It also includes methyl chloride (CH_3Cl) and isopropyl alcohol (C_3H8O) used in cleaning and etching processes, and hydrogen peroxide ($H2O2$), sodium fluoride ($NaCl$), and methanol (CH_3OH) used in utility processes.

Improving Occupational Health Monitoring

Through research on the risks of exposure to the aforementioned chemical substances, the limitations in health and safety protection for semiconductor industry workers become evident. The semiconductor industry, due to corporate trade secret protection policies and its relatively short history, lacks scientific evidence regarding industrial health. To address this, I propose to establish and continually enhance a monitoring process involving collaboration between companies, nations, and international organizations.

International organizations would establish management standards, nations would implement standardized exposure monitoring systems, and companies would maintain a system that regularly updates information. Companies would regularly assess the exposure levels to hazardous factors for all workers, and record and maintain results along with basic information about workers (job responsibilities, exposure processes, etc.). Nations would analyze macroscopic changes such as standardized industry or occupation-specific mortality, disease, and accident rates based on company data, identifying specific risk groups for prioritized management. Furthermore, through collaboration with international organizations, it may be possible to prevent health risks in countries with insufficient infrastructure and inadequate ongoing government supervision.

Conclusion

  The rapid development of the semiconductor industry plays a central role in modern technology, but the resulting chemical exposure poses a serious risk to workers' health. A variety of chemicals used in semiconductor manufacturing cause respiratory problems, skin diseases, carcinogenicity, and reproductive and developmental effects, which can lead to long-term health problems for workers. In particular, research results suggest that workers exposed to carcinogens have an increased risk of developing leukemia and blood cancer. Accordingly, effective surveillance and monitoring systems must be actively introduced to protect the safety and health of workers in the semiconductor industry, and efforts are needed to improve occupational health standards through international cooperation. Local governments and companies must work together to systematically respond to health and safety issues through regular and transparent data sharing. By combining these efforts to create a safe working environment, sustainable development and innovation can be achieved.

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Capitalist Motives in California and How They Affect the Media's Portrayal of South Asian Victims of Domestic Abuse By Aanya Mittu

Abstract

Using Stuart Hall's framework and applying it to South Asians in the Bay Area, this paper outlines the intersections between capitalism, media, and race that ultimately make representation more difficult for people of color. Using case studies of a South Asian woman and a white woman in the Bay Area, both victims of domestic abuse, I offer insight into the varying ways each story was handled not only by the public but also by the media outlets themselves. Finally, the paper concludes with the unfortunate result that South Asians are rarely represented when it comes to cases of domestic abuse, and if they are represented, it is typically inaccurate. To solve this issue, I propose a new perspective for media moguls to adopt, instead of the current capitalistic one that prioritizes marketability and profits over authentic storytelling.

Introduction

There have long been inequalities between a person of color and a white person in accurate representation–economically, socially, or culturally. How the media handles people of color is one important example of this discrepancy, whether it is white directors forcing South Asian actors to learn Indian accents, stereotyping East Asians as incredibly intelligent, or typecasting black people as aggressive or sassy. At first glance, some stereotypes, such as generalizing East Asians as geniuses, may not seem harmful; but to those East Asians who are not considered "intelligent", they are harmed when viewed as failures by other racial groups. Furthermore, the creation of a model minority increases negative opinions about other groups, only intensifying and deepening discrimination. These examples have had profoundly negative effects on how people of color perceive themselves and how others perceive them.

In contemporary societies, the media consumed by children in their formative years cements their understanding of different nationalities and races. It is one explanation of why echoes of these stereotypes are seen throughout society and life, especially when it comes to news outlets and the way they handle stories about people of color. The media intensifies and promotes these stereotypes by communicating them directly to an audience. Stereotypes have always formed an important part of society's interaction with race; however, the media's reflection and expansion of these stereotypes infiltrated homes. For instance, in the late 19th century minstrel shows in America began to pop up, where white actors would paint their faces black to mock slaves or other black people. Although the racism we see today in media is rarely ever as blatantly racist, the small microaggressions or misrepresentations eventually snowball and cause the issues we see today–a lack of representation or a horrible misrepresentation of people of color.

This paper explains the social reasons that underpin by focusing on a specific crime that is often reported on news outlets–domestic violence. This crime is commonly seen across the Bay Area, but it is widely accepted as a regular part of marriage by many South Asians. To bring a fresh understanding to this problem, I explore how capitalist social relations in California influence the media's portrayal of South Asian women who are victims of domestic abuse. The

media inherits a responsibility to inform the public; however, the profit (capitalist) motive eventually reigns supreme.

   I do this in three steps. First, I provide a theoretical framework for the topic by appealing to the cultural theorist Stuart Hall's writings on media and race. These provide a framework for understanding the intersection between capitalism, media, and racism, as well as how this framework can be applied to another population. Next, I apply this framework to the context of South Asian women in the Bay Area. I explore this through the case studies of a South Asian woman and a white woman in the Bay Area, both victims of domestic abuse, offering insight that will provide a glimpse into the varying ways each story was handled not only by the public but also by the media outlets themselves. Finally, the paper concludes with the unfortunate result that South Asians are rarely represented when it comes to cases of domestic abuse, and if they are represented it is typically inaccurate. To solve this issue, I propose a new perspective for media moguls to adopt, instead of the current capitalistic one used right now that prioritizes marketability and profits over authentic storytelling.

The Intersection Between Capitalism, Race, and Media

   In his piece *Media Power: The Double Bind*, Stuart Hall draws a link between capitalism and media, expressing how a capitalistic society has profound effects on the news we consume[1]. Although there are countless forms of news outlets, newspapers, magazines, and more, a few select elites in society have effective control over the majority of them. As Hall explains, capitalist societies emphasize the notion that money equals power—the power to control life, the power to control others, and even the power to control the news. Capitalism has put a price on everything, from heads to people's perceptions, so the right amount of money can allow news outlets to run certain pieces with certain implications. The media may benefit from the appearance of defending equality by upholding freedom of speech, but underpinning this freedom of speech are serious power imbalances that enable those with effective control over media organizations to direct the narrative.

   For instance, instead of garnering the public's honest opinion, politicians now target low-income communities that are known to not be as educated. Instead of using media as a tool to spread their messages or spread knowledge itself, the elite have opportunities to use the media as a means to promote their own interests and world views. As the most infamous lying politician in the United States, Donald Trump is widely known for his tendency to mislead the public through false claims and lies, about 30,573 times in his presidency according to *The Washington Post*[2]. Trump has been caught sending misleading fundraising emails to his supporters, in which he claims Joe Biden is enforcing a gag rule that would make it "impossible" for Trump to speak out against him. When fact-checked, journalists found that this new rule was in no way interfering with Trump's freedom of speech; in fact, the Biden administration simply wants Trump to stop spreading more misinformation regarding the 2020 election[3]. However, even after countless accounts of Trump lying, the PEW Research Center still reports that 49% of voters believe that he keeps his promises, and 72% of Republican voters believe he is trustworthy[4].

Capitalism only drills in this idea of money trumping all, and as long as we as a society conform to this structure, the media will be tainted by the rich.

The outcome of structural power in the media is not limited to financial issues. As Hall argues in *Black Men, White Media,* the problems also have dangerous effects when it comes to issues of race. He writes about how the mainstream media has continuously struggled with accurately portraying immigrant families[5]. In an industry dominated by white people, immigrants rarely feel seen or heard in society. As Bhoomi Thakore develops in *South Asians on the U.S. Screen: Just Like Everyone Else?*, one of these harms relates to false representation. For instance, people of color in the media are put into three categories–stereotypes, model minorities, or assimilated Americans[6]. There is practically no room left for people to accurately share their stories due to the lack of immigrants in the industry. Both Hall and Thakore explain how media industries stabilize racism through their broadcasting strategies.

This relationship between racism and the media is clear when we consider media consumption. People consume news and television media at enormous volumes daily; they are fed new information at such a pace that they often lack opportunities to reflect on what they are viewing. When inaccurate stereotypes of groups are put in the media, it further perpetuates these standards, making it even harder for people of color to escape this narrative. Although these stories were written by white people in boardrooms, the plot infiltrates every aspect of a person of color's life—Asians are assumed to be geniuses, the model minority, and more—but these general blanket statements erase the stories of anyone who does not fit these broad definitions. It raises questions, in the consumers' eyes, of the authenticity of Asians who do not align with these stereotypes.

The issue with racism in media is that it continues to generalize instead of specify; the beauty of media is the freedom that comes with it. Scriptwriters, directors, journalists, and others have the power to write stories that relate to them, but we lose that unique aspect the second we start to generalize through stereotypes. As consumers, we need to begin by first recognizing when the media focuses on harmful stereotypes, rather than taking the generalizations at face value. Informing media conglomerates that these stereotypes, often placed for comedic relief, are racist ensures that they know consumers will not tolerate microaggressions any longer.

This media dynamic is exacerbated by the relationship between capitalism and racism. In *Race, Articulation, and Societies Structured in Dominance*, Hall connects capitalism with racism and explains how capitalist societies perpetuate systemic issues of racialization and prejudice[7]. Racism is often explained through different lenses, one being an economic lens, but it is vital to understand why we see it that way. In a capitalist society, we are taught to believe that money equates to success—there is no concept of an intangible or inner success. More significantly, these financial advantages result in clear material benefits; for example, wealthy people have easier access to healthcare, higher life expectancies, higher education levels, and more. Economic or financial inequality reinforces the different life trajectories people of color must take, as compared to wealthy individuals. Essentially, if other people cannot witness someone's success (their money), that person has no ground to say they are "successful."

Capitalism provides a rigid class structure, which is often complexly intertwined with race. Even from the earliest days, race was used as a distinguishing factor to give one party of people power and to justify their actions. Hall explains that in contemporary capitalist societies, race is a concrete manifestation of that phenomenon–class structures are heavily based on race. With people of color often being ranked below white people, white people are given this false sense of superiority, and this is the issue. Capitalism distributes wealth in an extremely disproportionate way, often in favor of the white majority, so the "feeling" of superiority is not the only problem–the issue is the actual economic and social power that reinforces this complex. Capitalism has put too much of an emphasis on monetary success, but society's structure historically and innately gives a preference to white people. Harmful processes such as gerrymandering, systemic racism, generational debt, and more are obstacles people of color have to face consistently to become "successful." However, white people never have to think about these adversities, further proving the fundamental difference between the two parties. White people are inherently given an upper hand simply because of their race, and in no way is that a just world to live in.

Now that the relationship between each individual entity of racism, the media, and capitalism has been explained, we must understand the complex spider web that connects the three together. Racism, media, and capitalism are all nuanced topics that cannot be explained through a straight line; each influences the other. At the crux of the issue, capitalism perpetuates racist ideologies while also giving a platform to the media. The media typically has no choice but to succumb to capitalism's racist principles in order to succeed, even if the "winners" of capitalism–the people who benefit the most–often achieve their success through exploitation. Keeping this flimsy medal of success dear to their hearts, most entrepreneurs of television shows, production companies, newspapers, and other media outlets would do anything to keep their businesses up and running, even if it meant sacrificing personal morals.

In what follows, this paper critiques institutional and fundamental structures that cause racism and misrepresentation in media, rather than looking at certain accounts of journalists being discriminatory. If the building blocks of society have been formed on the backs of marginalized groups, it is not surprising that these same groups still struggle to find a place in society centuries later. By providing solutions for the accurate representation of people of color, I hope to lessen the impact of these struggles.

How Does Hall's Framework Apply to South Asians?

Although Hall's framework is based in the United Kingdom, his insights can be applied to the greater South Asian population in the Bay Area. In his piece *The Whites of Their Eyes: Racist Ideologies and the Media*, Hall explains the lingering effects of misrepresentation in media–how media moguls are responsible for this portrayal and its perpetuation in daily life[8]. Large media companies, typically ruled by a total of just six major companies, control the narrative consumers are fed in America[9]. Not only in entertainment television but also in news outlets, we see the long-term effects of colonialism and racism in America through popular

characters such as Apu Nahasapeemapetilon from *The Simpsons,* or Raj Koothrappali from *The Big Bang Theory*. Screenwriters for *The Simpsons* combined multiple stereotypes into Apu; he simultaneously has a Ph.D. in computer science and runs a convenience store. Apu's character was even voiced by a white man who feigned a thick Indian accent, rather than just hiring an Indian voice actor or allowing the character to have an American accent. Similarly, Raj from *The Big Bang Theory* also has a Ph.D. to his name, and his main character trait is his geeky inability to talk to women. His over-involved family also plays into a common South Asian stereotype that families struggle to set their children free. As innocent as these stereotypes may seem, the underlying meanings continue to form internal biases in the general population, making it easier for broad generalizations about South Asians to be made. Apart from television, news outlets often adopt these stereotypes, either subliminally or explicitly. One of the cruelest ways news outlets defer responsibility for informing the public of domestic violence cases, especially when it comes to people of color as victims, is this capitalistic notion that their stories must be appealing. If the story is not appealing, no one will read it, meaning the news outlet does not profit from the resources spent making the story.

Noam Chomsky's and Edward S. Herman's writings on the media add important context to this. In their book *Manufacturing Consent: The Political Economy of the Mass Media,* they criticize the media for distinguishing between "worthy" and "unworthy" stories based on what is deemed as marketable. However, this practice only serves to invalidate the stories of various victims of domestic abuse, and other crimes. Chomsky and Herman identify filters that raw stories go through to be "ready" to be mass-produced, yet these filters only serve the elite few at the heads of these media companies[10]. As minorities, South Asian women in the Bay Area already are at a disadvantage when it comes to proper representation; however, when looking at the specific issue of domestic abuse, it is significant to view it from a cultural lens. South Asia personifies the typical "women should be seen and not heard" ideology, especially when it comes to married women speaking out against their husbands. Although these women now live in America, years of cultural responsibility weigh down on them, even from thousands of miles away. Thus, South Asian women are already hesitant to speak out if they are victims of domestic abuse, but America's capitalist mindset only perpetuates this fear—if a woman risks her livelihood to earn justice but no one listens to her, it is all a waste.

The intersections of race, capitalism, and media can, therefore, clearly be applied to South Asian women. The pressure of needing a "marketable story" only reinforces this idea that South Asian women should not and cannot speak out against their husbands. When this framework is placed within the specific social expectations of the Bay Area–the hub of capitalism in the heart of Silicon Valley–South Asian women are placed in a perfect storm, urging them to do anything but earn justice. As I now show, this perfect storm is clarified when we consider the case studies of domestic violence of South Asian women in the Bay Area.

According to Nagaswami and Yeung, a total of 47% of South Asian women suffered from domestic violence within the past three years during the COVID-19 pandemic[11]. However, the whopping statistic of nearly half of South Asian women is nowhere to be seen in these news

outlets' coverings. In San Francisco's Family Violence Report from 2020, only 38% of South Asian women reported being victims of domestic abuse, as compared to the 51% of white women who felt comfortable enough to speak out[12]. Although 38% and 51%–in the grand scheme of things–are not too far apart, the discrepancy can be clearly seen when looking for certain cases where female victims of domestic abuse have reported their abuse.

The contrasting lived experiences of South Asian women in the Bay Area compared to those of white women are illuminated by comparing reported cases of domestic abuse. Currently, a quick Google search of domestic abuse cases in the Bay Area will reveal thousands of links. However, the first few pages only cover white women. The only reported cases of South Asian women suffering from domestic abuse are written by South Asian sources themselves. As of today, there is only one major South Asian domestic abuse case that took the Bay Area by storm–the case of Neha Rastogi and Abhishek Gattani[13].

Rastogi, a well-educated Apple engineer, found herself trapped in a decade-long abusive marriage to Gattani, and she finally spoke out in 2017. She recorded a six-minute long audio clip of Gattani's abusive words and cruel actions, in which he even explicitly details the crimes he would commit, right in front of their two-year-old daughter; however, when taken to court, the judge took pity on Gattani, stating that he would be deported for as serious a crime as domestic abuse. Thus, the charges were reduced to a minor felony for "inappropriate touching," and Gattani spent a total of thirteen days in jail. Thirteen days–not even a total of two weeks–was meant to make up for ten years of violence, shaming, and abuse. This presentation is in striking contrast to how white women who were victims of domestic abuse were covered. Grace Goodman sadly passed away in early September of 2023 as a victim of gun violence and domestic abuse[14]. Similarly, her husband taunted Goodman in front of their children, ultimately shooting her with the kids watching.

Comparing the amount of coverage over the two cases, a Google search with the prompt "Abhishek Gattani domestic violence case" yields 8,770 results in 0.35 seconds. A Google search with the prompt "Grace Goodman domestic violence case" yields a massive 17,200,000 results in 0.40 seconds. The prompt "South Asian women victims of domestic abuse in Bay Area" gives 6,110,000 results in 0.46 seconds. A similar prompt, "White women victims of domestic abuse in Bay Area" gives 8,920,000 results in just 0.49 seconds. The discrepancies in news reporting cannot only be due to capitalism, racism, or the media outlets. As nice as it would be to simply wrap up a nuanced topic with a pretty bow, there is no one answer for the main culprit of the lack of media reporting. These examples illuminate the core concern of this paper, namely that South Asian women's experiences of injustice in the U.S. lack the representation they deserve. This paper has pointed to the obstacles raised by cultural ties, racism, and capitalism to achieving representation.

It is beyond the scope of the paper to identify how we as a society can move toward positive representation and accurate representation. However, the analysis forwarded in the paper should imply that adequate representation in the media requires a change in the motivations driving the industry. The second we stop viewing every story as a money-grab, or as a personal

opportunity to "get ahead," and we start seeing stories as people desperate to have their voices heard, that is when change will happen. People share their stories to know they are not alone and to let others know they are not alone. Forcing stories to fit a certain narrative to be "interesting" or to be told only pushes people farther away from ever reaching a point of comfort in society.

Conclusion

How do capitalist motives in California affect the media's portrayal of South Asian women who are victims of domestic abuse? What makes the issue of misrepresentation so nuanced is that there is no one factor specifically pushing against accurate representation–it is a combination of racism, history, media incentives, capitalism, and more. All these different variables combine to form a perfect storm in which representation, at least for South Asians, seems almost impossible in entertainment television and news outlets. Through Rastogi's and Goodman's case studies, we can see the difference in how each story is handled simply through the amount of coverage of one story. Although it is important to note that South Asians themselves have external factors that make them hesitant to speak up, the American resistance to their stories only perpetuates these trepidations.

To ease this issue, there are two possible solutions: add people of color to the media rooms or simply stop viewing each opportunity as a new way to make a profit. In reality, the latter is a much more difficult stance to achieve simply because a large majority of the world revolves around capitalism, where every single thing is marketed to profit from. The former–introducing people of color into these jobs–seems much more realistic. Allowing South Asians to join these news outlets directly correlates to an increase in South Asian stories. Already, independent South Asian reporters are solely covering the stories of South Asian domestic abuse victims, so if we were to put them in major news companies such as *CNN* or *The New York Times*, representation would only increase.

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The Limitless Power of Fear By Juhyun Oh

The first day of school. The woman in the red dress. The first kiss. Happy memories can live on forever, serving as a sweet moment of escape from not-so-sweet reality. The first bone fracture. The pool you nearly drowned in. The first "F." Scary memories can also live on forever, but they are very different creatures than happy memories because they generate fear that can seize control of your life. For instance, Elbert Hubbard, a renowned American writer and publisher, professes "Of all mental and physical polluters of life, nothing exercises such a poisonous effect as fear," suggesting fear has the power to impale and cripple both people's psyche and body. This essay will explore the power of fear, which can knock us down by putting both intense stress on our mentality and immense pressure on our physiological systems.

Examining the impact of fear on people's psychology is a strong starting point for the foundation of this essay. According to a professor at University of Minnesota who specializes in research on mindfulness and well-being, the immediate effects of fear can disrupt our ability to regulate emotions, interpret non-verbal cues, think rationally, and make ethical decisions, which can lead to impulsive reactions and hinder the ability to respond appropriately (Delagran, n.d.). To elaborate, fear targets various brain activities, disrupting the normal processes of the rational human mind to bring about irrational and irregular responses. In addition to these immediate effects that hinder rationality of the human mind, the long term effects of fear are even more significant. Fear can hinder long-term memory formation, harm the brain, especially the hippocampus, and intensify anxiety (Delagran, n.d.). In other words, fear can cripple mental health by permanently injuring the hippocampus, a vital part of the brain that regulates learning and memory encoding. Excessive damage to the hippocampus may even induce amnesia, a condition that prohibits the mind from forming new memories (Spanò, et al, 2020). Thus, fear is capable of permanently robbing the intellectual capacity of the brain. Individuals who chronically experience fear not only suffer from irrationality but also permanently deteriorate in mental wellbeing as fear erodes their intellect to synthesize memory. It is critical to realize being vulnerable to fear can mean being deprived of the mind's abilities to reason and recollect, making fear a terrifying mind-killer.

In addition to impairing the mind, fear is capable of damaging physical health. The emotion of fear can manifest into physical form as medical symptoms, making the severity of fear physically detectable. According to the medical director of the Substance Abuse Treatment Program at the Atlanta VA Medical Center, some of the physical symptoms of fear include the increase in respiratory and heart rate, digestive changes, nausea, sweating, and muscle tension (Casarella, 2022). These examples demonstrate that the cardiovascular, digestive, nervous, and muscular systems are just some of the biological pathways that fear can infiltrate to wreak havoc on the human body. As some of these physical manifestations of fear can be unbearable on the body, a person triggered by intense fear instinctively resorts to the built-in fight-or-flight response to defend themselves. According to a Psychosocial Rehabilitation Specialist, the fight-or-flight response is categorized as a physiological response that makes people either fight back against the threat or flee from the threat for the purpose of self-preservation (Cherry, 2022). Therefore, our bodies have been programmed to follow the fight-or-flight response whenever we

encounter fear. This proves how fear can diffuse through the human body's biological systems to provoke varying physical symptoms and stimulate physiological responses.

Perhaps the most persuasive demonstration of the devastating power of fear, on both the mind and body, is a personal anecdote. I learned what fear was as a young boy, and this traumatic memory still has a tight grip over me today. When I turned nine, my mother and I moved to Canada to learn English. I had a hard time adjusting to all the unfamiliar ways of the Western world, and the language barrier aggravated the troubles. I was too scared and embarrassed to talk to Canadians in English, so I remained close to my mother at all times. One day, on a trip to a local Walmart, I lost sight of my mother because I was too distracted by the fancy electronics at the appliance section of the mart. I became dazzled by the big colorful television screens that featured cartoons about how superheroes climatically overcame odds to defeat evil, a proven entertainment formula for all boys at my age. (I think it was a rerun of Spiderman.) When the end credits rolled, I quickly turned around to find a different screen featuring a different superhero tale. At that moment, I realized my mother was nowhere within my sight. My fear of losing my mother in a public space became a reality. I immediately froze and felt my fingertips become numb. I felt as if life was draining out of my body and my heart falling out of its place. Immediately, a storm of questions bombarded my mind: "What's going to happen to me? What if I never find my mother? How can I make my way out of this?" I was helpless at the time since I didn't have a phone to call my mother, and my English wasn't proficient enough to ask for help. On the inside, I couldn't control my emotions as fear rushed in and took over my body; on the outside, I couldn't contain my fits of anxiety and distress. After 30 minutes of utter fright and panic that shattered me into pieces, I reunited with my mother who also had been desperately searching for me. After this haunting experience, I was genuinely terrified of losing my mother again, while my mother was also scared of losing me, so I never again left her out of my sight whenever we visited anywhere in Canada. Even today, I make sure to be accountable for her whereabouts when traveling abroad. This childhood ordeal introduced me to fear for the first time as an oppressive monster that still preys on both my mind and body. Even the slightest reminder of the experience inflicts immense mental stress, making my palms sweat and hands shake uncontrollably. I wonder if I can ever escape my fear because I know fear never lets go of its victim.

Once settled in, fear never leaves. Triggering a "flight or fight" response, fear is a survival instinct ingrained into the very DNA of the human species. In other words, it is a safety mechanism meant to preserve humans. However, when fear is unbearably intense, the human capacity to intelligently process reason disintegrates, completely impairing the human mind. Moreover, this psychological effect on the mind also translates to physical disability, disrupting various physiological systems of the human body. In short, fear seizes both the mind and the body. For instance, personal childhood traumas, including getting lost, can attest to the power of the hold fear can exert on a person. To this end, the power of fear is monstrous. Then, perhaps the power to defeat fear, including the power to reconcile childhood trauma, can attest to the true strength of an individual, making the limitless power of fear second to the limitless power of an

individual to evolve, adapt, and grow. Yes, fathoming the limitless power of an individual to overcome fear is even more awe-inspiring. And, yes, this is why fear shall never be a roadblock but a roundabout in life.

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A Comparison of Immigration and Labor Policy of the United States And The United Arab Emirates By Sahil Polepalle

Immigration has played a major role in shaping the world as we know it today. The concept of migrating from one region to another has existed since the time people first started forming organized societies.[3] There are several drivers that motivate an individual to seek out a new place to live, including social, political, economic, religious, and geographic factors.[4] When immigrants arrive in a new country, their priority is to integrate into the economy by seeking gainful employment in an occupation that matches their skill set.[5] As they do so, certain segments of the existing population benefit greatly, while others experience a sense of net economic disadvantage.[6] Ultimately, as immigrants become part of the workforce, they not only improve their personal socioeconomic status, but also help bolster the overall economy.

In addition to their economic contributions, immigrants also influence a society's social policy and culture.[7] A more permissive immigration policy, such as one that allows for chain migration, leads to the transmigration of a larger number of immigrants in a relatively short time span than a more restrictive one. While the immigrants themselves may not directly influence the creation of social policies, gradually, their presence in a society has a profound effect on what the general populace perceives is an appropriate level of benefits to render to such individuals.[8] Immigrants start on the lowest rung of the socioeconomic ladder and are greatly affected by policies relating to health care, housing, disability and worker's compensation, and unemployment benefits.[9] As immigrants develop long-term roots in their new homeland, they typically weave into the fabric of society and contribute to its social and cultural path forward.[10] This results in diversification and enrichment of the culture through the assimilation of new foods, languages, traditions, and even intermarriage, to the point that these elements no longer become identified as "foreign."

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There are a variety of economic benefits that accrue to a region from the presence of immigrants. Demographically, immigrants are young and eager to enter the labor force.[11] They are most attracted to wealthy countries with mature economies, where there are already enough desirable jobs for the native population that the most arduous ones are readily available for the new arrivals.[12] These immigrants bring with them a plethora of occupational skills that society may presently lack or need, thereby stimulating the economy.[13] If there is no such fit, they may try acquiring the skills needed for a new occupation, or simply assume roles in manual labor that do not require any specialized knowledge.[14] As immigrants thus enter the workforce, it is rare that their presence results in job replacement of the native population.[15] Instead, they have a positive effect of net job creation, as well as augmentation of the available labor pool, which supports industrial growth. Immigrants are highly motivated to advance economically and provide an infusion of entrepreneurial and intellectual energy to a society that may have otherwise stagnated.[16] Indeed, such economies come to rely on this source of labor to enhance overall productivity.[17] As they establish new lives, they create families and increase the birth rate, by which they stimulate the consumption economy and rejuvenate a mature society that is often experiencing a falling birth rate.[18] As immigrants integrate into society, the social and labor policies of a country have a profound impact on their respective living circumstances, standard of living, and long-term outlook. The United States (US) and the United Arab Emirates (UAE) serve as real-world examples of the outsized impact that immigration can have on a

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society.   Labor and social policy, however, varies tremendously across the two nations. While the US and the UAE have both historically enjoyed significant inflows of immigrants, each country's distinct social and labor policies regarding immigration have resulted in dichotomous long-term trajectories in the life of the typical immigrant.

While immigration is vital to the economies of both the US and the UAE, each country has taken a radically different approach to its policy. US immigration is based on the premise that immigrants have a long-term vision to plant roots in their new homeland by seeking employment, finding housing, and eventually starting a family. Hence, immigration policy is centered upon an immigrant obtaining permanent residency with a path to eventual citizenship. In contrast, UAE policy focuses on short-term labor contracts that serve the needs of the economy, whereby an individual is granted a 3- to 5-year time period of residency with temporary housing, with the contract subject to periodic renewal by the employer. Foreign workers are welcomed as "guests" who may stay only for a short period of time, with no possibility of obtaining permanent residency, owning a business or property, or establishing a family.

To better understand each country's current immigration policy, it is best to examine each country's approach through the lens of history. "Give me your tired, your poor, your huddled masses yearning to breathe free," is famously inscribed at the base of the Statue of Liberty[19], but is also inscribed in the American ethos by the successive waves of migrants that have arrived since its founding.[20] Immigrants have been attracted to the US for a variety of reasons, ranging from religious freedom to economic advancement, but have always shared the common goal of emigrating and remaining in the country.[21] European immigration dominated the early years of American history as colonies were created in the New World.[22] These colonists took advantage of the plentiful land available to establish agrarian lifestyles.[23] During this time, involuntary immigration also took place, as slaves were brought from Africa to work in the fields of the southern colonies.[24] The next wave consisted of displaced immigrants fleeing war, famine, and

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strife in Ireland, Italy, and France.[25] In the 1860's, thousands of Chinese immigrants were brought to the US to help construct the transcontinental railroad, doing backbreaking work that the established population eschewed.[26] Despite America's reputation as a hospitable destination, nativistic tendencies were ever present, with the existing population questioning if society could handle the many new arrivals, both economically and socially.[27]

US immigration policy went through major changes beginning in the late 1800's. The nation had no formal policy until 1875, when the US Supreme Court ruled that immigration fell under the purview of the federal government, leading to the creation of the immigration gateway of Ellis Island.[28] Initial regulations concerned restriction of Chinese immigration which had surged during the building of the transcontinental railroad.[29] In 1891, the first federal office to regulate immigration was established through the Treasury Department.[30] Despite these efforts, European immigration continued unabated, prompting passage of the Immigration Act of 1924, which introduced the concept of quotas to control the number of arrivals from various countries and regions of the world.[31] These interventions had little effect, as the economic, religious, and political freedoms found in the US continued to act as a magnet for immigrants worldwide, which led to the rise of xenophobia and the push to further restrict immigrants from "less desired" areas globally.[32] In reality, extenuating international circumstances, such as World War II and the Cuban revolution, which resulted in a vast number of refugees, prompted additional

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surges in the immigration rate.[33] Other factors, such as the needs of the economy, played a part as well. Labor shortages after World War II led to the establishment of the Bracero program to provide a source of migrant labor for America's agriculture sector. Low wages, harsh labor conditions, and discrimination were endemic to the program.[34] The next major policy change, which created the framework for modern-day regulation, was the passage of the Immigration and Nationality Act of 1965, where quotas were replaced by categories of professions deemed in need by the Department of Labor, and establishment of a preferential category solely for refugees.[35] This act also resulted in the institutionalization of chain migration, emphasizing familial relationships to immigrants already in the US. Subsequent to this act, immigration spikes occurred during the 1960's and later, in the 1990's, when the amount of individuals permitted to enter the country annually was increased. The cumulative effect of these surges resulted in the percentage of immigrants making up the US population to jump from just 5% in 1965 to over 15% by 2015.[36]

In addition to the above policies, the Immigration and Nationality Act of 1952 established the H-1 and H-2 visa program, allowing employers to procure employees in labor sectors with critical shortages.[37] These visas, still issued today, are valid for a period of 3 to 5 years, can be renewed, and must be sponsored by an employer. Employees must eventually return to their native countries unless they can find an employer willing to sponsor them for permanent residency status, known as "green cards."[38] The J1 visa program was established after World War II to help the United States inculcate democratic values globally.[39] It has since evolved into a program that also allows international visitors to gain business and medical skills here and subsequently return to their country of origin after two years.[40] In addition, special categories

[33] immigrationhistory.org/timeline/.

[34] Kratz, Jessie, "The Bracero Program: Prelude to Cesar Chavez and the Farm Worker Movement," National Archives - Pieces of Hisory, https://prologue.blogs.archives.gov/2023/09/27/the-bracero-program-prelude-to-cesar-chavez-and-the-farm-worker-movement/

[35]"Immigration and Nationality Act of 1965 (Hart-Celler Act)," *A Project of the Immigration and Ethnic History Society*, 2019. immigrationhistory.org/item/hart-celler-act/.

[36] "Historical Overview of Immigration Policy." *Center for Immigration Studies*, Accessed 2023. cis.org/Historical-Overview-Immigration-Policy.

[37]"Immigration and Nationality Act." *U.S. Citizen and Immigration Services*, July 10, 2019. www.uscis.gov/laws-and-policy/legislation/immigration-and-nationality-act.

[38]"H-2B Temporary Non-Agricultural Workers," *U.S. Citizen and Immigration Services*, January 12, 2024. www.uscis.gov/working-in-the-united-states/temporary-workers/h-2b-temporary-non-agricultural-workers.

[39]"The History and Purpose of J1 Visas," *Hacking Immigration Law*, Accessed 2024. hackinglawpractice.com/the-history-and-purpose-of-j1-visas/.

[40]"Waiver of the Exchange Visitor Two-Year Home-Country Physical Presence Requirement," *U.S. Department of State - Bureau of Consular Affairs*, Accessed 2024. travel.state.gov/content/travel/en/us-visas/st

exist for individuals fleeing religious persecution or seeking political asylum.[41] Apart from these legal avenues, illegal immigration is another major source of inflows that has been present since the founding of the country, with the annual number of such arrivals correlated to the whims of federal policy enforcement and deportation protocols.[42]

The holy grail for any immigrant coming to America is obtaining a green card. Stemming from the appearance of the original alien registration card,[43] such status has now come to represent that one has the unfettered ability to live and work in the US at will. After five years of continuous residency, an individual can apply for citizenship.[44] The spouses of individuals with a green card are permitted to enter the country as well.[45] Minor children of green card holders automatically become citizens through birth on US soil, or otherwise follow the ultimate status of their parents.[46]

As immigrants became established and vested in their new homeland, their mindset shifted from a focus on day-to-day survival to long-term goals like raising families and becoming productive members of society. As new arrivals, the occupations that were readily accessible were amongst the least desired and most strenuous, including agriculture, construction, meat packing, and factory work.[47] Such workers were exposed to a raft of dangerous and exploitative working conditions, including unscrupulous employers and minimal job security.[48] Over time, as these workers had the opportunity to establish deeper family roots and create stronger social networks, it became increasingly clear that they would remain in the US permanently. Indeed,

udy/exchange/waiver-of-the-exchange-visitor.html#:~:text=Some%20exchange%20visitors%20with%20J,%2C%20Section%2021(2(e).

[41]"Green Card Eligibility Categories," *U.S. Citizen and Immigration Services*, July 11, 2022. www.uscis.gov/green-card/green-card-eligibility-categories.

[42]Phillips, Keri. "The History of Illegal Immigration in the United States," *Listen*, August 19, 2014. www.abc.net.au/listen/programs/rearvision/the-history-of-illegal-immigration-in-the-united-states/5678670.

[43]"The Colorful History of the Green Card," *U.S. Citizen and Immigration Services*, March 29, 2023. www.uscis.gov/about-us/our-history/stories-from-the-archives/the-colorful-history-of-the-green-card.

[44]"U.S. Citizenship Requirements for 5-Year Permanent Resident," *Citizenship Path*, Accessed 2024. citizenpath.com/citizenship-requirements-5-year-permanent-resident/.

[45]"Family of Green Card Holders Permanent Residents," *U.S. Citizen and Immigration Services*, July 14, 2015. www.uscis.gov/family/family-of-green-card-holders-permanent-residents.

[46] www.uscis.gov/family/family-of-green-card-holders-permanent-residents.

[47] Abramitsky, Ran and Boustan, Leah. "Immigration in American Economic History,"*Journal of Economic Literature*, vol 55, no4, December, 2017, pages 1311–1345.

[48] Kratz, Jessie, "The Bracero Program: Prelude to Cesar Chavez and the Farm Worker Movement," National Archives - Pieces of Hisory, https://prologue.blogs.archives.gov/2023/09/27/the-bracero-program-prelude-to-cesar-chavez-and-the-farm-worker-movement/

less than 30% of immigrants ultimately returned to their country of origin, though a large percentage had initially harbored thoughts of doing so.[49] In tandem with the development of tighter social connections, issues like worker safety and protections, job security, healthcare, and rate of pay gained increasing importance. As individuals, however, they were powerless to create meaningful change.[50] This scenario laid the groundwork for the movement to establish labor unions in the US.[51] The labor movement grew in fits and starts, with notable events like the Haymarket Riot and the Pullman strike highlighting the rising tensions between workers and employers.[52] The Clayton Act of 1914, granting labor unions the right to be exempt from antitrust enforcement, followed by the Norris LaGuardia Anti-injunction Act of 1932, helped labor unions gain traction in their fight for workers' rights.[53] Unions continued to strengthen in the years following World War II and were championed by individuals like Cesar Chavez. By organizing, immigrants were able to achieve meaningful gains in wages, worker protection, pension benefits, and medical benefits, advantages which eventually percolated through to benefit all workers.[54]

To better understand the perspective of immigrants to the US, I recently interviewed a cross-section of individuals who migrated here over the last 50 years, in professions ranging from physicians to taxi drivers to illegal immigrants in the hospitality industry. I posed a series of 22 questions delving into their motivations for migrating to the US, the drawbacks of having done so, their future plans, and how their perspective had changed over time. Interestingly, the majority of individuals cited economic advancement, coupled with the ability to provide a better quality of life for their families, as the primary drivers for having migrated. A key theme that reverberated across all of the interviews was the notion that the economic opportunities found in the US are not found anywhere else in the world. While they missed the company of their extended families, this tradeoff was more than offset by the ability to establish nuclear families here and create strong social ties with other immigrants from their respective homelands.

Like the United States, the United Arab Emirates has also undergone large influxes of migrant labor since its founding in 1971. Prior to the production of oil in the 1960s, its economy

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[49] Shashkevich, Alex. "New Stanford Research Explores Immigrants' Decision to Return to Europe," *Stanford News Service*, September 12, 2017. www.news.stanford.edu.

[50] "Labor Movement," *History.com*, March 31, 2020, www.history.com/topics/19th-century/labor.

[51] "Key Events in Labor History," *ALF-CIO America's Unions*, Accessed 2024. aflcio.org/about-us/history/labor-history-events.

[52]"Haymarket Riot," *History.com*, May 1, 2020. www.history.com/topics/19th-century/haymarket-riot. Pruitt, Sarah, "How a Deadly Railroad Strike Led to the Labor Day Holiday," *History.com*, August 25, 2023. www.history.com/news/labor-day-pullman-railway-strike-origins.

[53]"Labor Movement," *History.com*, March 31, 2020. www.history.com/topics/19th-century/labor.

[54]Rextmk, "HIstory of Labor in the U.S.," Accessed 2024. www.timetoast.com/timelines/history-of-labor-3cb6ae70-d368-4185-8a61-accf7faf7a3c.

was based on fishing, pearling, agriculture, and a nomadic desert lifestyle.[55] The oil industry did not develop fully until the early 1970s, after the country gained independence from Great Britain.[56] The country lacked the industrial backbone, technological know-how, and the manpower needed to support the petroleum infrastructure. Industrial conglomerates like Shell and British Petroleum provided the necessary knowledge for the development of an adequate industrial base.[57] However, the country still needed to quickly procure the appropriate labor force to support this industry. It resorted to medium and long-term contracts with skilled labor from countries worldwide, especially from Asia, the Philippines and Africa.[58] The UAE benefited greatly from the oil boom of the 1970s, and due to the trickle-down effect of petrodollars, there was a building boom as the country modernized and its economy experienced significant growth.[59] This, in turn, necessitated the rapid expansion of the skilled and unskilled labor pool, ranging from white-collar jobs like physicians, architects and accountants, to blue-collar jobs like domestic help, construction workers, and sanitation employees. In all areas, the UAE resorted to migrant labor to fill the gaps.[60] Immigrants started arriving in the 1970s and early 1980s, with a significant acceleration in the late 1990s and 2000s.[61] Today, they constitute 90% of the population, the highest percentage of immigrants in any country in the world.[62]

In the UAE immigration model, individuals are guest workers that may remain in the UAE for only a set period of time before they must leave.[63] They are granted temporary work visas that last 3 to 5 years and that must be renewed regularly, or they are subject to deportation.[64] These work visas are sponsored by an employer under a system termed Kafala.[65]

[55]Malit, Froilan T. and Youha, Ali Al. "Labor Migration in the United Arab Emirates: Challenges and Responses." *Migration Information Source*, September 18, 2013. www.migrationpolicy.org/article/labor-migration-united-arab-emirates-challenges-and-responses.

[56] www.migrationpolicy.org/article/labor-migration-united-arab-emirates-challenges-and-responses.

[57] "Oil and Natural Gas in UAE," Accessed 2024. https://countrystudies.us/persian-gulf-states/85.htm.
[58]"UAE Immigration Statistics 1960-2024," Macrotrends, Accessed 2024. www.macrotrends.net/global-metrics/countries/ARE/uae/immigration-statistics.

[59]Suter, Brigitte, "Labor Migration in the United Arab Emirates: Field Study on Regular and Irregular Migration in Dubai," Malmo University, Sweden, 2005. www.diva-portal.org/smash/get/diva2:1482547/FULLTEXT01.pdf.
[60]www.migrationpolicy.org/article/labor-migration-united-arab-emirates-challenges-and-responses.

[61]www.macrotrends.net/global-metrics/countries/ARE/uae/immigration-statistics.

[62]"UAE Population 1950-2024" *Macrotrends*, Accessed 2023. www.macrotrends.net/countries/ARE/uae/population.

[63]"Residence Visa for Working in the UAE," *United Arab Emirates Government Portal*, Accessed 2024. u.ae/en/information-and-services/visa-and-emirates-id/residence-visas/residence-visa-for-working-in-the-uae.

[64]u.ae/en/information-and-services/visa-and-emirates-id/residence-visas/residence-visa-for-working-in-the-uae.

[65] Malit, Froilan T. and Youha, Ali Al. "Labor Migration in the United Arab Emirates: Challenges and Responses." *Migration Information Source*, September 18, 2013. www.migrationpolicy.org/article/labor-migration-united-arab-emirates-challenges-and-responses.

Under this system, the immigrant population regularly experiences high turnover, as there is no path to obtain permanent residency status.[66] Workers do not fully participate or integrate into society and they live in segregated housing located in the outskirts of town centers.[67] While families are permitted, immigrants typically are unaccompanied and live in joint housing with others from their home country. Also, there are no opportunities for chain migration to occur. Instead, immigrants render remittances to their native countries, which become a source of significant hard currency for these nations.[68] Furthermore, the immigrant population cannot acquire property and may not engage in any type of business without a majority stake owned by a local Emirati financial partner.[69] Recent changes have established the concept of a Golden Visa that permits semi-permanent residency status with sponsorship of immediate family members and domestic help, but most migrants do not meet its stringent eligibility criteria.[70]

While there is a perception in Western media that the UAE immigration model, which is replicated throughout the Middle East, results in exploitation of its migrant labor workforce, on-the-ground interviews conducted by me in the UAE in December 2022 with a cross-section of society revealed that the majority of immigrants felt that their career goals, as well as their overall quality of life, had been positively impacted by their decision to work abroad. I interviewed employees as well as small business owners, who were all immigrants, involved in a variety of industries, ranging from physicians to retail outlet managers to domestic help. I assured them of anonymity and posed a series of questions on topics ranging from their motivation to work in the UAE to the benefits and drawbacks of having decided to do so, as well as their future goals and aspirations. The responses I received from all individuals who participated in my study were uniformly positive. They felt that they had gained significant economic benefit by working in the UAE, with minimal regrets. By regularly repatriating remittances back home, they were also able to substantially elevate their families' overall standard of living. In their minds, whatever trade-offs they experienced, such as long separations from their families, were well worth the advantages accrued. Even though the immigrant population has no political power or freedom of speech, and enjoy limited freedom of religion,[71]

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[66]"How to Get Permanent Residency in the UAE: Ways to Obtain Citizenship," *Visit World*, Accessed 2024. visitworld.today/blog/1630/how-to-get-permanent-residency-in-the-uae-ways-to-obtain-citizenship.

[67] McPhillips, Deirdre, "UAE No Paradise for Migrant Workers," U.S. News and World Report, July 10, 2017. www.usnews.com/news/best-countries/articles/2017-07-10/uae-is-no-paradise-for-migrant-workers.

[68] Naufal, George and Termos, Ali. "Remittances From GCC COuntries: A Brief Outlook," *Middle East Institute*, February 2, 2010. www.mei.edu/publications/remittances-gcc-countries-brief-outlook.

[69] Bhaumik, Gayatri. "Starting a Business in the UAE," *Expatica*, March 1, 2024. www.expatica.com/ae/working/self-employment/starting-a-business-in-the-uae-72286/.

[70] "UAE Residence Visa," *Immigrant Invest*, Accessed 2024. immigrantinvest.com/golden-visa-uae-en/.

[71] Various interviews of immigrants living in Abu Dhabi and Dubai. Conducted by Sahil Polepalle, December, 2022.

the workers were aware of these restrictions from the get-go and did not harbor unrealistic aspirations of wanting, nor desiring, such liberties. Further, my research concluded that workers felt that there were adequate governmental protections that emphasized safety and fairness, and prioritized their health care, without subjecting them to exploitation by a powerful employer.

Strict government regulation governs many aspects of the immigrant work experience. Upon arrival in the Emirates, all workers must attend a mandatory class taught in their native language that discusses, at length, their labor rights.[72] All migrants receive comprehensive healthcare insurance that is widely accepted.[73] Employers are mandated to maintain a government controlled app that tracks all payments rendered to employees to ensure that there is no opportunity for fraud or abuse.[74] From an organized labor standpoint, unions are not permitted to form in the country.[75] Despite this ban, my interviews revealed that immigrants did not feel the need to organize to achieve better labor conditions, given the significant protections that they already enjoyed.

In the Kafala model, immigrants experience limited integration into Emirati society, due to the many rules and regulations affecting their length of stay and the typical absence of a nuclear family being present in the UAE. Despite this, my research in the UAE showed that South Asian immigrants have tremendously influenced the overarching culture, as their food, language, and traditions have come to dominate the country through their minority/majority status. South Asian food is commonplace and unofficially represents the country's major staple diet. Apart from English, Hindi is the most widely spoken language in the UAE.[76] Major Indian festivals such as Diwali are observed and well known by the population at-large. Indeed, one can go for days conducting everyday business without ever encountering a member of the minority Emirati population.

Both the United States and the United Arab Emirates have borne witness to the tremendous contributions made by immigrants to their respective societies. The gains are bidirectional, with the economy of each country benefiting from the productivity and drive of its respective immigrant population, and the immigrants benefiting socioeconomically, by both living and working in their new homeland, temporary or otherwise. With its model of limited

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[72] Sayed, Afez, CEO of Al Haifa Construction LTD. Interview conducted by Sahil Polepalle. December, 2022.

[73]"Healthcare," *Embassy of the United Arab Emirates*, Accessed 2024. www.uae-embassy.org/discover-uae/society/healthcare#:~:text=UAE%20law%20requires%20sponsors%20to,%2C%20dialysis%2C%20polytrauma%20and%20disability.

[74]"What is WPS in the UAE," *Zimyo*, September 6, 2023. www.zimyo.com/resources/insights/what-is-wps-in-uae/#:~:text=As%20long%20as%20you%20are,account%20registered%20in%20the%20UAE.

[75]Brown, Ben. "United Arab Emirates: Labor and Employment Comparative Guide," Mondaq, January 8, 2024. www.mondaq.com/employment-and-hr/1187512/labour-and-employment-comparative-guide#:~:text=Trade%20unions%20are%20not%20formally,Resources%20and%20Emiratisation%20(MoHRE).

[76]"What Languages Do People Speak in the UAE?" *The UAE Blog*, February 6, 2022. theuaeblog.com/travel-tips/what-languages-do-people-speak-in-uae/.

integration, the UAE exemplifies a society that can offer immigrants significant economic opportunities, yet grant them little to no political or labor rights. The US model becomes a case study of how immigrants seeking a new life can gain both social and economic benefits through hard work, coupled with the right to organize. Each model has its own advantages and challenges. While the US remains a magnet for worldwide immigration, it remains to be seen how receptive the nation will be to continuing inflows of immigrants in the future, with rising sentiments of populism dominating the national conversation. Despite its relatively short existence, the UAE has jump-started its economic engine by embracing immigrants, but has simultaneously chosen to severely restrict their societal integration. It remains to be seen how an improving standard of living currently occurring worldwide will affect this equation, and alter the UAE's ability to attract such a labor force in the future. Perhaps the introduction of the Golden Visa may be the first step toward assimilation of these individuals into society at large. Notwithstanding these challenges, people will continue to strive for a better life for themselves and their families, and immigration will continue to be crucial to the economies of these two countries for the foreseeable future.

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travel.state.gov/content/travel/en/us-visas/study/exchange/waiver-of-the-exchange-visitor.html#:~:text=Some%20exchange%20visitors%20with%20J,%2C%20Section%20212(e).

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Fuel Prices in India and How They Affect Energy Consumption Choices By Yashasvi Yadavalli

Abstract

Fuel prices in India have risen, impacting consumer decision-making for transportation, cooking, and lifestyle. This paper discusses the causes and effects of fuel price volatility from 2020-2023. This consists of supply shocks caused by the lack of a kerosene subsidy, the repercussions of price freezing in diesel and petrol, and the volatility caused by political elections. Furthermore, whether the government should subsidize fuel for rural households in Uttar Pradesh, India, is uncovered. Results from a survey of 201 households show a rise in fuel prices, which have caused homes to shift from kerosene (a source of light and cooking) to solid fuels such as dung cakes, firewood, and plastic. Lastly, the paper finds that the government could subsidize fuel for households in rural India to support necessities like cooking fuel. A preliminary literature review and original research collection were conducted in Uttar Pradesh, India, to discover these findings. Survey questions about income, fuel use, and fuel type were gathered.

Introduction

Fuel, one of life's necessities, is integral to Indian households. It runs tractors, irrigation pumps, and other agricultural machinery for farmers. Fuels such as diesel and petrol are essential in the workings of the large agriculture sector in the rural parts of the country. Another necessary fuel is kerosene, which is used as a source of light and cooking fuel for the lower economic strata of the country. Kerosene is a driving force for rural India.

This paper considers fuel as a basket term containing three different fuel sources: petrol, diesel and kerosene.

From 2020-2023, fuel prices sharply rose, specifically in Uttar Pradesh. In this Indian state, the price of diesel increased from 62.87 rupees (USD 0.76) per liter in April 2020 to 89.74 rupees (USD 1.09) per liter in 2023.[1] Petrol meanwhile increased from 71.92 rupees (USD 0.87) per liter to 96.62 rupees (USD 1.17) per liter in 2023.[2] The cost of diesel and petrol increased in 2020 due to increased government tax rates on these fuels. This was done to cope with the loss of government revenue from the COVID-19 pandemic.[3] There has also been an increase in the price of kerosene caused by supply shocks and increased inflation in the country. The supply of kerosene has drastically reduced in Uttar Pradesh, as the Indian government's Ujjwala Yojana initiative has been attempting to minimize kerosene usage in the country in hopes of shifting rural India towards a cleaner energy source: Liquid petroleum gas (LPG). Furthermore, the price of kerosene had risen due to the government halts on fuel subsidies.

Furthermore, fuel rates increased exponentially in 2022 in Uttar Pradesh due to earlier price freezes during state elections.[4] This freezing of prices was done when international prices for crude oil were high during the Russian invasion of Ukraine. Therefore, this sudden unfreezing in the state led to an exponential increase, as shown in *Figure 1*.
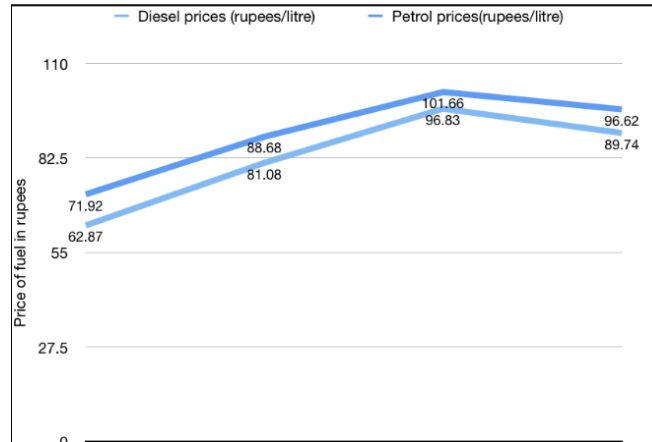
Figure 1: Trend in the price of diesel and petrol in the state of Uttar Pradesh from April 1, 2020, till April 1, 2023. The voluntary supply shocks of kerosene evolved in multiple states - including Uttar Pradesh. The government hoped to shift India through the Pradhan Mantri Ujjwala Yojana programme, which sought to increase the use of LPG in the country by reducing the number of solid fuels burnt as cooking fuels. To further this program's goal, the government has been reducing the supply of kerosene in the country. However, according to Farzana Afridi (2021), despite rapid increases in LPG access in rural areas and subsidized LPG refill consumption, regular LPG use in India still needs to grow. In June 2019, the average annual usage of LPG in rural households remained less than half of what is thought to be required to eliminate solid fuel use. The leading causes of low LPG use are the need for more information regarding the health benefits of using the fuel, lack of knowledge of available subsidies, and household financial constraints. The state of Uttar Pradesh voluntarily surrendered 68,632,000 liters of kerosene on October 7, 2019.[5] This led to Uttar Pradesh receiving 75,764,000 liters of kerosene in the 4th quarter of 2019.[6] The kerosene distributed to Uttar Pradesh was further reduced to 52,969,000 liters in the 2nd quarter of 2020.[7] Finally, the kerosene distributed in the 4th quarter of 2020 was 0 liters. This sudden decrease in kerosene supply caused a spike in the prices in the state.

Rising fuel prices can trap people in poverty in a country by significantly burdening households with limited incomes. As fuel prices increase, transportation costs escalate, affecting the prices of essential goods and services. This leads to a higher cost of living, making it increasingly difficult for low-income individuals and families to meet their basic needs. The additional financial strain can push people closer to or deeper into poverty, as a substantial portion of their income is allocated to fuel expenses, especially as fuel is an essential need that cannot be substituted. Moreover, rising fuel prices can affect the overall economy, leading to inflationary pressure. This can reduce the purchasing power of individuals, making it harder for them to afford essential goods and services. Additionally, sectors dependent on fuel, such as agriculture and transportation, may need more, reducing job opportunities and hindering individuals' ability to escape poverty. Therefore, rising fuel prices can perpetuate poverty traps by negatively affecting economic stability in a country.

Furthermore, due to the inaccessibility of kerosene in Uttar Pradesh, households are forced to switch to more unhealthy fuel sources such as wood, dung cakes, and plastic. This is

because most of the population needs LPG and electricity connections as alternative methods for cooking fuel and light. This leaves them vulnerable to unhealthy and potentially life-threatening gasses.

Thus, this paper explores:

1. **How have rising fuel prices affected households' fuel consumption and financial decisions in rural India?**
2. **How much are families willing to pay for fuel, and should the government subsidize it again?**

The Pradhan Mantri Ujjwala Yojana's goal has been to increase the use of LPG in the country by reducing the amount of solid fuels burnt as cooking fuels. To further this program's goal, the government has been reducing the supply of kerosene. However, according to Farzana Afridi (2021), despite rapid increases in LPG, access in rural areas, and subsidized LPG refill consumption, regular LPG use in India remains low.[8] In June 2019, the paper talks about how the average annual usage of LPG in rural households remains less than half of what is thought to be needed to eliminate solid fuel use. The leading causes of this low LPG use are the need for more information regarding the health and subsidy benefits of using fuel and household financial constraints.

Despite the subsidy, the cost of LPG can still be high for poor households in India. The study's results highlighted the financial constraints that rural households face in India. Moreover, implementing an LPG connection to a home can be seen as capital intensive for the lower economic strata of India, as there is an upfront cost of 3200 rupees (45 USD). This is approximately 47.8% of the household income in the Bulandshahr district, Uttar Pradesh. According to another study done by the Council of Energy, Environment and Water (CEEW; 2019), it was indicated that if LPG was used as the exclusive source of cooking fuel, a typical household would have to allocate a significantly higher share of its overall monthly expenditure, approximately 9.3% in rural India.[9]

LPG is too expensive for households to use as their only source of cooking fuel. This point has been further presented in another paper written by Farzana Afridi (2023), which demonstrated that while 67.5% of the sample reported using LPG for cooking in the previous month, a large share of households reported also using dirty fuels (74.8% firewood, 87.8% dung cakes, and 11.3% crop residue) for cooking.[10] Households tend to use solid fuels frequently and regularly for cooking regardless of LPG account status.

Farzana Afridi (2023) explains how the lack of awareness regarding the health benefits and available subsidies of LPG has caused many not to use their LPG connections regularly, as households assume the LPG connection was a one-time "gift" from the government.[11] An LPG connection provides access to liquefied petroleum gas (LPG) for domestic use. LPG is a flammable hydrocarbon gas commonly used as a clean-burning fuel. In the Pradhan Mantri Ujjwala Yojana Programme, an LPG connection provides households with the necessary equipment, such as a gas cylinder, regulator, and pipes, to access and use LPG safely and conveniently for cooking.

The paper results show that the sample group that received health and subsidy information was the most likely to refill their LPG purchase. To explain, the experimental group–which was only provided with the health benefit–was seen to have behavioral changes that reduced smoke inhalation in households. These results were similar to Madajewicz (2007), in which households in Bangladesh that used arsenic-contaminated wells were more likely to switch to a safer water source once the well was marked unsafe.[12] The information provided to the households in Bangladesh led to a change in their behavior regarding the source of water they would use. These results show the impact of the unawareness of health benefits, not only in energy.

Furthermore, the findings in Afridi's research highlight the complementarity between health and subsidy awareness. Another group presented with both the health and the subsidy information showed the most significant increase in LPG refills. This further suggests the importance of increasing information regarding the subsidy. It also shows financial constraints' critical role in household decision-making regarding chosen fuel sources.

Methods

Primary and secondary data were analyzed to investigate **how** rising fuel prices have affected households' finances and consumption decisions. Understanding the cause of increased fuel prices over the last three years in Uttar Pradesh is essential.

For this, secondary data was collected: papers, government sites and data think-tank websites. A literature review was done for these papers to understand the cause of price increases and critically understand the roles that the income effect* and the substitution effect** have played in household consumption decisions over the last three years. It is also essential to observe the changes in fuel prices in the state of Uttar Pradesh from 2020-2023, along with changes in average wages/income.

Primary data is crucial to collect to understand the extent of the income and substitution effects. This was done through a survey, a wealth index, and an expenditure table. The survey consisted of 14 questions found in *Table 1* below:

1. What is the number of household members you have?
2. What is the number of household members aged 17 or under?
3. What is your household income per month?
4. What are your areas of expenditure per month?
5. Have your expenditures in these areas changed over the last 3 years?
6. In what daily activities do you use fossil fuels (such as kerosene, diesel, petrol, coke/coal)?
7. In the activity of cooking, what source of energy did you use earlier (3 years ago)?
8. Now, has the amount of this energy source increased, decreased or stayed the same?

9. If it has decreased, what alternatives have you started to use more in the area of cooking?
10. What source of energy did you use as a source of light earlier (3 years ago)? (To be used as a form of light to study, or to have a lit home for dinner, or having company over)
11. Now, has the amount of this energy source increased, decreased or stayed the same?
12. If it has decreased, what alternatives have you started to use more?
13. What is your monthly expenditure on fossil fuels?
14. Do you think fuel is more expensive now, or was fuel more expensive a year ago?

Table 1: List of Survey Questions

Each question was asked to uncover differences in the following household variables from 2020 to 2023:

- The change in income
- The daily fuel usage
- Whether there was a change in the cooking fuel
- Whether there was a change in the fuel used for a light source
- What the population would be willing to spend on fuel

Along with these results, the Bulandshahr, Uttar Pradesh district's sampled population was asked to complete a wealth index survey. The purpose of the wealth index was to determine the approximate wealth of the person sampled, considering that those with higher wealth would be less affected by price changes than those with a lower wealth level. Considering the area of study is one of the poorest districts in India, the difference between high and low levels of wealth is marginal.

The sample population includes farmers who send their children to a (Non-Governmental Organization) NGO school called Pardada Pardadi Educational Society. This sample population was explicitly targeted due to the relationship with the school and a lesser reluctance for these families to share private information in surveys. Additionally, it could be assessed if a household sends their child with no tuition cost. Two hundred-one households were surveyed and selected within the sample population, thus allowing the results of this paper to be generalized to the sample population. To limit the variability of the results, specific control variable questions were asked:

- Whether the household was under the Pradhan Mantri Ujjwala Yojana government scheme
- What material is the house made of
- Number of household members
- Number of household members 17 years old or younger.

After analyzing the survey data, an evaluation of whether the government should subsidize kerosene was completed

Results and Discussion

The data for the graphs were collected through the wealth index and the question survey. The 201 responses were then tabulated, and multiple graphs were drawn to show correlations between different parameters of the survey and the wealth index score.

Participation in the Government Program

Figure 2 represents the number of households under the government LPG subsidy program. This is important as it justifies the point made in the literature review regarding the lack of families under the LPG program.

Whether the household is under the Pradhan Mantri Ujjwala Yojana Programme
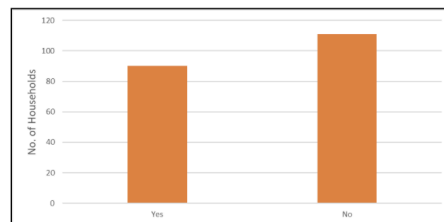
Figure 2: Bar graph displaying the number of households under the government subsidy program. Ninety farmers out of the two hundred-one participants are under the program and one hundred-eleven farmers are not under the program.

As seen in *Figure 3*, out of 201 farmers, only 90 are under the government program. This justifies the point made in the literature review regarding the lack of families under the LPG program because households are forced to use cheaper, more toxic alternatives. Despite 314,000,000 crore families being provided an LPG connection, a large portion of the Indian population has not installed LPG pipelines in their houses.

The following chart shows results between the average wealth index score for a family under the government subsidy scheme and a family not under the plan.

Average Wealth Index Score vs. Whether the household is under the Pradhan Mantri Ujjwala Yojana Programme
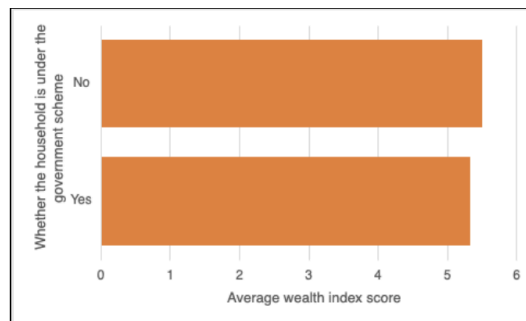
Figure 3: The bar graph shows the average wealth index score for a family under the government subsidy scheme and a family not under the government subsidy scheme.

Households under the subsidy program have a lower wealth index, which could be attributed to a lack of income to spend on wealth indicators such as beds, chairs, and other parameters considered in the wealth index, leading to a lower score. This claim is made with the assumption that those with an LPG connection are more likely to purchase the gas more frequently than those households without the connection.

As the bar graph shows, the average wealth index score for families not under the government subsidy scheme can be seen as larger than those under the government scheme. Although the difference in the average wealth index is only marginal, this may support another claim made in the literature review and the introduction: LPG is too expensive.

Changes in fuel use and income over time

In *Figure 4*, it can be seen that over the last three years, the survey responses show a decrease in the usage of LPG from 84 (out of 201) in 2020 to 77 participants using the source regularly. Moreover, there was a slight decrease in the usage of dung cakes, from 185 out of 201 participants using it in 2020 to 166 participants using the source regularly in 2023. In 2020, 73 out of 201 survey respondents were using firewood as a source of cooking fuel. However, there was a decrease in its usage for 29 participants until 2023.

Three years ago, 121 out of 201 survey responders used kerosene as a source of fuel for cooking; however, now, only five responders use kerosene as a cooking fuel source. Moreover, 101 out of 201 survey responders used kerosene as a source of fuel for light. However, now, only 18 responders use kerosene as a light source.

Number of participants using kerosene (in 3 years) vs. Type of activity

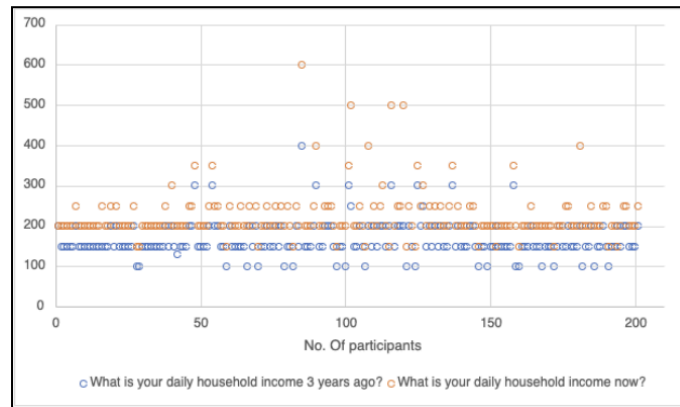**Figure 4**: The graph above shows the change in kerosene usage ov
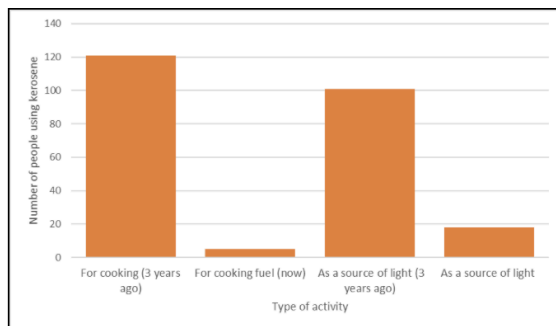
er the last three years as a source of light and cooking fuel. The number of participants using kerosene for cooking decreased from 121 to 5, and those using the fuel as a source of light decreased from 101 to 18.

The increase in price due to supply shocks has subsequently decreased the quantity demanded of kerosene. The graph shows the drop in the kerosene usage as a source of light and cooking fuel.

Additional analysis shows that a single fuel is rarely used for cooking. Rural households utilize a combination of fuel sources and see a decrease in the usage of LPG. There is also a

more significant percentage of the survey responders using dung cakes as a fuel source, approximately 82.5% in 2023. The results from the change in income are shown in *Figure 5*. The average income three years ago was 165.8209 rupees (USD 1.99) per day. Whereas now, the average income is reported to be 223.1343 rupees (USD 2.68) per day, and 23 participants of the sample surveyed showed an increase of income greater than the average change of 57.3 rupees (USD 0.69) per day.

Change in Income over 3 years

Figure 5: The graph above shows the daily income of each farmer sampled three years ago and their income now. The graph indicates that the daily income is much greater for most farmers than three years ago. More specifically, out of the 201 sampled, 198 survey responders showed an increase in their average daily gain. While two responders showed no change, and for one person, the difference in income was negative.

Due to the large proportion of the survey responders showcasing a positive change in their income, people may have higher incomes to compensate for the higher prices. However, due to the marginal difference in the average income, it is possible that any increase did not affect the quantity demanded of fuel by households.

Willingness to pay and perceived fair price for fuel

The percentage of people surveyed who believe fuel is more expensive now is 99.0%. This provides evidence of increased fuel prices over the last three years. Furthermore, the average expenditure on fuel is 346 rupees (USD 4.19) (monthly), while the average reasonable price reported for fuel is 260.199 rupees (USD 3.15) (monthly) among the survey respondents. We can learn that 98.5% of respondents believe their total expenditure has increased by analyzing the survey data.

According to a distributor in West Uttar Pradesh, kerosene prices are 120 rupees per liter (USD 1.45), while the average monthly expenditure on the basket of fuels is 346 rupees (USD 4.19). This shows that one liter of kerosene covers 34.6% of the monthly expenditure on fuel. Hence, we can conclude that the prices are too high and must be reduced. Therefore, the government must subsidize this particular fuel source since their initial plan to promote LPG has

yet to create a significant enough impact to reduce the usage of solid fuels ultimately. Stopping the supply of kerosene was not the solution, as evidenced by the results of this research showing an increase in the use of solid fuels, such as dung cakes, instead of a more significant rise in LPG usage.

Conclusion

This paper documents the cause of the rise in fuel prices in Uttar Pradesh. It discusses how such rises have subsequently affected fuel consumption decision-making for rural households in India. It has been found that the kerosene price increase has been caused by massive supply shocks by the state government and the state's complete stoppage of the kerosene subsidy. Furthermore, high price fluctuations in the fuel sources diesel and petrol have been caused by political influence when the Uttar Pradesh government froze prices during the global fuel price instability from the Ukrainian-Russian wars. Moreover, the government increased kerosene prices to reduce this fuel usage and promote the use of LPG. The usage of LPG as a cooking source was further promoted through the government subsidy Pradhan Mantri Ujjwala Yojana. However, as seen in the literature review, there are still many areas where the government must improve this subsidy program for fuel sources. These areas include a need for more information regarding the health and subsidy benefits of using fuel and the financial constraints of households. Due to the rising kerosene prices, families were forced to switch to solid sources, such as dung cakes and firewood, which can cause health and environmental problems.

As the results show, the survey responders spend an average of 364 rupees (USD 4.41) per month on fuel and believe a reasonable price is 260 rupees (USD 3.15) per month. Therefore, the government could subsidize fuel at least 100 rupees (USD 1.21). This subsidy amount could be larger, based on the argument that higher prices over the last three years have led households to use less than necessary fuel in their day-to-day lives. If true, the subsidy rate should be greater than 100 rupees monthly.

Implementing this subsidy would be difficult (since fuel has been considered a basket term for diesel, petrol, and kerosene) but practical. Since the Ujjwala Yojana program is a "cash back subsidy" program, instead of a direct subsidy on gas, households cannot afford it, as rural households in India are not liquid in cash (Afridi, 2023). Hence, the government could use another method of providing a subsidy, for instance:

1. Give rural households monthly "vouchers" of 100 rupees that they must use on fuel. This method is simple and easy, allowing homes to spend on any fuel necessary, excluding solid fuels such as dung cakes.
2. Make it mandatory that households provide proof that they have spent money on fuel. Since the infrastructure is already constructed for this through the Ujjwala Yojana, the government can use it.
3. When the proof is approved, households automatically receive monthly vouchers for three months. By providing vouchers for three months, any technical delays in approval

would not negatively affect the lives of families, as we would recommend they send the proof every month.

This subsidy method would help rural households in states such as Uttar Pradesh.

Although the Pradhan Mantri Ujjwala Yojana programme has increased access to clean cooking fuel through financial support, LPG still needs to be cheaper for households to refill annually. Furthermore, there is a need for adequate awareness and education campaigns to ensure safe usage of fuel.

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Review of Corporate Social Responsibility Reporting Frameworks By Daylan Kim

Abstract

In the wake of increased globalization and rapid technological advancement, organizations are facing increasingly complex business issues and problems with their stakeholders, who now have access to more information about the business practices of the organization. One of the most challenging issues organizations must deal with is their performance of the corporate social responsibility (CSR) and sustainability. Businesses are expected to not only make profits but also conduct socially responsible behaviors and environment friendly practices in their business operations. In addition, they need to communicate such practices to their stakeholders by disclosing their CSR performance on a regular basis. There are several types of CSR reporting frameworks that corporations can adopt as a guideline or tool to prepare their CSR and sustainability performance reporting. This paper reviews the most widely adopted CSR reporting frameworks by global companies across different industries or countries and evaluates advantages, disadvantages, and rationale for adopting certain framework. ESG reporting framework is discussed in detail as a key framework for CSR reporting. The content of this paper can be used as a reference for the companies in need of implementing an internal CSR guideline or reporting CSR performances.

Introduction

After some restrictions on business practices were deregulated and liberalized to aid the recovery from the economic recession, major global corporate corruptions and scandals early in the New Millennium were reported, most of which were caused by the lack of business ethics and social responsibility of certain business leaders (Heath and Norman, 2004). Following these incidents, the government and regulatory institutions reinforced business regulations for ethical conduct (for example, Sarbanes-Oxley Laws, Global Reporting Initiatives, the United Nations Global Compact, etc.) and firms have been forced to strictly follow the new regulations (Val et al., 2011). However, for the past decade, the new mega-trend of globalization and the rise of emerging markets has allowed global manufacturing firms to take advantage of offshore outsourcing of their supply chain activities to developing countries, and to avoid being exposed to risks associated with business ethics.

Recent developments concerning some Fortune 500 companies' violations of socially responsible business conduct and subsequent allegations of wrongdoing have raised concerns among stakeholders about CSR and sustainability, beyond mere environmental protectionism (Tate et al., 2010). Moreover, the rapid advancement of internet-based technologies has allowed stakeholders, including consumers, communities, social protection groups, and regulators, to obtain extensive information about an organization's practice and performance (Heizer and Render, 2014). As a result of increased visibility, many firms are more concerned than ever with practicing business in a way that is both ethical and beneficial to stakeholders.

According to a 2009 survey conducted on Fortune 500 firms, CSR became an important part of the corporate strategy agenda (Smith and Alexander, 2013). An organization's social performance and its impact on the environment have become critical elements in its overall

performance and its ability to continue operating efficiently (ISO 26000, 2010). Traditionally, economic and social objectives were perceived to conflict with each other (Friedman, 1970). It is now generally accepted that, since firms do not function in isolation, but rather as part of their local environment and society, social and economic goals are fundamentally connected and complement each other (Porter and Kramer, 2002). Werther and Chandler (2005) contended that the concepts of CSR and profit maximization in business strategy have become increasingly inseparable in the 21st century.

CSR is such a hot topic that it has received considerable attention from both practitioners and scholars. The management of firms and their shareholders want to know what benefits the investment in CSR can bring them. Due to the increase of such concerns in the past decade, there has been a surge in research and development related to the relationship between CSR and many types of business performance. Consequently, organizations and their stakeholders are increasingly concerned about the need for and benefits of socially responsible corporate behaviors (Walker and Jones, 2012). In recent years, CSR has gained momentum in global corporations as a critical agenda, along with the increased concerns for environmental protection and sustainable growth (Carter and Easton, 2011). As a result, consumers, governments, and non-governmental organizations (NGOs) are demanding that companies be held more accountable for social issues and environmental concerns and disclose transparent information about their CSR and sustainability performance by reporting CSR activities in their annual reports using selected frameworks and guidelines.

In this paper, various CSR reporting frameworks are reviewed and examined to analyze pros and cons of each framework and illustrate which framework would serve best for the purpose and objective of the organization based on the nature and intent of the business functions and circumstances.

CSR Reporting

CSR reporting was once for only some large public companies to comply with SEC requirements or to showcase their social contribution and improve their corporate reputation. Recently CSR reporting has become a widely practiced form of self-regulation across organizations of all sizes (IBM Envizi). Just like organizations are obligated to periodically report their financial performance using financial statements and other SEC reports to their external stakeholders, they voluntarily report their non-financial performance on CSR. In some regulated jurisdictions, CSR reporting is also mandatory for publicly traded companies to provide non-financial performance information to external stakeholders.

Historically the information in CSR report was limited to social aspects, for example, concerns for employees' welfare or workplace conditions and contribution to the communities. CSR report nowadays contains a broad spectrum of performance result on non-financial aspects ranging from socially responsible practices to environmental activities and corporate governance structures. There are several CSR reporting frameworks available to organizations to support CSR reporting, depending on which CSR area the organization intends to focus on to highlight their non-financial performance. Currently, one of the most widely used and accepted reporting frameworks is Environmental Social and Governance (ESG) reporting. ESG reporting specializes in quantifying environmental and sustainability efforts as well as communicating social responsibility. It measures sustainability performance against comparable metrics and sets exact

targets for the future, making ESG reporting more relevant to our current situation with the climate crisis and the demand for organizations to be ethical. In this paper, ESG reporting using various supportive frameworks and standards will be particularly discussed as a main CSR reporting framework.

ESG Reporting

ESG reporting is a process of identifying, collecting, documenting, and disclosing the information related to organizational performance on CSR using various types of ESG frameworks and standards. The frameworks and standards provide a set of criteria for evaluating an organization's performance in environmental, social, and corporate governance areas (Quantive.com):

- Environmental – This area is where a company shows its impact on the environment by reducing greenhouse gas and other toxic chemicals involved in business operations and measuring the company's carbon footprint and achieving sustainability objectives.
- Social – In this area, a company reports its business practice on social issues related to both internal and external stakeholders including the broader community. Social factors would include gender equality, racial diversity, and inclusion in employee relationship management and hiring practices.
- Governance – This area includes management's practice on compliance and integrity of the ownership structure and corporate decisions on issues ranging from executive pay, diversity in leadership, and transparency with shareholders.

Therefore, ESG is a practical and business suited process for addressing how a company serves and meets stakeholder expectations by managing ESG efforts to comply with regulations and managing risks and opportunities. Additional benefits of adopting ESG reporting include providing a competitive advantage for the company and attracting new capital investments.

ESG Reporting Frameworks

ESG reporting frameworks are composed of guidelines, standards, and principles, which encompass a range of ESG performance measurements, including board diversity, greenhouse gas emissions, and social issues including diversity, equity, and inclusion. While ESG frameworks provide guidance and best practices, ESG standards are benchmarks of ESG commitment a company must meet. ESG reporting can be structured and customized to target three major types of stakeholders using the following several supportive frameworks and standards:

- Investors: To help investors make decisions by providing information on a potential investment's CSR performance, Global Reporting Initiative (GRI), Dow Jones Sustainability Indices (DJSI), and World Economic Forum (WEF) reporting framework are most pervasively used for ESG reporting (Fernandez-Feijoo et al, 2014).
- Government: To serve as guidelines for governments as well as private organizations to provide sustainability-related services and support, Carbon Disclosure Project (CDP) and United Nations Sustainable Development Goals (UN-SDG) are most widely used for ESG reporting (Bose, 2020).

- Management: To provide conceptual and technical guidelines for a management to systematically produce sustainability performance outcomes, International Organization for Standards (ISO), SA8000, and Science Based Targets initiative (SBTi) are most frequently referred to for ESG reporting (Chiarini and Emidia, 2017).

There are a handful of other CSR reporting frameworks and tools available, however, in this paper the above selected ones will be discussed as they are considered most representative according to the researched literature.

Global Reporting Initiative (GRI)

Sustainable development has become increasingly important in corporate agenda after the Brundtland report was launched in 1987. Social and environmental accounting and reporting plays a relevant role in sustainability performance of the organizations (Moneva et al, 2006). GRI sustainability reporting guidelines were developed to help organizations communicate their impacts on CSR through producing sustainability reports that integrate social, environmental, and economic impacts of business. GRI has developed the leading standards for CSR reporting and is considered the most prominent and widely used reporting tool for environmental impacts (Isaksson and Ulrich, 2009).

Environmental issues have become increasingly important in recent years in the business world and in society at large. Due to the growing importance of environmental concerns and the subsequent need to disclose environmental information to stakeholders, companies have tended to voluntarily disclose more information about their environmental impacts (Gallego-Álvarez et al, 2018). This disclosure is of great relevance because of the current interest in both companies and society in environmental issues. GRI can provide an opportunity for companies to communicate their performance of managing greenhouse gas emissions. Therefore, companies are implementing GRI to improve the environment and inform stakeholders about their dedication and efforts towards the environment (Lee, 2012).

GRI consists of a modular system set of three series of standards (universal, sector, and topic standards) focusing on material issues relevant to stakeholders and offers in-depth understanding and insights of environment, economic, and societal impacts by calculating key performance indicators (KPI) which can be adopted by companies to improve CSR performance (GRI Homepage). However, the extensive number of KPIs in the GRI framework makes selections challenging and complex and time-consuming to implement for particularly small businesses. It also focuses on disclosure versus ESG performance, where organizations may just report on ESG impact without improving it or behaving in a responsible way (Laskar, 2018).

Dow Jones Sustainability Indices (DJSI)

DJSI was launched in 1999 as the first pioneering series of global sustainability benchmarks available in the market for CSR reporting framework to track CSR performance of top 10% of the largest 2,500 companies in the S&P Global BMI based on long-term economic, environmental and social criteria. The DJSI benchmarks are comprised of three geographical breakdowns: DJSI World DJSI Regions, and DJSI Countries (S&P Dow Jones Indices Homepage). The indices evaluate and assess companies within their respective industry based on

a broad range of ESG factors, providing a holistic evaluation. The indices have earned worldwide credibility as the benchmark for sustainability performance. However, because the benchmark is exclusively for publicly listed companies, small or private companies cannot adopt the framework due to lack of resources and accessibility. The indices rely on subjective evaluations for some qualitative assessment, which can lead to inconsistencies or inaccuracies.

World Economic Forum (WEF)

WEF is a public interest, not-for-profit organization committed to improving the state of the world. ESG reporting framework helps institutions report their ESG performance using the Measuring Stakeholder Metrics, 21 core and 34 expanded metrics across four pillars — governance, planet, people, and prosperity. The framework aligns with other ESG reporting standards and covers a broad, comprehensive range of ESG metrics (World Economic Forum Homepage). However, the framework is still relatively new, making it difficult for companies to benchmark themselves. It also relies on self-reporting, which may lead to a lack of transparency and accuracy in reporting.

Carbon Disclosure Project (CDP)

CDP was established in 2000 and helps institutions to disclose and report their impact on the climate. The CDP framework uses a questionnaire covering climate change, deforestation, and water usage, which then calculates a sustainability score and provides benchmark compared to peers and feedback on potential ESG risks and opportunities (CDP Homepage). It facilitates transparency with stakeholders on carbon emissions and environmental impact and helps identify environmental risks. CDP is considered the gold standard of environmental reporting with the world's most comprehensive collection of self-reported data. However, the framework can be time-consuming and resource intensive. It has a limited scope on carbon emissions and environmental impact and doesn't enforce sustainability targets or hold companies accountable.

United Nations Sustainable Development Goals (UN SDGs)

UN SDGs was established in 2015, listing 17 goals that help create a more sustainable and equitable future. These goals aim to end poverty, protect the planet, and promote peace and prosperity through education, healthcare, gender equality, and clean energy. The goals address the most urgent issues for action in all countries (United Nations Homepage). The goals have clear ESG metrics and indicators, allowing for better progress tracking and accountability. Some goals may be overwhelming and contain unrealistic targets. The goals also prioritize economic growth over social and environmental issues and may require significant funding to achieve.

International Organization for Standards (ISO)

ISO is an independent, non-governmental organization that provides institutions with standards across hundreds of ESG topics, namely, ISO 14000 and ISO 26000. The ISO 14000 sets out the criteria for an environmental management system, practical tools designed for any type of companies to manage their environmental responsibilities and get certified for completing the requirements. The ISO 26000 was published in November 2010, aiming at promoting sustainable development by providing a CSR framework for companies to measure their level of engagement

in socially responsible behaviors. The guideline provides best practices and recommendations on CSR for organizations seeking to incorporate them into their operations. The guideline addresses a range of core subjects related to social and environmental issues with the aim of promoting sustainable development (ISO Homepage).

One of the evident benefits of adopting ISO 26000 is that all types of organizations can apply the ISO 26000 guidelines (ISO, 2010). Any organization choosing to adopt the guidelines will optimize its processes, management systems and activities relating to social responsibility and contribute towards global sustainable development. In contrast, Schwartz and Tilling (2009) criticized the generalized approach of ISO 26000 as being too generic: Its "one management standard fits all organizations and contexts" approach can be questioned, not only for its assumptions on organizational rationality but also for being "slippery" and more concerned with symbolic value than actual results. Given these critical voices, as well as ISO's own assessment of ISO 26000, whether the new standard is a useful tool for structuring strategic management processes for the highly diverse domain of CSR is questionable (Schwartz and Tilling, 2009). Another drawback of the guidelines is the fact that they are voluntary and do not offer a certification resulting in a lack of enforceability of compliance.

SA 8000

SA8000 is an international certification standard that encourages organizations to develop, maintain and apply socially acceptable practices in the workplace. The standard is viewed as the most globally accepted independent workplace guidelines, which can be applied to any company, of any size, worldwide. Adopting SA8000 certification enables organizations to consider the social impact of their operations and to develop and improve social accountability across the operations. The SA8000 certification standard can help companies demonstrate a commitment to social accountability and allows them to ensure compliance with global standards and reduce the risk of negligence, public exposure and possible litigation (Social Responsibility International Homepage). However, because SA8000 is not a standard specifically developed for environmental management, the standard lacks the capability of disclosing the impact on the environment.

Science Based Targets initiative (SBTi)

Science Based Targets initiative (SBTi) was set up in 2015 as a partnership for collaboration between multiple organizations (e.g., UN Global Compact, CDP, and World Resources Institute) to help reduce greenhouse gas emissions by providing technical assistance and expert resources to companies who set science-based targets in line with the latest climate science. The SBTi's Corporate Net-Zero Standard is the world's only framework for corporate net-zero target setting in line with climate science offering guidelines for science-based targets across the value chain (Science Based Targets Homepage). It assists institutions in futureproofing, preparing them for upcoming regulations and helps institutions become greener, reducing reliance on fossil fuels. The reporting also improves investor confidence, with SBTi adherence improving business longevity. However, the reporting can be time-consuming and resource-intensive due to the complex technicality and because it focuses on reducing greenhouse gas emissions it doesn't consider other sustainability issues.

Discussions

In the previous section, eight CSR reporting frameworks that can measure an organization's ESG reporting were selected and reviewed, depending on what aspects of the framework are most relevant to the organization and most informational to its respective stakeholders.

Investors are primarily concerned with an investee company's specific ESG actions and practices that can create sustainable value. GRI provides a framework for identifying the key environmental, social, and economic impacts the company has based on the nature of its business. According to the KPMG survey of sustainability reporting for 2020, 73% of the largest 250 companies in the world reporting on sustainability use GRI and 67% of the largest 100 companies in 52 countries reporting on sustainability use GRI (The KPMG Survey, 2020). GRI offers the only reporting standards used by most surveyed companies in all regions (75% in the Americas, 68% in Asia-Pacific and Europe, 62% in ME & Africa) (GRI Homepage). For example, companies in the mining, metals, and electric utility sectors will likely best engage and meet the interests of investors by choosing the GRI topic-specific standards (Conserive.com).

DJSI is considered a best-in-class benchmark for investors who recognize that a company's sustainable business practices can play a critical role in generating long-term shareholder value. WEF framework has become more popular as reported in 2023 WEF Meeting, over 150 companies have implemented Stakeholder Metrics in reporting sustainability reports. The new Future of Growth Framework introduces a multidimensional approach with the aim of identifying countries most closely related in their growth characteristics and facing similar constraints and opportunities (World Economic Forum Homepage).

Companies and governments can use CDP questionnaires and its scoring methodologies to measure and manage environmental impacts and report their carbon footprint and greenhouse gas emissions. Since European Union Carbon Border Adjustment Mechanism (CBAM) has become effective from October 1, 2023, affected EU importer companies must determine and document direct and indirect emissions that occur during the production process of the imported goods as a requirement during the transitional phase of the implementation. The CDP framework can support the CBAM report for recording and determining carbon dioxide equivalent emissions.

UN SDGs and SBTi framework can help organizations set targets that show how much- and how quickly they need to reduce their greenhouse gas emissions to prevent the worst effects of climate change from happening. Governments can refer to those targets in setting their nationally determined contributions and implementing policies to eradicate poverty and achieve their sustainability goals and objectives.

Other ESG reporting frameworks including ISO standards and SA8000 can support companies to set up their internal ESG reporting process and implement sustainability management policies, particularly in managing employee related matters and providing safe working environment.

Conclusions

Preparing an ESG report is not a simple task because gathering data alone is complex and time consuming, but understanding what business aspects to focus on and which framework to adopt can be the biggest challenge for many organizations. Reporting methodologies and approaches require a substantial in-depth business process analysis, requiring professional knowledge and expertise and must be backed up with robust sustainability strategies and risk

management processes. Requirements for ESG reporting differ between geographical regions, and there are few, if any, widely agreed-upon standards, meaning that the content, length and style of ESG reports can vary widely between organizations. Which framework and standard is best for your organization will depend on your company's operations, industry, location and what existing reports and sustainability programs your company already has in place.

Due to the lack of common CSR reporting frameworks and standards, organizations can select the only information they intend to stress for their achievements and highlight them in their reports. This can not only make it difficult to draw accurate comparisons between organizations but can also lead to accusations of greenwashing and reputational damage. If there was a standard ESG criterion, analyzing and understanding the data would be more efficient and the ability to greenwash would be reduced (ClimatePartner.com). Organizations should try to be as open as possible in their reporting by disclosing their CSR shortcomings and areas where they need to improve, as well as their successes. Success is often rewarded prematurely with policies and procedures that are being measured, not the performance of how well they are doing. The more transparent the organization, the more likely consumers are to trust that these issues really matter to the organization.

CSR reporting is now so universally adopted that companies not yet reporting will find themselves seriously disadvantageous and behind global trends and norms. The managers of those non-reporting companies must realize that such misalignment with accepted global practice poses critical risks to many aspects of business operations and must take immediate actions to define the CSR strategy, set up goals and priorities, and select a reporting framework that best suits the company's industry and region. Implementation of adequate processes and policies for CSR reporting is an important task for governments, companies and consumers which need to accept responsibility for their external effects on societies and the environment.

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The Increasing Use of Artificial Intelligence (AI) in Finance by Huanyu Liu

Abstract

AI (Artificial Intelligence) in finance is a transformative technology that revolutionizes various aspects of the financial services industry. It enables personalized services, risk management, fraud detection, compliance, automation, and more. Machine Learning (ML), a subset of AI, allows systems to learn from data without explicit programming. One area in which machine learning is used in finance is credit scoring, where credit models can be continuously refined to make them more accurate. Machine learning can also be used to develop forecasting models for securities prices. AI applications in finance include speech recognition, sentiment analysis, anomaly detection, recommendations, translation, document processing, image recognition, and cybersecurity.

Introduction

The benefits of AI in finance encompass automation, accuracy, efficiency, speed, availability, and innovation. It automates tasks, reduces errors, enhances efficiency, processes data quickly, offers services anytime and anywhere, and drives innovation through data analysis. The future of AI in finance entails personalized customer engagement, safer product recommendations and trust-building through AI-powered concierge services, which are used to help consumers better manage their finances. Financial institutions will reduce the problem of data silos, which are collections of data that are not readily available to all users within an organization. Financial institutions can also apply AI and combine human interaction to create tailored experiences that meet customer needs while scaling effectively (i.e., increasing the efficiency of decision making.)

AI is changing finance, potentially saving banks $447 billion by 2023. It's used for tasks like chatbots (programs that simulate human interaction), fraud detection, and helping manage money. About 80% of banks know AI's benefits. It makes banking easier, prevents fraud, and helps businesses assess risks. For example, Capital One's Eno gives insights through texting. JPMorgan Chase uses AI to stop fraud, earning trust. The U.S. Bank fights money laundering with AI. Benefits include 24/7 help, making less mistakes, and big savings.

Fintech (financial technology) is pushing AI's future. Young people want digital banking. The pandemic sped up this shift to online banking. By 2024, most Americans will use online and mobile banking. Banks will find it increasingly necessary to use AI to compete with other financial institutions.

Banking virtual assistants use AI to help with routine money tasks, like checking accounting balances and paying bills online. These assistants can help determine what customers wish to do and then offer them the appropriate choices. For more complex choices, human assistants will be used. This helps reduce the volume of routine queries faced by a bank's customer service department, freeing them up to work closely on problems that require human intervention.

Benefits

Information is easier and quicker to obtain than would be the case with human assistants. Obtaining customer service often requires waiting for the next available representative, whereas interacting with an AI program happens immediately.

Further, the likelihood of errors is lower with AI. Routine transactions can also be completed quickly and accurately.

1. Easily obtained information

Basic information can be obtained very quickly with AI whereas this process can be very time consuming when dealing with human assistants.

2. Talk, not type

It is typically quicker to communicate with an AI assistant than a human assistant. It is not necessary to use a phone to contact an AI assistant, and customers can type questions through a chat box or by speaking to the assistant. Dealing with human assistants is typically much slower.

3. Simple transactions:

AI assistants can quickly and easily carry out routine transactions such as shifting funds between accounts or paying bills by entering the appropriate information or using voice commands.

4. Safe alerts

AI can be used to warn consumers about strange activities, keeping customer accounts secure from fraud.

5. Smart Insights

They show spending patterns and more details about your revenues and expenses. They can also show recurring charges and offer to cancel these charges. They may also suggest ways to save money.

The future of AI in finance

As the benefits of using digital banking continue to increase more and more people take advantage of its efficiency and convenience. The use of AI assistants accelerates this trend as it becomes easier for customers to manage most of their own transactions.

Banks are using technology to make banking easier, and these assistants are part of this process. In the future, AI assistants will likely become more user-friendly and capable of providing even better service, which will attract even more customers to digital banking.

AI is reshaping banking by making processes faster, safer, and more efficient. The industry is expected to grow to $64.03 billion by 2030. AI affects all aspects of banking, from customer service to fraud protection. Traditional banks are using AI-powered chatbots and virtual assistants to enhance customer support. Ally Financial and Capital One have integrated AI chatbots for mobile banking, making transactions and inquiries easier. The software company Kasisto offers conversational

AI for digital-first banks, while another software company that focuses on AI, Affectiva, offers a robot named Pepper that helps customers at HSBC branches.

AI is also transforming fraud protection. Socure uses AI to verify identities by analyzing online and offline data. Vectra AI detects cyber threats targeting banks, and FIS uses AI for compliance and credit analysis. Ayasdi's AI combats money laundering by spotting suspicious anomalies. DataVisor employs machine learning to counteract application and transaction fraud.

In lending and risk management, AI influences credit underwriting and risk assessment. Kensho Technologies provides analytics for financial institutions, while PNC Financial's PINNACLE predicts a company's financial future using AI. ZestFinance creates fairer lending models by downgrading biased credit data. Feedzai uses AI to monitor transactions for risk and suspicious behavior.

Overall, AI is revolutionizing the banking processes, enhancing customer service, fraud protection, and risk management.

Artificial intelligence (AI) is making waves across the business world, including in the field of finance. Fintech companies and traditional banks are using AI for various purposes, such as customer service, fraud detection, and risk management. Examples include Upstart using AI models for accurate credit assessments, AI algorithms in fraud detection for spotting suspicious activities, Lemonade employing AI for fast claims processing in insurance, banks using AI chatbots for customer service, and platforms like Robinhood utilizing AI to personalize investment recommendations. AI's adoption is growing in finance due to its efficiency, potential cost savings, and ability to enhance decision-making. As technology advances, AI's role in the financial industry is likely to expand further.

Deep learning and reinforcement learning are two essential branches of artificial intelligence (AI) that offer significant economic impact. Deep learning, characterized by neural networks identifying patterns in data, is widely used for tasks like image recognition and language processing. Reinforcement learning, on the other hand, focuses on teaching agents to make decisions to achieve specific goals through trial-and-error interactions.

The key distinction is that deep learning is data-driven, whereas reinforcement learning is goal-driven. Deep learning algorithms analyze data to learn, while reinforcement learning requires feedback to guide the agent toward desired outcomes.

In practical applications, deep learning is vital in areas like finance for stock prediction and sentiment analysis, healthcare for cancer diagnosis and drug discovery, and marketing for customer segmentation and campaign optimization. Reinforcement learning, with its focus on automation and optimization, finds use in fields such as industrial processes, climate change solutions, and advertising campaign improvement.

Akkio offers a no-code AI platform, simplifying the adoption of both deep learning and reinforcement learning by automating model creation and deployment. This democratizes AI usage, enabling businesses to harness its benefits without coding expertise.

AI can enhance credit scoring in several ways:
1. Enhanced Data Analysis: AI analyzes diverse data sources to identify hidden patterns, aiding accurate credit predictions.
2. Improved Risk Assessment: AI builds predictive models considering factors like income and history for better risk evaluation.
3. Reduced Bias: AI mitigates bias by focusing on objective criteria, reducing the influence of personal characteristics.
4. Faster Processing: AI automates tasks, expediting credit assessment and decision-making, crucial for online lending platforms.
5. Personalized Experience: AI tailors loan offerings based on individual needs and preferences for a more customer-centric approach.

AI is gradually penetrating credit rating agencies (such as Moody's and Standard and Poor's), impacting various sectors such as the Municipal Bond industry and personal loans. In the Municipal Bond market, AI is utilized by credit rating agencies using services from companies such as Bitvore to monitor changes in bond issuers' economic environments and provide necessary alerts. AI scores are also supplementing traditional FICO scores for customer assessment in personal loans, analyzing payment data from various sources. However, AI's black box nature poses challenges for regulators, as understanding and regulating AI-driven credit scoring models becomes complex and potentially difficult to oversee.

Banks and finance companies are using these smart programs more. They can help clients with investing, loans, and checking IDs. These programs also save time and money for banks. In particular, the use of AI and ML can reduce the time spent by humans on routine tasks, which can reduce labor costs.

Financial institutions that do not invest sufficiently in artificial intelligence and machine learning will find themselves at a competitive disadvantage, leading to lost profits and jobs.

Countries and companies need to work together to help everyone. They can share knowledge and give support. Using AI and ML is good, but we need to be careful about problems like mistakes and bias. It is important to be able to balance these technologies with human judgment in order to continuously improve customer services and increase profits. In the end, this paper says using AI and ML in finance is good, but we need to be smart and work together.

This section highlights the growing influence of artificial intelligence (AI) and machine learning (ML) in the financial sector, encompassing various key areas:
A. Forecasting: AI/ML is being used to predict economic, financial, and risk events, offering more flexibility than traditional methods. It can discover hidden relationships between variables, improving forecasting accuracy. The speed with which AI/ML can process data has the potential to lead to many improvements in forecasting techniques. However, using nontraditional data sources, like social media, raises concerns about legality, ethics, and data

quality. Even with sophisticated forecasting techniques, human judgment will be required to interpret the results and make appropriate decisions based on these results.

B. Investment and Banking Services: AI/ML has significantly impacted investment management, enabling personalized advice, better analytics, and cost reduction. While adoption in banking has been slower due to data privacy concerns, it's on the rise, driven by fintech competition and customer-oriented improvements.

C. Risk and Compliance Management: AI/ML has transformed regulatory technology (regtech), automating compliance tasks and enhancing risk management. Applications span identity verification, anti-money laundering, fraud detection, stress testing, and COVID-19 relief efforts.

D. Prudential Supervision: Supervisory technology (suptech) is leveraging AI/ML to analyze data, detect anomalies, and improve market conduct supervision. It enhances risk assessment, and governance analysis, and provides predictive insights.

E. Central Banking: AI/ML can aid central banks in policy implementation, enhancing understanding of economic trends, improving policy decisions, and strengthening systemic risk monitoring. However, challenges include data biases, sudden shifts, and resource limitations.

Central banks have started experimenting with AI/ML applications for forecasting, market sentiment analysis, uncertainty monitoring, and internal process improvements. In 2020, the Bank of England introduced the "Bank of England Bot" or "Bob" which is intended to help with the gathering of key data, forecasting, financial supervision and the analysis of monetary policy.

Overall, AI/ML offers substantial benefits to the financial sector, improving predictions, enhancing services, and strengthening regulatory and supervisory functions. However, challenges like data quality, privacy, and bias need careful consideration.

Conclusion

Artificial Intelligence is rapidly being adopted by all types of business applications due to its potential to improve efficiency, provide better customer service, develop new products, identify important market trends, and provide better predictions of future economic activity. Currently, AI is heavily used in online applications and has become an important part of customer service applications.

In short, the benefits of AI/ML far outweigh the costs. AI/ML approaches have the potential to significantly increase efficiency, facilitate the development of new products and services, improve customer service, trigger further improvements in financial technology, increase the efficiency of risk management and credit modeling, and ultimately increase the profitability of the financial industry. Some of the potential costs include potential problems if decision makers rely too much on AI/ML

and not enough on human judgment. Additionally, privacy issues must be carefully monitored as advances in technology can provide criminals with more tools for identity theft, fraud, etc.

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