Figure 1. A map of intersections and all known biking accidents on Stanford campus.
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Stanford University
Department of Human Biology
A LETTER
FROM THE EDITORS

Thank you for joining us for the seventh issue of the Stanford Journal of Public Health (SJPH)! We are incredibly excited to share with you a wide variety of pieces, written by students at Stanford and around the country, that showcase diverse approaches to some of today’s most pressing public health challenges.

In this issue, we are fortunate to feature a great diversity of subjects, divided into four broadly defined categories: Experience, Investigation, Policy, and Research. We invite you to read about different cultural views of childbirth and the resulting struggles that women endure, to dive into studies of nicotine addiction and neurodegenerative diseases, and to work through the mathematics of developing spaces that might keep people safe from mass shootings. We encourage you to learn about how socioeconomic status affects the field of medicine, from clinical trials to mental health care.

It goes without saying that even an aliquot of topics above is especially relevant in today’s political climate. Our government does not provide equitable healthcare to women, LGBTQ+ communities, and people of color. Mental health care is still an aspect of medicine that is not being sufficiently supported by the government and is heavily stigmatized by many communities. And the tragedy of gun violence and mass shootings is now becoming a common occurrence.

We do, however, have reason to hope. We are seeing a rise in the number of young people who are instigating change. Reading, writing, and sharing are vital in this process, and we are happy to see that so many people are doing those things with SJPH. With this kind of support, we hope that we see positive change in the near future, and we would love for you to continue reading to support those who are trying to be part of this important conversation.

Before leaving you to the stories that follow, we would like to thank all of the students, faculty, and staff who support this journal and seek to educate and learn about public health. We are especially grateful to The Program in Human Biology and Student Activities and Leadership (SAL) at Stanford for their continued support. And of course, we would like to thank the SJPH staff for their passionate, diligent work to make this publication possible.

We welcome any questions, comments, or concerns that you might have, and we invite you to contact us at sjph.stanford@gmail.com. We hope you enjoy the pieces as much as we did.

Warm Regards,

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Aprotim C. Bhowmik ’18
Lauren Killingsworth ’18
Aprotim “Cory” Bhowmik is a senior majoring in Electrical Engineering and pursuing a career in medicine. He does research in computational neuroscience, by applying algorithms from signal processing and machine learning to analyze neural signals. More specifically, he is analyzing EEG signals to better understand anesthetic states in patients. Cory also serves as the Co-President of HELP4Kids, an organization that teaches health education to middle school students in Redwood City, CA. He is also an RA in a dorm and a TA in chemistry and mathematics courses at Stanford. In his spare time, Cory enjoys watching soccer, eating dark chocolate, and drinking coffee.

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Michelle Bach is a junior from Dallas, Texas. This will be her second year serving as the Editor-In-Chief of Stanford Journal of Public Health. She is interested in infectious diseases and global health. She is currently involved in Pacific Free Clinic and conducts research at the School of Medicine. Michelle is a huge foodie, and loves to swim, travel, and sing during her free time. Michelle is excited to work with the editorial staff this year to produce the annual SJPH publication.

Lillian Liao is a Master’s student in Epidemiology and Clinical Research passionate about identifying health disparities through population health research and addressing them through sustainable community engagement. She is also interested in identifying areas of improvement in public health and using modeling to simulate potential interventions. In her spare time, Lillian enjoys dancing, playing the violin, and exploring the world. She will attending medical school at Columbia University College of Physician and Surgeons this upcoming fall.

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The policy section explores the intersection of public health research and innovation and its deployment in the real world. The section approaches health topics at the forefront of scientific debate by integrating legislative, ethical, and economic perspectives.
Herman Shaw was a young humble man who lived on a small plot of land and took pride in farming from dusk till dawn to provide for his wife and two kids. When he decided the family needed a new house, he built it himself, hammering away until four or five in the early mornings[1]. Thus, the day he heard about the announcements made in local churches and cotton fields about an opportunity to receive free medical care, he thought it was a reward from God. Herman, along with several of his friends and neighbors, showed up early at the church where the doctors from the U.S. Public Health Service were going to present the program to hundreds of excited men - men who were unaware that the “free medical examination” was a study designed to follow the effect of untreated syphilis in black men; men who were unaware of the high price that would be paid over the next forty years; men who were suffering from bone deformities and dying of heart failures and various infections. Even as some men went blind and insane from advanced (tertiary) syphilis, the government doctors withheld treatment; remaining committed to observing their subjects to the study’s predetermined “end point”: autopsy[2]. To ensure that the families would agree to autopsies, the doctors offered burial allowances and gave them a free meal once a year. This was half a century ago; perhaps we can call it history.

Unfortunately, the racial mythology, the medical exploitation of black bodies for profit, and even the instances of medical sadism that threatened African-Americans in the past, have been exported to Africa[3]. On May 16, 1997, President Clinton stood a few feet away from the last five survivors of the Tuskegee Syphilis Study and made a heart-wrenching apology on behalf of the nation, admitting the injustices that had been committed. In President Clinton’s own words, “it was a time when our nation failed to live up to its ideals, when our nation broke the trust… did something that was wrong, deeply, profoundly, morally wrong”[4]. This speech and the work that followed set forth basic ethical principles for medical research involving human subjects, such as the requirement that each subject must give informed consent before participating in an experiment. Undoubtedly, the adoption of informed consent regulations was a critical development. However, in practice, informed consent does not effectively address the needs of research participants who are relatively powerless, such as those who originate from disadvantaged communities, are enduring severe poverty, have limited formal schooling, and lack access to health services to begin with.

For the most part, this description fits research that is being conducted in sub-Saharan countries, where current scientists and scholars from Western institutions have now moved the physical setting of numerous therapeutic studies on vaccines, drugs, or medical devices for the treatment of a disease. In many “developing” countries in sub-Saharan Africa, the heavy burden of disease is combined with a lack of adequate access to healthcare. Institutions in these countries often lack the resources to fund and carry out extensive biomedical research and limited resources are spent mainly on primary health care. This situation leaves a space in which these institutions rely heavily on research sponsored by “developed” countries. The pace of biomedical research is particularly fast in southern Africa, where research ethics capacity is reportedly in danger of falling behind the pace of research activities [5]. Considering this, it is patently clear that there exists an endless possibility for the exploitation of economically disadvantaged minorities in medical research studies. While the concept of informed consent has its advantages in confirming voluntary participation, it does not account for the majority of participants who live in impoverished settings with limited education and support systems, and hence do not have the option to make fully autonomous and non-coerced decisions.
The Controversy of Informed Consent

In the recent discourse around informed consent, biomedical investigations conducted by researchers from “developed” countries in “developing” countries has been, and still is, a topic of significant controversy in regard to medical ethics. On the one hand, as stated by the Code of Medical Ethics of the American Medical Association, the principle objective of the medical profession is to render service to humanity with full respect for the dignity of man [6]. In other words, physicians should merit the confidence of patients entrusted to their care, rendering to each a full measure of service and devotion. On the other hand, some argue that once a promising drug is identified, it is of utmost importance that it goes through clinical trials (i.e. stringent testing on human volunteers). In the modern world, this involves informed consent, a legal requirement and a fundamental part of medical ethics that ensures that the participation of subjects in the study is in fact entirely voluntary. According to the standards set forth by the World Health Organization (WHO) and National Institute of Health (NIH), informed consent involves educating subjects about: their own rights, the purpose of the study, the procedures to be undertaken, potential risks and benefits of participation, the expected duration of study, and the extent of confidentiality for personal identification and demographic data [7]. The remainder of this paper will delve deeper into the prioritization, relevance, application, and consequences of informed consent. Furthermore, this paper aims to provide an introductory evaluation of whether or not most research subjects living rural and impoverished areas in sub-Saharan nations really have the option and ability to refuse participating in research studies.

Challenges to Obtaining Informed Consent in Sub-Saharan Africa

Despite this, sub-Saharan African nations host countless studies by Western researchers, scientists, and pharmaceutical companies, who clearly see the exigency of doing clinical research in a fairly unregulated and uncompetitive environment. Between 2002 and 2008, the number of U.S. Food and Drug Administration–regulated investigators carrying out biomedical research outside the USA increased by 15% annually, while the number of U.S.-based researchers declined by 5.5% [11]. Just a decade ago, in 2006, research funded by the U.K. Medical Research Council and Rockefeller Foundation conducted an open, randomized Development of Anti-Retroviral Therapy (DART) trial by recruiting 3,300 volunteers in Kampala, Uganda. SOMO, a scientific magazine, later exposed the research: revealing that the study had enrolled patients desperate to get free treatment, had insufficient arrangements for post-trial treatment access, used a drug regimen that is not readily available to the general population, and omitted important risks in the consent forms (9). Once the researchers were forced to switch to acceptable therapy, the situation of the participants deteriorated and some of the patients died during the interruption period. This was because a significant portion of HIV-infected participants were at risk of an undetected mutation that was a result of taking the experimental drug, and these patients developed antiretroviral resistance that compromised their second-line therapy options. These findings have important implications for the broader domain of targeted participants who are struggling to put food on their table and a roof over their heads, making “choice” a tricky concept and “voluntary participation” a potential slippery slope.

In addition to lack of resources, differences in language proficiencies and literacy levels make the process of acquiring informed consent in sub-Saharan Africa even more complicated. To begin with, issues involving communication are the most frequent...
root causes of serious adverse events [13]; even after signing a consent form, subjects typically do not understand the risks, benefits and alternatives involved in an experiment. In 2005, Family Health International ran a clinical trial in Cameroon funded by the Bill and Melinda Gates Foundation involving 400 participants, mostly sex workers, who were at high risk of becoming infected with HIV. Before the study was suspended, five women became HIV-infected while enrolled, and NGOs claim that the subjects were not adequately informed about the risks and that only English information was given to mostly French-speaking volunteers. The study’s end highlights how certain (and often incorrectly assumed) language comprehension is necessary to understand and complete most consent forms that are required for participation in clinical research studies [14]. It is unreasonable to have a formally uneducated study participant sign a lengthy consent form that they are unable to read, let alone comprehend. Going to even further conservative measures, one could even claim that no matter how extensively researchers verbally explain the details and essence of a particular study, it is virtually impossible for most formally uneducated participants to fully grasp the scientific concept of what is being presented to them and voluntarily join a clinical trial with complete informed consent.

Another factor that can affect the welfare of clinical trials is the culture, politics and socio-economic stability of the particular nation. For instance, recent research shows that participants in developing countries appear to be less likely than those in developed countries to say they can refuse participation in or withdraw from a trial, and are more likely to worry about the consequences of refusal or withdrawal [15]. There is evidence that the act of offering money for participating in human subject research studies can highly distort the judgment of destitute participants and compromise the voluntariness of their informed consent. A deeper analysis shows that the recent history of medical research in sub-Saharan Africa closely parallels that of African-Americans in the United States a few decades ago. As reported by the Berkeley Journal of International Law, sponsors of clinical research tend to search out the least expensive and least burdensome regulatory environment with the lowest liability exposure, in order to avoid litigation in the event of injury to participants [16].

In the book, Medical Apartheid: The Dark History of Medical Experimentation on Black Americans from Colonial Times to the Present, Harriet Washington writes about the cultural memory of medical experimentation, abuse, research and the complex relationship between racism and medicine. Washington claims that U.S. researchers who can no longer conduct trials at home without intense scrutiny from the FDA and the news media have moved their operations to sub-Saharan Africa to exploit the public-health vacuum that once condemned black Americans [17]. Consider the scandalous experiment piloted in 1996 by Pfizer, the world’s largest research-based pharmaceutical company, which conducted an unregistered drug trial in Kano, Nigeria, during one of the nation’s worst meningitis epidemics. Pfizer came along with other international organizations such as Doctors without Borders “to assist and treat patients.” The study immediately recruited two hundred children and conducted a clinical trial that involved ingesting one of three oral antibiotics: Trovan, Ceftriaxone or Chloramphenicol. Pfizer was sued after 11 children died within three weeks of the clinical trial and others developed conditions including brain damage, paralysis, and slurred speech. The allegations against Pfizer included:

1. Pfizer never obtained ethical clearance before conducting the study;
2. Pfizer did not obtain informed consent before recruiting participants and did not inform the study participants that the drug was an experimental drug;
3. Pfizer capitalized on the poor, illiterate, and desperate situation of the participants and their communities; and,
4. Pfizer left the town after conducting the study despite the fact that the epidemic was still ongoing [18].

Understandably, some may claim that, currently, clinical trials are firmly regulated and researchers attempt to comply with ethical requirements to the best of their ability while maintaining high scientific standards. In fact, some scholars might challenge this paper by insisting that as long as participants are accurately informed of the purpose, methods, risks, benefits, and alternatives to the research, they are able to understand the information and can make a voluntary decision about whether to participate or not. By focusing on the general definition of informed consent, such critics overlook the deeper
problem at hand, which is the fact that clinical trials have become a big business with the imperative of getting the work done as quickly as possible with minimal obstacles is prioritized [19]. The examples mentioned in the previous paragraphs of incidents in Uganda, Cameroon and Nigeria are current case studies that clearly illustrate the ethical challenges that may arise in conducting clinical trials in “developing” countries. Though I concede that clinical trials are extremely useful tools that are much needed to address the burden of disease and have yielded exciting results that have improved health care, I maintain that many studies that are done in sub-Saharan Africa could never be conducted in the countries sponsoring the work.

Future Directions

Despite the existence of international guidelines, standards, and protocols that govern biomedical researches, many gaps and challenges relating to ethical issues still need to be addressed to ensure a fair, transparent, and moral research processes. The first step is to create awareness about the grossly immoral injustices that are inflicted on the most vulnerable of populations. The difficulties in finding scientifically published unethical clinical trials, despite the numerous reports and research that are being conducted, suggests that we are aware of a small fraction of the number of abuses that occur as many go unreported. Domestically, there is a huge prospect for laws to be successfully applied and upheld to protect participants from persecution and exploitation in clinical trials. Eventually, we have to admit that it has come to a point where we, sub-Saharan Africans, need to take a stand and stop allowing this perpetuation of exploitation from continuing. The fact that only Malawi and South Africa contain a provision which makes specific reference to clinical research [20] is clear evidence that civilians and local governments need to work harder to uphold the guarantees of human right protections written on their constitutions.

The goal of clinical research is to develop information that improves human health and increases the understanding of life. In order to achieve this, researchers need to understand that the act of a participant signing a consent form does not necessarily equate granting full informed consent. Signing the form is only part of the process, the most important part being the conversation with the patient, which allows for informed consent. It is of utmost importance that the content of these trials is given to the potential participants in linguistically and culturally acceptable formats. This might mean something as simple as improving the presentation through the use of instructional graphics and accompanying videos, or something more complicated, such as involving local communities in establishing the criteria for recruiting participants, as well as determining the incentives for participation. Furthermore, research must begin with a clear plan for what will happen to the participants once the trial has ended. In order to accomplish these goals, we need to hold researchers to a higher standard of moral conscience and ensure that funding agencies are giving money to ethically sound research. Ultimately, while we need all the cures we can find for HIV, malaria, TB and countless other diseases, it is imperative that we conduct our clinical trials in a humane way.

The blood, sweat and tears of people like Herman Shaw has brought us to a time where there exists a law that any U.S. organization conducting federally funded research must have an institutional review board (IRB) to ensure compliance with federal regulations [21]. Despite their good intentions, even such guidelines have proved to be inadequate in ensuring the safety of human subjects. It is a shame that after all the extremely painful lessons we learnt from the Tuskegee Syphilis Study, we are still targeting populations who are defenseless to fight for their own interests against high-risk research. For some of us today, breakthroughs in medicine can no longer bring the joy and celebration they used to, as they remind us of the mandatory preface to such achievements, their commercialization, and how it has frequently brought pain to many families in sub-Saharan Africa. I challenge you to be part of the movement; As you close the lid of your laptop and walk towards your top drawer to grab riboflavin to deal with the aftereffects of a bright screen, to just take a moment and appreciate the shoulders of the unfortunate people it took to develop the drug. Perhaps then, there will be a spark of hope for a positive change.
References


How a nation upholds the well-being of its vulnerable populations takes precedence in outlining the foundation of general welfare for society as a whole. Both age and immigrant status are characteristics that indicate the vulnerability of an individual. \(^1,2\) Considering the large and growing population in Maryland of immigrants, refugees, and other displaced persons, this paper addresses the sources of vulnerability and the mechanisms that construct a disproportionate risk of negative health and social outcomes for individuals at the intersection of these subpopulations: foreign-born youth ages five through nineteen residing and attending schools in Baltimore City. \(^3\)

Children of immigration, displacement, and refuge not only have greater biological and social sensitivities to environmental exposures and familial circumstances, respectively, but they also (1) bring prior exposures and experiences unique to their backgrounds, and (2) face barriers in assimilation that may compete with their past and are exclusive to their experience as minors. Factors within these outstanding categories aggregate and precipitate as an array of physical, psychological, and social burdens. \(^4\) Health profiles of refugee children in the nation reveal elevated blood levels (EBLs) as a major concern for individuals from major countries of departure, which compounds the issues of lead already found in Baltimore. \(^5,6\) Evidence thus draws attention to environmental health among foreign-born youth as a concern that should be prioritized for policy intervention.

Children who have immigrated to Baltimore City, whether by choice or by necessity, are shown to endure disproportionate burden by toxic environmental exposures and psychological distress. According to the Agency for Toxic Substances and Disease Registry, low levels of lead exposure in children are evidenced to affect neurodevelopment such that no dose is safe; these biological changes are expressed as a reduced growth rate, which causes problems in learning, hearing, speech, behavior, and downstream academic achievement. \(^7,8\) Coupled with the sensitive, immature biology and the unique behaviors of children, who have (a) intake patterns greater than that of the average American adult (drinking more water, breathing more air, and eating more pounds of food per pound of body weight) and (b) social and play patterns prolonging confrontation with environmental elements, lead exposure presents a significant burden on children, especially for the foreign-born immigrating with previous exposure to lead. \(^1\) Life-long effects of childhood exposure to lead have thus been justifiably linked to a seven-fold increase in dropout rates, higher poverty rates, and criminality in adulthood. \(^10\) Further consideration of psychological traits that arise from childhood lead exposure, such as aggressive behavior, paired with the psychological stressors of immigration substantiates the ideas behind vulnerability among foreign-born youth and the mechanisms leading to disproportionate risk. \(^4,10\)

Considering that the advantages of addressing these vulnerabilities extends to greater populations of Baltimore City, the burdens imparted by intervention are assuredly outweighed. Policies targeted at reducing lead exposure among youth in the city would benefit a greater range of vulnerable populations, including the one in six children found to have EBLs in Baltimore and biologically vulnerable women of reproductive age, mitigating not only physical health concerns but also psychological stressors and the social issues that emerge. \(^5,9\) Historically, efforts to reduce lead exposure, such as the removal of lead from gasoline by the Clean Air Act, have directly (1) prevented the development of cognitive deficits associated with aggressive and impulsive behaviors such that legislation was also responsible for a majority of the decline in violent crime, and (2) restored intelligence quotients (IQ) by 2.8–4.9 IQ points, raising worker productivity by 4.9–11.7%, and yielding an economic benefit from $110–319B, thus empowering the overall population. \(^7,10\)

Maryland Department of Education may establish a blood sampling requirement for all new students entering the Baltimore City Public School system to determine pre-existing lead concentrations. By having newly-arrived children test their blood lead levels and report the values, attention would be brought to
the health implications of lead exposure, conferring caution regarding exposure and ultimately deterring further accrual of lead, especially among foreign-born youth. Additionally, institutions would not only receive novel data associating blood lead levels with location of departure, revealing detailed trends between local and foreign-born populations, but also adopt greater awareness of developmental challenges among children with EBLs, promoting adjustment of education and counseling to better suit affected groups.

Baltimore City Public Schools may also call for regular lead screening of drinking water to safeguard youth from further negative impact. By (1) testing water in fountains and sinks in schools for lead at stricter levels than nationally enforced, and (2) requiring them to display informative signs should elevated levels be detected until addressed within a certain period of time, foreign-born youth would avoid accumulating more exposure than allowed for an individual born in the country, and the displays would deter immigrant parents and refugee case managers from enrolling children at the institutions until adequate filtration is installed.

Maryland State legislation may facilitate the financing of lead abatement on the basis of financial accountability. Considering that lead hazards found within building infrastructures such as lead paint were utilized until the nationwide ban in 1978 by manufacturing agencies such as Sherwin-Williams, a major industrial entity in Baltimore City, liability may be attributed to these companies. Requiring lead paint manufacturers to finance a lead restitution fund for municipal renovations and preventative intervention, part of which would be allocated for foreign-born youth, would remove financial barriers and promote lead exposure reduction.

Baltimore City Public Schools should enact district policy requiring regular tests of drinking water with stringent standards and the requirement that signs are to be prominently displayed at locations of any hazard until tests show insignificant levels of lead. Screenings of newly-arrived children would yield beneficial data, but intervention would be reliant on institutional changes in educational methodology with barriers that may render the policy ineffective, especially considering that damages from lead would have already been committed. Although resources may be allocated to abatement of lead hazards, specifically by requiring lead paint agencies to contribute to funds financing intervention, it is difficult to retroactively establish liability of lead paint to a specific entity, and the capital garnered by such policy would be outweighed by economic returns obtained by efforts targeting prevention. Holding schools accountable for lead in drinking water at a standard higher than that held nationally takes prior lead exposure of foreign-born youth into consideration and empowers them with both a better understanding of the toxin and the ability to make informed decisions regarding exposure at their chosen school. Altogether, this prevents further accrual of lead and its negative health outcomes and promotes a positive social narrative and institutional attribution of developmental challenges.

School officials may suggest that labeling lead-tainted water would financially burden and inconvenience them to outsource services, as has occurred due to extreme levels in many Baltimore City schools that now spend ~$500K yearly on bottled water in addition to outsourced lunch. Considering that these efforts are reported to detract from education and that preventative measures have a return of $17 to $220 for every dollar invested, the effective course of action as a result of this policy would be to renovate water outputs with filters, which have a yearly cost less than that of bottled water.

Implementation of school-wide policy addressing lead exposure among foreign-born youth is contingent upon not only political sentiment towards both immigration/refugees and the environment but also stakeholder concern and support for the primary source of vulnerabilities (lead exposure) and the disproportionately affected population. Attitudes toward immigration translate into public backing of any policy targeted to benefit foreign-born individuals; should sentiment remain isolationist or anti-immigration, the recommended policy would face greater barriers to pass and effectively implement. Additionally, separate from the national sentiment towards non-U.S. citizens, attitudes towards the gravity of environmental considerations such as lead exposure and its downstream effects are a major factor of policy implementation. Should there be limited concern for the environment, perhaps as a result of limited public awareness of risk attributable to lead, even full public support for the vulnerabilities among foreign-born youth may prioritize other sources of
vulnerability and side-step the outstanding issue of lead exposure. Ultimately, the effectiveness and success of policy implementation relies on support from the schools themselves; as major stakeholders in this recommendation, they’re not only at liberty to divert attention to other vulnerabilities within the education system, but also, even upon implementation, schools must take initiative upon the identification of non-compliance (demonstrated lead in drinking water) and act as intended by both installing filters and/or replacing lead piping and acknowledging the significant adverse health and social effects of lead exposure as an institution.

Successful intervention targeting the adverse health and social outcomes of lead exposure among foreign-born youth should consider collaboration between (a) local, state, and federal agencies and philanthropic organizations, (b) state and federal health agencies and insurance programs, and (c) schools and the parents of lead-poisoned children. Schools that participate in the National School Lunch (NSLP) and Child and Adult Care Food (CACFP) programs must provide children with free potable water as a requirement of the Healthy, Hunger-Free Kids Act, overseen by the U.S. Department of Agriculture. Both federal and state government agencies such as the U.S. Departments of Health and Human Services (HHS) and Education and the Maryland State Department of Education would organize a task force to regularly test and enforce compliance of screening policy. Baltimore City Health Department, Maryland Health Care Commission, and other health agencies would coordinate with Baltimore City Public Schools as well as Medicaid and the Children’s Health Insurance Program to provide financial resources facilitating the testing and reporting of lead levels as required by the proposed policy. Concurrent with the screening policy, schools would ideally provide targeted academic and behavioral interventions to lead-exposed children to decrease the likelihood of the vulnerable population engaging in destructive practices and increase chances of earning a high school diploma. Assessment of psychological and developmental needs may be facilitated by the Centers for Medicaid and Medicare Services and education and care programs may be financed by HHS as well as federal and state departments of education. If given the structural and financial resources to execute the recommended policy, such a program’s overall success may be measured in the short-term by reduction of schools with lead-contaminated water and in the long-term by the attributable increase in academic performance (e.g. improved standardized test scores, higher graduation rates).

Baltimore City Public Schools may both implement the regular testing policy and provide the means necessary for its implementation, but additional policy measures are necessary to improve adverse health and social outcomes among foreign-born youth in the context of lead exposure. First, housing policy encouraging the removal of lead from infrastructure carrying drinking water to urban residences, which are disproportionate to low-income families, especially those with foreign-born children, would target another major origin of lead risk for youth. By identifying and remediating these lead-containing pipelines that service low-income homes built before the ban on lead in construction, the acting policy would facilitate the reduction of a significant source of lead and the downstream health and social outcomes. Second, educational policy may facilitate access to education and care programs, financed by the HHS and U.S. Department of Education, that utilize an evidence-based approach for academic and behavioral intervention targeted towards children with EBLs. Consideration of the developmental challenges of children with EBLs, especially among foreign-born youth who may need additional specialized attention, would circumvent unjustified attribution of negative performance to the individual as opposed to environmental predisposition. Third, nutritional policy may expand upon the services provided by U.S. Department of Agriculture food programs such as National School Lunch Program and the Supplemental Nutrition Assistance Program such that beneficiaries of nutrition-related services also receive advice concerning lead reduction in the home; within experimental implementation, children in the intervention group exhibited improved educational achievement and reduced antisocial behavior. Considering that these additional policy measures target a major source of vulnerability systematically, provide equity to those already made vulnerable through education, and avoid further vulnerability through behavior change, the primary policy recommendation is only a stepping stone in upholding health and general welfare among foreign-born youth in Baltimore City and beyond.
References


When a friend of mine recently admitted that he is suffering from schizophrenia, I started thinking about the disparities in access to the psychiatric treatment. Despite multiple functional difficulties that he faces in an academic setting on an everyday basis, he is still able to continue his studies at a prestigious institution, while being supported with professional treatment and special accommodations provided by psychiatrists, psychotherapists, and multiple academic advisors. Meanwhile, many homeless people living on the streets who talk to themselves, have hallucinations or act violently are simply considered lunatics by the public. In the case of individuals who are marginalized because of their ethnic identity or socio-economic status, bizarre behavior is often quickly reduced to craziness and ignored, even though it often represents symptoms of severe mental illnesses, especially psychotic disorders such as schizophrenia or schizoaffective disorder. The prospect of equality in psychiatry and clinical psychology will not be achieved as long as classist and racial prejudices influence the approach of mental health care professionals towards patients, and socio-economic class determines access to proper diagnosis and treatment.

Lack of access to professional care

The results of the 2016 National Survey on Drug Use and Health conducted by Substance Abuse and Mental Health Services Administration within the U.S. Department of Health and Human Services suggest that about 18.3 percent of American adults experienced any mental illness in the past year and 4.2 percent suffered from a serious mental illness, defined as any mental, behavioral, or emotional disorder that substantially interfered with or limited one or more major life activities (1). Yet, only 43.1 percent of the population with mental illness received mental health services in the past year, and about one-third of adults coping with both severe mental illness and substance use disorder did not receive either mental health care or specialty substance use treatment.

Economic stratification and mental illness

The relationship between socio-economic class and psychiatric illnesses remains extremely complex. On one hand, financial difficulties and low status stand for additional psychosocial stressors that increase vulnerability to mental disorders. On the other hand, visible symptoms of mental problems stigmatize and often lead to lower income, unemployment, and deprivation from a certain social status. As a result, economic disadvantage correlates with the distribution of the most common mental disorders among the society.

While there is an established association between low socioeconomic status and incidence of schizophrenia, major depressive disorder, anxiety disorders, and substance use disorders (2), the negative consequences of mental illnesses remain the most harmful for the poorest, partially due to inadequate access to psychiatric treatment (3). Additionally, condition of mental health is especially acute in homeless individuals for whom psychiatric diagnosis tends to co-occur with substance abuse and physical disabilities. Homelessness is often considered a drawback of deinstitutionalization when patients discharged from in-patient facilities are not provided with support to settle back in the community and re-adjust to normal functioning within a society. Meanwhile, mental illness combined with homelessness contributes to the vicious circle of victimization and crime, and increases the risk of early death (4).

Financial barriers to treatment

According to the National Comorbidity Study, 47 percent of respondents with anxiety, affective or substance-use disorders who were aware of their need for mental health care admitted that the lack of appropriate health insurance or financial barriers stopped them from undergoing treatment. Among working-age adults suffering from severe mental illnesses, the percentage of people without health insurance is significantly higher than in the general population (5). Researchers from University of Min-
nesota (5) found that among people with mental illnesses a more dramatic decline in private coverage has been observed which highlights the importance of covering the costs of mental health care with public insurance. Yet, having an insurance still does not directly guarantee access to mental health care. Cost sharing, commonly known as “co-pay”, constitutes a financial obstacle and is especially hard to be overcome by psychiatric patients for whom impairment in occupational functioning, and therefore employment opportunities, stands for a diagnostic criterion itself. Those who cannot afford specialized psychiatric treatment often resort to the primary care. More than a half of patients with mental disorders receive some mental health treatment from a primary care provider and for almost a third of them it is the only opportunity for such treatment (6).

Ethnic identity and access to psychiatric care

Access to mental health care remains linked not only to economic privilege of middle and upper class but also to white privilege, given that white people stand for the only subpopulation in which most people struggling with mental problems manage to get professional help (7). While generally there is a pattern of increasing access to mental health care, such growth is not observable among the black people. The meta-analysis conducted by Timothy A. Smith and other co-authors of “Foundations of Multicultural Psychology” demonstrates that in comparison to European-Americans, African-Americans are 21% less likely to use mental health services. Yet, this number is even greater for Latino population and Asian-Americans – 25% and 51% accordingly. The authors argue that we cannot simply relate these dramatic differences to socioeconomic disparities, but we need to acknowledge that race itself is a separate factor and a strong predictor of the access to mental health care. The American Psychological Association indicates that ethnic minorities are especially at risk for mental disorders and what makes the situation even more tragic, “minority individuals may experience symptoms that are undiagnosed, under-diagnosed or misdiagnosed for cultural, linguistic or historical reasons” (8).

Undoubtedly, we need to train a more diverse mental health workforce as there is a high and still unmet demand for psychiatrists, psychotherapists, social workers and psychiatry nurses who would be culturally and linguistically compatible with minority patients. Accommodation for language is especially crucial in psychotherapy sessions, since limited language proficiency hinders ability to freely communicate feelings and express emotional states.

Racial discrimination among mental health providers

Underrepresentation of people of color in the medical field poses a huge challenge in psychiatry as racial match with a healthcare provider gives patients a sense of comfort, facilitates building a long-term relationship based on mutual trust and can even determine the prospects of treatment follow up. A meta-analysis published in the Journal of Counseling Psychology explicitly demonstrated that patients suffering from mental disorders exhibit a moderately strong preference for therapists of their own ethnicity or race and perceive them more positively. Even though the results of this investigation did not show any significant difference in objective treatment outcomes depending on the racial or ethnic matching, the lack of trust that patients of color often have towards white doctors seems reasonable if we take into account subjective experience of interpersonal interaction. There are numerous cases of medical providers discriminating minority patients, even though some forms of discrimination might remain subtle or almost invisible. For instance, an audit study conducted by a researcher from Princeton University who is interested in implicit biases among mental health professionals revealed that psychiatrists and therapists are more likely to accept white patients than patients of color, and while scheduling appointments give priority to the middle class over the lower-class representatives (10).

Public health actions needed

Economic opportunities, healthcare insurance coverage and issues related to ethnic and racial inequalities often determine whether the symptoms of psychiatric disorders are clinically diagnosed and properly treated. In a sense, socio-economic stratification has turned mental health into a privilege. Patients who cannot afford private insurance or out-of-pocket costs may lack treatment so that developing mental illness impairs their functioning and further contributes to their poverty. Apart from the subjec-
tive experience of tremendous psychological distress, mental disorders also lead to disability and deterioration of physical health. In long-term perspective inequalities in the access to mental health care pose a significant burden to workforce and economy.

Therefore, to decrease to effect of wage gap on the accessibility of mental health services, efforts should be made to:

- Assign equal importance to mental or substance-use disorders and physical illnesses in insurance coverage
- Advocate for increasing reimbursement of medical services related to mental and behavioral health, including appointments with clinical psychologists, and expand the number of limited psychotherapy sessions to treat given disorder
- Increase expertise of primary care providers in evaluating mental health condition
- Promote close cooperation between in-patient psychiatric wards, out-patient psychiatric clinics and non-clinical community-based support centers to ensure continuous recovery and smooth transition between facilities.

In order to alleviate the extent of racial and ethnic disparities in access to quality psychiatric and psychological care, policies should be introduced to:

- Increase the presence of underrepresented minorities in mental health care setting by applying the principle of affirmative action to medical school and psychiatry residency programs,
- Appreciate the importance of ethnic and racial concordance in patient-clinician dyad,
- Improve cultural competency among mental health professionals,
- Provide medical interpreter services to patients with limited language proficiency.

Equity of access to healthcare has been a major point of concern of American public health for many years but most of the policies introduced by the public health authorities are intended primarily to improve the physical health. However, population’s health has to be assessed more holistically and the relationship between the condition of mental health and the level social and economic functioning should be recognized by the policymakers.

Occurrence of mental disorders, prevalence of psychosocial stressors and accessibility of treatment should be carefully monitored across different groups and communities within the society in order to respond with effective financial interventions and political support. If we want to eliminate, or at least alleviate present economic, ethnic and racial disparities in mental health, we need to first conceptualize mental health problem as a fully valid public health problem so that it can become recognized, prioritized and addressed by the public health experts, healthcare providers and legislators.

References


INVESTIGATION

The investigation section presents and analyzes pressing public health issues through the lens of epidemiological, medical, and scientific perspectives.
Introduction

In his seminal essay *Nietzsche, Genealogy, History*, the French philosopher and social theoretician Michel Foucault noted that “humanity does not gradually progress from combat to combat until it arrives at universal reciprocity, where the rule of law finally replaces warfare; humanity installs each of its violences in a system of rules and thus proceeds from domination to domination” (Foucault 151). This statement rings especially true for members of minority groups, whose ancestors may have faced colonialism and abject prejudice, and whose current relatives might be tangled in a web of institutionalized injustice, unconscious prejudgment, and biosocial and biopolitical disadvantage. The indigenous people of the Canadian North are one such minority group. Though the many groups of this region differ in language and cultural norms, they all share a history of state-sponsored oppression, which in many communities has manifested itself in adverse health outcomes. As Laurence Kirmayer explained, “cultural discontinuity has been linked to high rates of depression, alcoholism, suicide, and violence in many communities” (Kirmayer et al). And yet, recent attempts to ameliorate these public health crises using primarily biomedical strategies for intervention were not successful in a number of North American minority populations (Castro et al). This result suggests that alternative modes of delivering medical care to these groups should be explored. The goal of this paper is to review current literature on culturally appropriate intervention strategies among indigenous populations in the Canadian North, and to offer some suggestions for how community-based health networks might be enacted in this region.

A Short History of Indigenous Health in the Canadian North

According to oral history, the incidence of modern disease epidemics like tuberculosis and suicide was relatively low in the Canadian North prior to contact with European explorers (Waldram). This was not simply because the indigenous groups of this region had superior genes or better diets: they also possessed effective methods for dealing with disease outbreaks. Bopp and Lane describe how the community of Nuxalk, Canada survived a smallpox epidemic by creating and following a plan that involved scattering in pairs while keeping within shouting distance. “If your partner died, you were to bury them. If you were the last one left alive, and you were sick, you were to bury yourself in a shallow grave before you died” (Bopp and Lane 7). Though unconventional, this strategy allowed the indigenous community of Nuxalk to survive near certain annihilation, and thus proves that the people of the Canadian North had the ability to manage their own public health crises prior to European contact.

Over time, the systemic destabilization of indigenous economies by factors including extractive mining by transnational corporations and changes in animal migration patterns due to anthropogenic climate change led to a disintegration of the traditional way of life for many indigenous people. While in some metrics, modern technologies have greatly bettered the quality of life for these people, “the disintegration at the most intimate level” of lived experience contributes to an ongoing sense of anomie in these communities (Million 110).

To make matters worse, as of September 2017, Canada’s Northwest Territories do not have centralized substance abuse and mental wellness services (Chatwood). Instead, such services are the discrete mandate of local governing organizations, health authorities, and indigenous groups. Often, these groups have neither the resources nor the staff to successfully support struggling individuals. Thus, it is common for these persons to be sent to better-equipped care facilities in south Canada, which has led to the separation of families and the dislocation of individuals from their native cultural environment. This problem is compounded by the colonial history of the Inuit and Dene people who were forcibly removed...
from their homes and sent for medical rehabilitation and cultural re-education in the South. This theme of cultural dislocation has recurred in the tuberculosis epidemic of the 1940s-1960s and in the suicide epidemic of the 1980s-present (Stevenson).

With this cultural context in mind, it is important to consider some somber statistics regarding public health in the Canadian North. A clear divide in health status exists between indigenous and non-indigenous groups. 54% of indigenous people (aged 15+) in the Northwest Territories show signs of hazardous drinking, compared to 25% of non-indigenous people. 51% of indigenous people (aged 15+) in this region are daily smokers, compared to 18% of non-indigenous people. Indigenous groups in the Northwest Territories are far more likely to use and abuse illicit substances like cocaine and cannabis (Report On Substance 20). Perhaps most troubling is the fact that in some parts of North Canada, the suicide rate can be as much as eight times the national average (Kue & Bjerregaard, 2008).

Furthermore, it is clear that standard biomedical intervention strategies are not wholly effective at combating these public health emergencies. This may be due in part to the fact that “notions of health and healing [rooted in biomedicine] do not match indigenous conceptions of wellbeing” (Stewart et al 80). It becomes apparent that medical interventions are not ‘one size fits all’, and that effective interventions must be designed with the patient in mind. In order to understand who ‘the patient’ is in the Canadian North, we now transition to a consideration of what it means to be ‘well’ in two different ethnomedical traditions: Western biomedicine and indigenous Canadian naturalistic medicine.

**Healing vs Curing: How Health is Understood Across Cultures**

In order to help an individual reach or maintain their ideal personal health status, it is important to understand how that person conceptualizes his or her own health. In the case of the minority groups of the Canadian north, such as the Inuit and the Dene, there are many factors that might affect a person’s perceived health status. There is the distinctly biological component of health, which is acknowledged by nearly all types of ethnomedicine around the world, including conventional Western medicine. This is the realm of health within which biomedicine most comfortably operates. There is also the spiritual aspect of indigenous Canadian medicine.

In her book Life Beside Itself, Lisa Stevenson describes how, to some indigenous groups, engagement in the spirit world is an essential process that is needed to maintain good health. There is a custom among the Inuit to name a newborn child after a recently deceased friend or relative. To the Inuit, a name is not just a moniker, it is the atiq, the ‘name-soul’ that carries part of the deceased into the newborn (Stevenson 105). Transference of the atiq in this way skews kinship so that familial ties follows the path of the atiq rather than simple biological relationships. One person that Stevenson interviews noted that “if I give my grandfather’s atiq to my baby daughter, she is my grandfather” (Stevenson 105). Fluid transmission of identity, an idea exemplified by the concept of the atiq, is just one example of how aspects of indigenous culture can challenge Western notions of rationality, and yet still be incredibly meaningful to the culture and community of that indigenous group. The atiq also intimates many indigenous groups’ essential connectedness to others, both spiritually in time and genetically to blood relatives. In his article Culturally Appropriate Means and Ends of Counseling, Rod McCormick states that “effective healing for First Nations people focuses on interconnectedness rather than autonomy, which is a more common goal for Western therapy” (McCormick 1995). McCormick goes on to note that that aim of healing for many indigenous people in the Canadian North is to maintain balance between four dimensions: “physical, mental, emotional, and spiritual” (McCormick 1995). Some might argue that conventional biomedicine weights the physical or biological aspects of health over everything else. This might be a reason why, as Castro noted, and as alluded to earlier in this paper, conventional biomedical intervention strategies are typically not successful in the long-term for North American minority populations.

Because notions of health are so different in the indigenous Canadian and Western imaginations, it is no surprise that the process of attaining wellness is also different in these two cultures. In most indigenous communities, the process of achieving a good health status is described as ‘healing’. In Anthropology of Alternative Medicine, Anamaria Ross defines
’healing’ in this context as “a therapeutic process or action that addresses the whole suffering person and illness, rather than just a specific body part of a particular problem, thus including emotional, mental, social, and spiritual needs and concerns in the treatment plan” (Ross 20). In contrast, Ross defines ‘curing’, the process of reaching a good health status as it is understood in most parts of the Western world, as “a narrower and more pragmatic approach, which has the goal of removing a particular problem completely and permanently” (Ross 20). With its intention to address the many components of personhood, it is clear that ‘healing’ is better equipped than ‘curing’ to address the four dimensions of health that McCormick described. But what does healing look like in practice?

What Can Healing Mean in a World of Connections?

The interconnectedness noted by McCormick and the notion of atiq as reported by Stevenson point to an indigenous worldview that closely associates the physical body and many connected domains, such as the spiritual world, the world of myth and tradition, and the natural world. These different conceptions of lived experience resemble the different ‘bodies’ first envisioned by Nancy Scheper-Hughes and Margaret Lock in their prolegomenon entitled The Mindful Body. This text explores ways in which the human body is conceptualized, with special attention paid to how a medicalized perception of the body is related to larger human structures like cultures and communities. Importantly, Scheper-Hughes and Lock note that “insofar as the body is both a physical and cultural artifact, it is not always possible to see where nature ends and culture begins” (Scheper-Hughes et al 19). This passage pertains to our present discussion because it closely relates the ‘physical body’ with ‘nature’, an association that is also often made by public health workers when designing culturally appropriate healing strategies in the Canadian North.

Dian Million, author of Therapeutic Nations, noted that in this region, “the land is imbued with sacredness by the indigenous [people]” and that experiences had on the land itself can be “individually and communally healing” (Million 115). Million goes on to describe a movement among some indigenous groups in Canada known as the Canoe Way. Simply put, Canoe Way is one among many resurging cultural practices that situates large groups of indigenous people in nature, specifically taking canoes into the watersheds of the Canadian North. At one point in time, the canoe was the primary means of transportation and thus the principal driver of local economies for many indigenous groups. With this in mind, engagement with this ancient practice through Canoe Way connects indigenous people with their traditions and their land, thus strengthening the mental and spiritual dimensions of health that were originally described by McCormick. In fact, when advertising Canoe Way to potential paddlers, it is “often portrayed as a healing activity” (Million 168) rather than purely recreational. The values highlighted in Canoe Way illustrate how a connection to culture and nature can be used in a therapeutic manner.

Another way of conceptualizing the therapeutic nature of a land-based medical intervention like Canoe Way is through the lens of sensation. A number of authors have “stressed the importance of attending to sensations in studying the illness experience” (Ross 123). Hinton, Howes, and Kirmayer further delineated the role of sensation in the practice of naturalistic medicine when they noted that “healing can entail sensations that invoke a script [which in turn] increases a sense of efficacy and promotes positive engagement in the life process” (Hinton et al 153). Put another way, sensations from the outside world (such as the vestibular sensation of being rocked by a canoe or the taste of salty water) can cause a shift in “embodied metaphor, memory, and self-image” (Hinton et al 154) such that one feels a greater sense of interconnectedness, to heritage, community, or self.

Another way of exploring the abstract concept and the actuality of healing in the Canadian North is by considering how the word itself can become a metaphor for resolving not only biological, but also biosocial ills. In Body Metaphors: Reading the Body in Contemporary Culture, Danica Škara describes how aspects of the human body are often projected through metaphors into the world around us. For example, “the arm of a chair”, “an ear of corn”, or “the foot of the mountain” are all body metaphors that are employed in common parlance (Škara 184). This is no less true in the practice of public health and medical anthropology, when we talk about ‘healing’ a broken home, ‘revitalizing’ (which literally means ‘to give life

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again) a community, or ‘diagnosing’ social problems in a bad neighborhood. Laurence Kirmayer recognized this truth when he described indigenous families and communities as the “primary locus of injury and thus the source of restoration and renewal” (Kirmayer et al 21). Even though an abstract concept like ‘community’ cannot literally sustain an injury, Kirmayer recognizes that political action that improves the quality of life, increases individuals’ sense of self-efficacy, and reduces anomie, can be defined as a form of healing, despite not being a directly biological intervention. Kirmayer more straightforwardly links the political with the biological when he notes that “the high suicide rates among indigenous young men can be related to a loss of value status” (Kirmayer et al 20) and that empowering youth by giving them the opportunity to “design and implement their own [mental health] programming” can sometimes “restore their positive mental health [status]” (Kirmayer et al 21). This type of biopolitical care stems from the recognition that a figurative wound in a family unit or a community can be ‘healed’ just as a biological wound can, through attentiveness and care. Noted anthropologist Mary Douglas recognized early on how metaphors tie together the human body with other causative forces in the environment. In her book Purity and Danger, Douglas stated: “just as it is true that everything symbolizes the body, so it is equally true that the body symbolizes everything else” (Douglas 122). This metaphorical conception of healing opens up new avenues for how healing can be actualized through language in indigenous communities.

**Healing Through Language**

One way that language can accelerate the process of biological and political healing is through the reclamation of appropriated words and ideas. For example, the renowned developmental psychologist Erik Erikson studied Lakota philosophy and incorporated many Lakota belief systems into his stage theories of childhood development (Million 154). Don Coyhis, an Alcoholics Anonymous leader from a Mohican reservation in Wisconsin, moved to re-appropriate Eriksonian mental psychology for Lakota culture, eventually coining the term “Eriksonian-Lakota” (Million 155). Importantly, as Dian Million notes, this has the effect of “[reclaiming] a practice that has found usefulness, moving it from its position as ‘whiteman’ knowledge, and into closer relations with indigenous lives” (Million 155). This repossession has two additional benefits: it helps to heal the psychic wounds inflicted when Lakota knowledge was taken without proper credit, and it sets the stage for new ways of framing medical interventions through clever manipulations of language.

Many modern drugs are refined derivatives of ancient remedies. Over 546 unique traditional plant remedies like poultices, decoctions, and pastes have been identified in the boreal forests of Canada alone (Uprety et al 1). Thus, it is conceivable that a public health promotion campaign could ‘reclaim’ modern drugs if they were described primarily in terms of the traditional preparation and geographic range of the original remedy. This could help cultivate a sense of familiarity and connection to heritage with valuable modern medications. In the same way that Erikson’s developmental psychology was reclaimed and actively appreciated for its “usefulness” by the Lakota, so too could ‘reclaimed’ pharmacologic strategies be employed in the Canadian North. It might sound like a strategy of deception at first, but if executed empathetically, and with the guidance of community leaders, it is likely that the beneficial aspects of pharmacology could be employed in the fight against serious health concerns.

In addition to uncovering the hidden links between biological and naturalistic medicine, language can also be a therapeutic tool in and of itself. Of what use might storytelling be to an addict or to someone struggling with a mental health crisis? Narrative therapy, an effective form of psychotherapy that explores the therapeutic potential of storytelling, seeks to answer some of these questions. In the process of storytelling “individuals are constantly in the process of creating themselves” (Crossley 2000). Narrative therapy makes use of storytelling as a creative tool to “imagine and promote the most positive, empowering conception of self” (Hammer 2012). One vignette that showcases the therapeutic potential of narrative storytelling occurred in the primarily indigenous Canadian community of Alkali Lake (Million 106). As the story goes, a young girl in this community refused to drive home with her parents because they were too drunk. Shamed by their daughter’s intelligence and their own recklessness, this girl’s parents committed to becoming sober. Shortly thereafter, they started to tell friends and family in this community the story...
of how they were shamed into becoming sober, and within several short months “it is estimated that Alkali Lake went from a 100 percent alcoholism rate to what is now around 85 percent of the community achieving and keeping sobriety” (Million 106). While anecdotal, this story demonstrates how shared stories can empower people to change their behavior to become healthier. As Dian Million noted, “narrating the story of their community was one of the myriad healing or community transformation techniques that Alkali Lake used [to overcome the addiction of alcoholism]” (Million 107).

The therapy of narration has been particularly embraced in Alcoholics Anonymous groups across Canada. Alcoholics Anonymous was particularly popular among indigenous groups mainly because indigenous peoples had formed “large socially active networks for managing their lives around alcohol subsistence” (Million 153) and because the flexibility of the Alcoholics Anonymous curriculum enabled indigenous peoples to “adapt its framework to include specific indigenous spiritualities and ceremonies” (Million 153). Significantly, Alcoholics Anonymous relies on “narrative strategies and frames” (Million 153) to engender honest sharing among community members. Thus, it represents a form of collective and cathartic storytelling, the recognition of shared burden, and the hope that with community action, a seemingly insurmountable health challenge can be defeated.

Conclusion

While there is no doubt that the indigenous people of the Canadian north currently struggle with some of the most severe public health crises on the planet, the results and stories presented above indicate that there is still hope for positive action. Current Canadian Prime Minister Justin Trudeau’s September 7th, 2017 apology to the indigenous people of Canada for the long history of the Canadian government’s institutionalized racism, injustices in the school system, and colonial oppression is a good first step in starting a dialogue about healing (Shaw and Coburn). This palliative step represents more than a simple recognition of political injustice: it metaphorically represents a recognition of wounds enacted on indigenous communities. As Kirmayer succinctly showed, an understanding of the figurative link between politics and health outcomes can actually lead to a resolution of, or at least engagement with, public health crises. Trudeau’s apology shows that he recognizes the power of metaphor and language as a therapeutic tool in indigenous communities.

Because indigenous notions of health more fully explore the four dimensions of wellness that McCormick first described, it is clear that alternative modes of care must be adopted to fully heal people in the Canadian North. More recently, dual intervention strategies that draw upon both traditional forms of healing and mainstream biomedical services are being implemented in many northern communities (Stewart et al 90). For example, a successful northern Manitoba First Nations substance abuse treatment program integrated counseling sessions and pharmacological interventions with expeditions to culturally resonant sites, powwow dances, and pipe ceremonies (Gone, 2011). A local cultural approach and an ethic of community ownership thus appears essential to providing holistic behavioral healthcare in these indigenous communities.

The central tenet of this work however, is that new medical interventions are developed with substantial input from indigenous communities themselves. In Red Skin White Mask, Glen Coulthard makes a call for indigenous action: “if indigenous peoples want the relationship between themselves and the Canadian state to be informed by their distinct worldviews, then they will have to engage the state’s legal and political discourses” (Coulthard 45). The reality is that the pursuit of autonomy, and biological, biosocial, and biopolitical healing is “in the end, an ongoing intergenerational struggle to define and redefine and practice what is wellness” (Million 107). There is no rulebook detailing how to heal from and reach a healthy status following centuries of oppression. What seems clear is that any intervention that is implemented should be a blend of evidence-based biomedical and indigenous care strategies, and that enactment of this intervention should be done with cognizance of the power of language and metaphor, understanding of alternate notions of healing and health, awareness of the historical contexts of suffering, and a familiarity with the interconnectedness of beliefs.
References


Neurodegenerative diseases (NDs) encompass a wide range of acute and chronic conditions characterised by the loss of neuron and glial cells in the brain or spinal cord. In acute conditions, due to stroke or spinal cord injury, different types of neurons within a restricted brain region die over a short amount of time. In chronic conditions, there is either a selective neuronal loss of specific sub-populations (such as dopamine neurons in PD or medium spiny neuron loss in HD), or widespread degradation of many neuronal types (such as in AD) over several years. For both types, no cures currently exist. Current clinical approaches adopted can only target symptomatic treatment and disease management, while clinical applications of novel therapies developed for NDs have been limited.

In this paper, I review the current literature on both implemented and developing therapies for Alzheimer’s (AD), Parkinson’s (PD), and Huntington’s (HD) disease, three of the most common and debilitating chronic NDs. The symptoms, affected brain regions, and some molecular changes have been identified for several NDs, some of which are summarized in Table 1. Novel therapies have been developed in animal models to target these observed pathological and molecular changes, but significant ethical, economic, regulatory, safety, and etiological weaknesses still hinder their widespread clinical application.

### Table 1: Overview of Neurodegenerative Disorders

<table>
<thead>
<tr>
<th>Disease</th>
<th>~Incidence (per year in UK)</th>
<th>Brain Region Affected</th>
<th>Molecular Changes</th>
<th>Symptoms</th>
</tr>
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</table>
| Alzheimer’s Disease (AD) | 225,000                     | Hippocampus, amygdala, neocortex, basal forebrain | · Neurofibrillary tangles (hyper-phosphorylation of tau proteins)  
· β-amyloid plaques (amyloid peptide aggregates) | Dementia (cognitive, psychiatric, behavioural) |
| Amyotrophic Lateral Sclerosis (ALS) | 1,300                     | Motor neurons                          | · Motor neuron degeneration in spinal cord, brain stem, primary motor cortex | Difficulty walking, weakness in limbs/arms, slurred speech, muscle cramps and twitching |
| Parkinson’s Disease (PD) | 60,000                      | Substantia nigra                       | · Dopaminergic neuron loss from nigrostriatum and substantia nigra pars  
· Build-up of Lewy bodies, α-synuclein aggregates | Tremors, bradykinesia, impaired balance and posture, loss of automatic movements |
| Huntington’s Disease (HD) | 2,000                      | Basal ganglia, neostriatum             | · Trinucleotide (CAG) repeat in IT15 huntington gene  
· Loss of medium spiny neurons (MSN)  
· Toxicity of mHTT: protein misfolding & aggregation | Muscle problems (rigidity, dystonia), involuntary jerking movements, abnormal eye movements |
| Spinal Muscular Atrophy (SMA) | 300                        | Motor neurons                          | Mutations in SMN1 gene                                                          | Muscular atrophy, balance and coordination deficits |
Within the context of the two main developing therapies examined, gene and stem cell therapy, I suggest specific focuses for research in their current fields. Major milestones in research that must be reached before clinical application begin with better understandings of disease initiation and progression. Molecular pathological classification through the identification of biomarkers can provide the greatest cross-methodological benefits in furthering effective and personalized treatment of NDs. Fundamentally, a more thorough understanding of underlying ND pathophysiology can be accomplished through biomarker identification, stem cell-based disease modelling, and genetic research. Combined, this knowledge will help develop more personalized and ultimately more effective novel therapies for treating neurodevelopmental disorders.

Part 1: Current Approaches: Disease Management

Section 1.0: Introduction

Current clinical approaches to addressing AD, PD, and HD all center on disease management and symptom alleviation. The use of pharmacological agents, physical therapy, and caregiving aid is efficient and affordable, but are ultimately only forms of palliative care rather than effective treatments.

Section 1.1: Current Management Techniques

Four acetylcholinesterase inhibitors (donepezil, galantamine, rivastigmine, tacrine) and one NMDA receptor antagonist (memantine) constitute the five main medications currently used to provide temporary symptomatic relief to AD patients (Desai & Grossberg, 2005). The first four enhance cholinergic function by reducing rates of acetylcholine breakdown (as reduced ACh levels is related to memory and cognitive decline in AD), while memantine reduces AD-related excitotoxicity (observed in AD & related to neuronal death). Further behavioural, psychosocial, and caregiving provisions are used to improve quality of life for AD patients.

Current therapies for PD are arguably the most well-developed and effective among these three discussed NDs. Drugs such as levodopa or dopamine agonists used in earlier stages of care can restore some motor function, but their efficacy decreases dramatically over time. Deep brain stimulation (DBS) and rehabilitation techniques provide further symptomatic therapies for PD (Mizuno, 2014).

Treatments for HD, like those for AD and PD, are only able to reduce symptom severity. Various pharmacological treatments are available to reduce Chorea, a disorder within Huntington’s characterized

<table>
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<tr>
<th>Disease</th>
<th>Pharmacological Treatments</th>
<th>Other Treatments</th>
</tr>
</thead>
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| Alzheimer's Disease (AD) | · Acetylcholinesterase inhibitors (donepezil, galantamine, rivastigmine, tacrine)  
· NMDA receptor antagonist (memantine) | · Caregiving  
· Behavioural therapy (reduce problem behaviours)  
· Psychosocial interventions (emotion and cognition regulation) |
| Parkinson's Disease (PD) | Dopamine replacement (levodopa, carbidopa, selegeline)                | · Deep brain stimulation (of thalamus, globus pallidus, subthalamic nucleus)  
· Physical therapy |
| Huntington’s Disease     | Chorea treatment (tetrabenazine, benzodiazepines, neuroleptics)       | · Caregiving  
· Physical therapy  
· Speech and language therapy |
by involuntary spasmodic movements (Busse et al., 2012). As the disease progresses, physical, speech, and language therapies are used to rehabilitate physical and cognitive function (Busse et al., 2012).

Section 1.2: Moving Forward

Techniques currently available to treat neurodegenerative diseases are able to provide temporary symptomatic relief, but are critically unable to halt the rapid deterioration and progression of neurodegeneration.

Though the complete causes of AD and PD have not been fully characterised, neurofibrillary tangles, β-amyloid plaques, decreased synaptic function, and cortical atrophy observed in AD and the loss of dopaminergic neurons characteristic of PD can be addressed by gene therapy and stem cell-based therapies. These two therapies can also be applied to treat the root causes of HD, which has been attributed to an expanded trinucleotide repeats, the mHTT protein, and consequent neostriatal neuronal loss. However, their widespread clinical application has been limited by underdeveloped understandings of disease etiology and mechanisms of therapeutic action. Insights into the molecular mechanisms of NDs lie at the crux for the development of novel targets of disease-modifying therapies. Therefore, efforts to further gene and stem cell-based therapies (discussed in Parts 2 & 3) will benefit from an increased focus on biomarker research (discussed in Part 4) to elucidate disease pathophysiology.

Part 2: Gene Therapy

Section 2.0: Introduction

The theory behind the use of gene therapy to treat neurodegenerative disease is simple: deliver a transgene that either corrects or replaces a defective gene to cure a complex disease using a transfer vector. However, the numerous technical difficulties associated with gene therapy are daunting in complexity: the transfer vector must be easy to produce, safe for patients and the environment, target specific cells efficiently, and not trigger a deleterious immune reaction; simultaneously, the appropriate transduced transgene must be expressed at the optimal level for an optimal duration (Sarkis & Mallet, 2005). All these factors that must be taken into consideration can only be optimized with increased knowledge of disease etiology, which can be mediated through biomarker research.

Section 2.1: Gene Therapy Trials

Gene therapy vectors are either viral or non-viral. Currently, the most common viral vectors are adeno-associated viruses (AAVs) and lentiviruses. Both infect non-dividing and dividing cells, but lentiviral vectors integrate into host genomes while AAVs do not. Thus, lentivirus integration can confer long-term, stable transgene expression, but poses a risk of integrational mutagenesis. Non-viral vectors (mostly used for HD treatment) have more localized effects, require higher dosage levels, and confer only transient gene expression that is normally insufficient to fully treat chronic ND.

2.1.1: Viral Techniques

A series of viral vector-mediated gene therapy trials has been conducted for AD and PD, summarized in the table below. In these trials, AAV2-mediated transgenes were injected into patients’ brains, but treatment results either fail to meet or achieve the same level of therapeutic benefit as current standards of care. It is important to emphasize that the efficacy of gene therapy depends critically on the therapeutic gene delivered; this can only be improved by better understandings of the etiology of neurodegenerative diseases.

2.1.2: Non-Viral Techniques

Huntington’s is a genetically acquired disease with a known etiology (CAG repeats in the IT15 huntington gene), for which non-viral gene therapy techniques carry significant therapeutic potential. Carroll et al. (2011) have developed antisense oligonucleotides (ASOs) that selectively bind to exonic and intronic SNP (single nucleotide polymorphisms) sites on the mutant huntingtin protein (mHTT), thus selectively silencing gene expression of mutated regions on the mHTT. The experiment used primary cells from HD-patients with transgenic mouse lines, and the devel-
### Table 2: Current Therapies for AD, PD, & HD

<table>
<thead>
<tr>
<th>Disease</th>
<th>Study / Trial Codes</th>
<th>Gene Therapy</th>
<th>Method of Delivery</th>
<th>Current status</th>
</tr>
</thead>
</table>
| Alzheimer’s Disease (AD) | Rafii et al., 2014 (NCT00876863) | AAV2-NGF | Injection into basal forebrain | • Phase 1 successful*, therapy well-tolerated, NGF-induced axonal sprouting observed  
• Phase II in progress |
| Parkinson’s Disease (PD) | LeWitt et al., 2011 (NCT00643890) | AAV2-GAD | Injection into subthalamic nucleus | Phase I & II successful, but symptom improvements achieved were not better than current standards of care |
| Parkinson’s Disease | Bartus et al., 2011 (NCT00400634; NCT00985517) | AAV2-NRTN | Injection into striatum & putamen | • Phase I successful, observed increased NRTN expression  
• Phase II showed no improvement in clinical outcome over controls |
| Parkinson’s Disease | Azzouz et al., 2002 (NCT00627588; NCT01856439) | Lentivirus-TH, AADC, GCH1 (*exciting tricistronic vector: cells transduced express all 3 enzymes) | Injection into striatum & putamen | • Phase I (open label) successful, improved motor function correlating with increasing dose  
• Currently optimizing delivery method before Phase II (double-blinded randomized trial) |
| Parkinson’s Disease | Muramatsu et al., 2015 (NCT02418598) | AAV2-AADC (as discussed above) | Injection into putamen | • Phase I safety trial successful, stable AADC expression 4 years post-delivery  
• Phase II recruiting, in progress |

*N*success defined by meeting safety requirements and showing functional improvement
oped ASOs achieved potent and selective allele-specific knockdown of mHTT both in vitro and in vivo.

This presents the most exciting potential treatment for Huntington’s, as ASO delivery to adult CNS can be achieved through simple intrathecal or intracerebroventricular infusion rather than viral delivery. Further, ASO dosing can be precisely controlled or stopped when necessary. Kordasiewicz et al. (2012) have shown that transient infusion of ASOs catalysing RNase H-mediated degradation of mHTT in mouse and non-human primate models delays disease progression and sustains HD disease reversal that outlasts ASO-mediated mHTT knockdown. Thus, clinical trials should be conducted to test the efficacy of gene therapy either through direct ASO infusion, or combined with iPSC-mediated transplantation (correcting disease mutations of patient-derived iPSCs with ASOs, then transplanting corrected NPCs).

Section 2.2: Conclusion

Promising proof-of-principle concepts have been presented in Phase I trials, which have shown that gene therapy techniques targeting AD & PD are safe and well-tolerated. However, therapeutic efficacy in further clinical trials remains weak, in that observed improvements failed to exceed placebo effect or current standards of care for AD and PD. Non-viral ASO-mediated silencing of mHTT expression has proved efficacious in HD-animal models but have not yet moved to clinical trials. In sum, success by design meets failure of efficacy within these gene therapy studies.

Moving forward, future research must focus first on expanding choices of possible transgenes for delivery, as improvements in vectors and delivery methods depend crucially on efficacy of the transgene delivered. Greater understanding in disease etiology will help identify these gene targets. A significant area of development lies in the identification of biomarkers of NDs, which would not only improve gene therapy techniques, but also allow for earlier diagnoses, continuous motoring of the progression of therapeutic effects, and the development of precision medicine.

Part 3: Stem Cell Therapy

Section 3.0: Introduction

Stem cell and iPSC research has significantly furthered neurodegenerative disease modelling, diagnosis, and transplant- and drug-based therapies. A plethora of therapies developed in animal models have failed to translate into effective clinical trials due to differences in mammalian genomes and embryonic development (Begley & Ellis, 2012). Human-based stem cell research generates not only potential ND therapies, but also presents clearer pathophysiological models for those diseases. In particular, the development of induced pluripotent stem (iPS) cells has presented a unique approach for studying signalling pathways, growth control, and disease mechanisms in previously inaccessible human brain tissue.

The main types of stem cells used for neurodegenerative therapies are embryonic, mesenchymal, progenitor, and iPSC cells (Singh et al., 2016). Embryonic stem cells are pluripotent and hold excellent potential to restore damage caused by brain injury or neurodegeneration; however, their ability for unlimited self-renewal poses a high risk for tumour formation post-engraftment, limiting the range of their clinical application. Mesenchymal stem cells are multipotent and immunomodulating (derived from autologous source; do not trigger a host immune response), and thus find a relatively widespread application for neurodegenerative treatment. However, their use in genetic diseases, wherein autologous sources contain the same genetic predisposition to the disease, is limited. Neural progenitor cells (NPC) and neural stem cells (NSC) are derived from either fetal or adult neural tissue, carry limited differentiation and tumour-formation potentials, but are difficult to isolate and thus lower in availability. iPSCs, generated from somatic tissue and reprogrammed using TFs into embryonic stem cell-like states, offer novel sources of autologous cellular therapy.

Application of the appropriately selected type of stem cell to treat neurodegenerative diseases is mediated through two primary mechanisms. First, stem cells can replace or stabilize neuronal networks that experience both widespread or specific subpopulation-based neuronal loss. Second, stem cells can provide environmental enrichment through neurotrophic support to prevent further neuronal degradation. These mechanisms will be discussed in the context of specific neurodegenerative diseases be-
Following this discussion, I’ll emphasize that the focus of stem cell research should first lie in exploiting its means of modelling disease pathophysiology and providing an in vitro screening tool for screening efficacy and safety of drugs, then on its direct therapeutic applications. I’ll then highlight the potential iPSC research holds in future developments of precision medicine.

Section 3.1: Alzheimer’s

Complementing current pharmacological AD treatments that regulate neurotransmitter activity (Section 1.1), stem cell (SC)-based therapies for AD can also help restore degeneration and loss of cholinergic neurons, and increase levels of brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) that are lowered in AD. In mouse models, combinatorial upregulation of BDNF with NPC transplants promoted neurogenesis and protected neuronal function. Thus, NPC-mediated stem cell-based therapy may offer an enhanced approach to preventing AD-associated degradation of cholinergic synapses and neurons (Tuszynski, 2007).

Wang et al. (2006) compared transplants of ESC-derived NSC to transplants of ESC alone into mouse AD models. As suggested in Section 3.0, ESC-transplanted mice developed teratomas (ESCs: unlimited self-renewal capabilities, high risk of tumour formation), while transplanted NSCs successfully differentiated into stable cholinergic neurons, improving memory and learning. Genetically modified NSCs for BDNF expression has been shown in many rodent studies to reduce AD symptoms (Lindvall & Kokaia, 2010). In these mouse models, increased hippocampal synaptic density, increased cognitive function, and enhanced cell-cell synaptic communication, as associated with increased BDNF expression (Blurton-Jones et al., 2009; Li et al., 2009; Xuan et al., 2008). NGF has also been implicated in preventing neurodegeneration and reducing amyloid toxicity (Tuszynski et al., 2007). In addition to AAV2-mediated gene therapy techniques discussed in Section 2.1.1, autologous fibroblasts genetically modified to express NGF implanted into patient forebrains have been found to slow rates of cognitive decline in an open-label phase 1 clinical trial (Tuszynski et al., 2005). However, fibroblasts are immobile and cannot slow degeneration across large brain regions. Transplanted stem cells can efficiently migrate and release growth factors to many damaged sites, but their use in AD treatment has yet to be fully explored. Another technique to increase NGF release to treat AD is with encapsulated cell bodelivery (ECB) implants, for which the first clinical trial was conducted in 2008 by the Danish company NsGene. Encapsulated retinal pigment epithelial cells releasing NGF were implanted into the basal forebrains of six AD patients (Wahlberg et al., 2012). At 12 months, implants were retrieved and low but persistent NGF secretion was detected in half of the subjects. Thus, both ECB implantation and stem cell-based gene therapy may provide future methods for enhancing NGF expression to counteract cholinergic neuronal death.

Although NSC transplantations into the adult forebrain of patients may be able to increase cholinergic and cognitive aptitude, they are unable to target the main molecular cause of the disease: accumulation of β-amyloid plaques (Blurton-Jones et al., 2009). Nonetheless, the ability of NSC transplants to enhance cholinergic function, synaptic transmission, and neuronal function is suggested by animal studies and replicated by initial clinical trials (Tuszynski, 2007). Combining growth factor overexpression with NPCs’ ability to integrate across many neural networks thus presents an exciting potential for limiting AD pathogenesis. Continued research must be conducted before established SC-based treatments can be developed for AD therapy.

Section 3.2: Parkinson’s

Earlier open-label studies of human fetal ventral mesencephalic tissue (hfVM) transplants in Parkinson’s patients yielded successful long-term PD symptomatic relief, but these results failed to replicate in subsequent placebo-controlled, double-blind trials (Brundin et al., 2010). Success has been observed in using genetically modified ESCs and iPSCs to derive neurons with the dopaminergic (DA) phenotype, but these techniques have not yet been translated into clinical studies.

Clinical trials using hfVM tissue transplants in the 1990s (Madrazo et al., 1988; Lindvall et al., 1990) found impressive restoration of dopaminergic neu-
rotransmission and motor-symptom alleviation. In these open-label clinical studies, PET scans showed long-lasting evidence of functionally-integrated dopaminergic neurons forming from transplanted tissue, restored DA release in vivo, and reactivation of cortical motor areas. However, the design of these open-label trials contains significant bias and thus deserve cautious interpretation. Further, the occurrence of recurring graft-induced dyskinesias (GIDs) in consequence double-blind trials, in addition to heavy ethical concerns raised over the use of fetal tissue as a therapeutic source, has heavily impeded the clinical development of this form of hfVM-based therapy (Brundin et al., 2010). Instead, the focus has been shifted to ESCs and iPSCs: mouse model studies have found that overexpression of Nurr1, FGF-8, and Shh signalling in mouse ESCs and iPSCs has successfully induced midbrain dopaminergic phenotypes and improved functional recovery (Kim et al., 2003; Cooper et al., 2010). A major concern for ESC clinical transplants, however, is the risk for tumour formation observed in animal models (Lindvall & Kokaia, 2010). As PD patients have normal life expectancies, even a slim risk of tumour formation is unacceptable.

Initial suggestions of hfVM transplant-mediated PD therapy have been significantly hindered by ethical and methodological issues, while the induction of ESCs and iPSCs into dopaminergic neurons is cumbersome, potentially nonhomogeneous (may contain traces of undifferentiated cells that can lead to teratomas), and currently unsubstantiated by clinical studies. Thus, progress made in stem cell-based PD treatments have been slower than for AD. However, iPSC-derived dopaminergic neurons have provided critical insights into the pathophysiology of PD, by providing a SC-based human disease model. Abnormalities in mitochondrial and dopamine homeostasis, as well as mutations in Parkin and PTEN-induced putative kinase 1 (PINK1) previously noted in animal models have been substantiated by similar data from studies using PD patient-derived iPSC neurons (Van Laar et al., 2010; Cai et al., 2012).

Though stem cell technology has yet to develop clinically-relevant PD therapies, it has proved effective in modelling Parkinson's. In particular, mutation-bearing iPSCs has helped study PD physiology, elucidate underlying signalling cascades modulating the disease, identify PD biochemical markers, and screen efficiency of therapeutic compounds.

Section 3.3: Huntington's

Applications of stem cell techniques in HD studies have paralleled those for AD and PD. More specifically, fetal striatal grafting into HD patients have provided transient symptom improvements, but its mechanisms are poorly understood and its use is limited by ethical constraints (Bachoud-Lévi et al., 2000). Both iPSCs and ESCs have been used to establish differentiation protocols for medium spiny neurons (MSN)— these transplantations have shown successful neural circuit development and integration, but are currently restricted to animal models (Viegas et al., 2011; Precious & Rosser, 2012).

Initial clinical trials using fetal-derived tissue, iPSCs, or ESCs as sources of MSNs have observed reduced motor and cognitive dysfunction in HD patients. In addition, decreased neuronal loss was observed in HD rodents with NPC transplants engineered to over-express GDNF, as compared to control mice with unmodified NSC transplants, emphasizing the potential of stem cell-based therapies to provide environmental enrichment and protect endogenous neurons (Pineda, 2007).

Section 3.4: Conclusion

For AD, PD, and HD, similar trends in stem cell-based therapies can be observed. Early cell-based therapies using fetal ventral mesencephalic tissue (for PD) and fetal striatal tissue (for HD) transplantations provided initial support for successful symptomatic relief. However, widespread clinical applications of human fetal tissue transplants has been limited by significant ethical and scarcity issues associated with the nature of the tissue source. Subsequent clinical trials have failed to consistently replicate initial data and observed deleterious side effects (teratoma formation, GID, immunorejection). Thus, the focus of stem cell therapies has shifted to ESCs derived NSCs induced to certain cell fates or gene expressions (increased BDNF/NGF expression for AD, dopaminergic phenotypes for PD, and MSN for HD); however, these induced populations are usually not pure, long-term graft survival is generally low, and any ES cells escaping in vitro differentiation carries the potential for yielding teratomas and tumours following transplan-
Above all, the development of effective stem cell-based therapies is ultimately hindered by our current lack of knowledge on the mechanisms of action of transplanted stem cells, and how stem cell proliferation, differentiation, survival, and migration are controlled in a pathological environment. The mechanisms of cellular protection provided by SC-mediated trophic support are also not fully understood (McBride et al., 2004). Because current potential risks outweigh validated benefits in their therapeutic applications, research on human stem cells and patient-derived iPSCs should first be focused on disease modelling and used for screening drugs and other therapeutics. Successful development of clinical therapies can begin once more precise disease pathophysiology and mechanisms of SC action post-transplantation are identified.

In sum, the use of stem cells for transplantation has generated enormous ethical, technical, efficacy, and safety-related debates. It is true that SC replacement therapy can stabilize and regenerate entire networks of neuronal loss and prevent further neurodegeneration by providing environmental and trophic factors against toxic, neurodegenerative factors. However, with current literature, the greatest functionally validated potential of SCs lies in their unique ability to model disease pathophysiology and mechanisms of action. Patient-derived iPSC cells may be a particularly tremendous treatment option for personalized medicine in the future, but for now serve as prominent tools for understanding disease etiology on a highly personalized level, as they carry the patient’s genotype, disease mutations, and also account for environmental influences on the individual’s disease.

### Part 4: Precision Medicine & Biomarkers

In discussing future developments of neurodegenerative therapies, it is critical to emphasize the importance of elucidating the molecular etiologies of NDs. Pathologically altered proteins and protein aggregations are fundamental characteristics of neurodegenerative diseases and should be of paramount focus for further research.

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**Table 4: Overview of Current Literature on SC-based ND therapies**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Stem Cell Applications</th>
<th>Goal of SC-based Therapies</th>
<th>Current Therapeutic Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer’s disease</td>
<td>· NSCs · ESCs</td>
<td>· Restore loss of cholinergic neurons · Increase BDNF &amp; NGF trophic factors to promote neurogenesis</td>
<td>· Successful basal forebrain grafts of NGF-secreting fibroblasts (open-label trial, Tuszynski, 2007) · Development of encapsulated cell biodelivery implants to increase NGF release (NsGene) · No current clinical trials testing SC-transplants in AD</td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>· ESCs</td>
<td>· Restore nigrostriatal dopaminergic neuronal loss</td>
<td>· Successful clinical open-label hFVM transplants (Lindvall et al., 1990; Madrazo et al., 1988) — provided long-term symptomatic relief, but failed to replicate in subsequent double-blind trials (which observed GIDs) · Successful animal studies using ESCs &amp; iPSCs to derive DA phenotype, not yet translated to clinical trials due to risk of tumour formation and technical difficulties</td>
</tr>
<tr>
<td>Huntington’s disease</td>
<td>· MSNs</td>
<td>· Restore medium spiny neuron loss</td>
<td>· Successful clinical fetal striatal grafting (Bachoud-Lévi et al., 2000)— provided transient symptom improvements, but limited by ethical constraints &amp; poorly-understood mechanism of action · Successful animal studies using ESCs &amp; iPSCs to restore MSN loss, not yet translated to clinical trials</td>
</tr>
</tbody>
</table>
I’ve alluded to the importance of biomarker research in aiding developments of novel therapies during Part 2 & 3’s discussion of gene therapy and stem-cell based treatments. This is because molecular classifications of NDs can detail the nature of pathologically dysfunctional proteins and correlate corresponding clinical symptoms to genetic abnormalities. Ongoing biomarker research has already identified extracellular deposits of Aβ fibrils and aggregation of abnormally-phosphorylated tau proteins in AD, the presence of Lewy body deposits, altered dopamine transporters in PD, and protein misfolding and aggregation associated with mHTT proteins in HD (Kovacs, 2016). Thus, the ability of biomarker data to identify core disease pathology has already been validated, and therapies targeting these protein abnormalities (through immunotherapy, gene therapy, SC-transplants) have yielded promising results in animal and some clinical models. However, the most exciting potential of biomarker research lies in its ability to characterise patient-specific environment-disease dynamics and gene variations, and consequently provide personalized diagnoses. In the emerging era of precision medicine, the use of biomarkers (detected in body fluids or PET imaging) can provide earlier and more accurate ND diagnosis, and their identified protein dysfunctions can be targeted in translational research using novel therapies.

Looking forward, biomarker research will contribute greatly to developing pathophysiological disease models, improving immunotherapy, gene therapy and SC-based transplant methods, and moving us closer to personalized cures for neurodegenerative diseases. Similarly, stem cell research can be applied to experimentally model NDs. Patient-derived iPSCs are especially well-suited to uncover specific disease pathophysiology as they carry the patient’s genotype and bear patient-specific disease mutations and gene-environment interactions. Thus, I believe that research focusing on biomarkers, patient-derived iPSCs, and genetic studies are currently most necessary and potentially most beneficial for current experimental and clinical endeavours for ND cures.

References


Abstract:
Addressing nicotine addiction is a critical public health priority, as millions of individuals continue to lose their lives to tobacco-related diseases despite many wanting to quit. Both smoking initiation and subsequent nicotine dependence are highly heritable, and recent research has uncovered genetic markers of predisposition. Variation in SNP (single nucleotide polymorphisms) and alleles for dopamine transporters in the mesolimbic dopamine pathway are tied to increased risk for heavy smoking and nicotine addiction. Incorporation of discussions of individual genetic predisposition can increase the personal relevance of existing prevention intervention messaging and offer greater specificity for cessation intervention recommendations.

Introduction
Every six seconds, someone dies due to a tobacco-related disease (Action on Smoking and Health, 2016). Nicotine, the primary addictive substance in tobacco products, is a highly addictive drug that acts on the brain's reward systems and produces cycles of intoxication, withdrawal, and preoccupation (U.S. Department of Health & Human Services, 2012). By hijacking neural circuitry relating to pleasure and learning, nicotine consumption results in neurophysiological changes that compels users to seek out more. Though 68% of adult smokers want to quit, 70-85% relapse within a year of attempting to stop (Centers for Disease Control and Prevention, 2016). These statistics are highly troubling, particularly considering causal links between smoking and cancers, stroke, heart disease, diabetes, lung diseases, and premature death (Centers for Disease Control and Prevention, 2016). Though environmental factors like socioeconomic status and education can influence likelihood of smoking persistence, numerous studies have also uncovered a genetic component to nicotine addiction susceptibility (Agrawal & Lynskey, 2008; Straub et al., 1998; Li et al., 2002). As nicotine dependence is highly heritable, individuals with certain genotypes are more likely to experience greater activation of reward systems upon nicotine exposure and worse withdrawal symptoms, thus making it more difficult for them to quit (Benowitz, 2010). Current methods of measuring genetic predisposition include tracing family lineages, scanning genomes, and direct-to-consumer testing (Dingel et al., 2012; Docherty et al. 2011). Although research on isolating specific genetic markers is still emerging, strategic implementation of these methods can increase efficacy of existing smoking prevention and cessation interventions by increasing personal relevance. Current educational programs can be supplemented by incorporating opportunities for individual participants to learn about their susceptibility and develop personalized plans of action.
Neurophysiological Effects of Nicotine and Nicotine Addiction

Nicotine was first identified in the early 1800s as one of 7,000 chemicals found in tobacco smoke and serves as the primary addictive substance in tobacco (U.S. Department of Health & Human Services, 2012). Each year, millions of Americans live with a tobacco-related illness and an estimated 500,000 face premature death as a result of tobacco’s harmful effects (Centers for Disease Control and Prevention, 2016). Capable of damaging almost every organ in the body and harming others through secondhand smoke, tobacco has been empirically linked to causing disability, disease, and mortality (Sullivan et al., 1999; U.S. Department of Health and Human Services). Despite known health risks and aggressive public health campaigns, 36.5 million Americans still smoke and thousands of adolescents begin smoking each day (Centers for Disease Control and Prevention, 2016; Lantz et al., 2017). Although many smokers want to stop, the strong addictive power of nicotine enacts physiological and psychological changes in the body that make cessation difficult.

Inhaling smoke from a cigarette – the most popular and widely used delivery device for tobacco consumption – allows 1-2 milligrams of nicotine to enter the bloodstream and quickly diffuse into brain tissue (Benowitz, 2010; Dani & Balfour, 2011). Nicotine functions as a stimulant by triggering epinephrine release, but can also work as a sedative with increased dosages (Benowitz, 2010). As an agonist, nicotine binds selectively to nicotinic cholinergic receptors (nAChRs), opening ligand-gated ion channels, stimulating the receptors, and facilitating neurotransmitter release (Mansvelder & McGehee, 2002). Dopamine is consequently released in the mesolimbic dopamine pathway, including neurons in the ventral tegmentum, frontal cortex, and nucleus accumbens. Activation of this reward system signals the experience of pleasure, playing a crucial role in the reinforcing effects of nicotine and facilitating dependence (Benowitz, 2010). Although initial exposure to nicotine produces aversive effects such as nausea or headache, continuous nicotine consumption results in pleasure, increased concentration, and relaxation. However, because nicotine is metabolized rapidly, its positive effects wear off quickly and regular smokers must continue to consume throughout the day or else experience withdrawal – contributing to the formation of habitual smoking and dependency (Mansvelder & McGehee, 2002; Benowitz, 2010). Extended use of nicotine can also cause tolerance, where higher dosages are required to feel the same effects (Mansvelder & McGehee, 2002).

The pharmacological basis of nicotine addiction is facilitated by positive reinforcement from mood and functional enhancement, as well as avoidance of negative consequences from withdrawal (Benowitz, 2010; Mansvelder & McGehee, 2002). Nicotine withdrawal can manifest in negative emotional, physical, and cognitive symptoms. During periods of abstinence such as nighttime sleep or attempted cessation, desensitized nicotinic cholinergic receptors (nAChRs) become responsive and can trigger intense cravings for nicotine (Benowitz, 2010). In addition, deficient dopamine release can cause reduced feelings of reward and hedonic dysregulation, a loss of pleasure in once-enjoyable activities, which can persist for years after quitting (Benowitz, 2010). Other emotional symptoms can include anxiety, depressed mood, irritability, and anhedonia. Untreated individuals with nicotine addiction withdrawal can experience mood disturbances comparable to those of psychiatric outpatients with clinical depression and anxiety disorders (Hughes, 2006). Physical symptoms such as nausea, headaches, and tremors can further exacerbate withdrawal. During the addictive phase of preoccupation and anticipation where individuals begin to crave nicotine and plan for consumption, lower amounts of dopamine and glutamate in the frontal cortex result in cognitive impairments to memory, attention, motor skills, and impulse control. Combined with the powerful effects of cravings and emotional disturbances, these withdrawal symptoms can make cessation more difficult to sustain.

In addition to withdrawal symptoms, the paired association of reward (nicotine consumption) with environmental or contextual cues can provide strong urges to smoke (Mansvelder & McGehee, 2002; Dani & Balfour, 2004). Through the psychological mechanism of conditioning, once-neutral stimuli such as specific locations, habits, or people become associated with smoking over time and can function as “cues” to smoke (Benowitz, 2010). For example, if a
smoker regularly smokes a cigarette while drinking coffee, exposure to the smell, taste, or sight of coffee can remind them of smoking and subsequently trigger cravings and relapse (Benowitz, 2010). Although certain environmental cues can be avoided, others – such as a workplace or family member – can be encountered frequently and serve as a challenge to continued cessation.

Enduring nicotine consumption causes neuroadaptation as the brain adapts to changing environments biologically and physiologically. As nicotine usage increases, there is an upregulation in response to nicotine-mediated desensitization of nAChr receptors and bindings sites (Benowitz, 2010). This facilitates nicotine dependence by necessitating increased amounts of nicotine to feel the same amount of pleasure. Although all regular smokers experience upregulation to some extent, a key component of interest is investigating why certain individuals experience more intense or faster upregulation than others (Mansvelder & McGehee, 2002). Recent advances in genetic sequencing technologies have shed light on several potential mechanisms of these differences.

Measures and Implications of Genetic Predisposition for Nicotine Addiction

Although nicotine has high addictive potential regardless of an individual’s genetic predisposition or environmental factors, studies involving genetic epidemiology and gene-sequencing have found that liability to nicotine use and dependence are highly heritable (Dingel et al., 2012; Agrawal & Lynskey 2008; Straub et al., 1998; Hawkins et al., 1992). Data from family, adoption, and twin studies support a substantial genetic influence on nicotine addiction, and recent advances in genomic technology have enabled the identification of candidate genes implicated in susceptibility (Philibert et al., 2008). In addition to furthering understanding of the mechanisms of addiction, these methods can also be utilized in improving the personal relevance of preventative and cessation interventions.

A behavioral analysis of smoking initiation and consumption habits found strong associations in prevalence of smoking among biologically related family members (Green, 1979). However, because family studies cannot parse heritable genetic factors from familial environmental factors, adoption studies investigated the smoking habits of children who were raised by adoptive parents with no biological relation. Eaves et al. (1980) found that adoptees were more similar to their biological parents than their adoptive parents in average cigarette consumption and nicotine dependence, supporting the heritability of liability to nicotine addiction. A later meta-analysis of twin studies comparing monozygotic and dizygotic pairs found that greater genetic similarity was strongly correlated with similar measures of nicotine dependence (Li et al., 2002). Review of literature finds that the interaction of genetic and environmental factors varies for smoking initiation and nicotine dependence (Li et al., 2002; Sullivan et al., 1999; Agrawal & Lynskey, 2008). Genetic factors account for 60% of liability to initiate smoking, while environmental factors play a significant role in accounting for 30% (Agrawal & Lynskey, 2008). In contrast, nicotine dependence is determined largely by genetic factors at a rate of 70%, while environmental factors are negligible (Sullivan et al., 1999; Agrawal & Lynskey, 2008).

Since the completion of the Human Genome Project, numerous studies have implemented genome scans to identify plausible genetic markers that increase susceptibility to nicotine dependence. Though strong empirical support exists supporting the role of genetic predisposition in nicotine addiction, it has been difficult to pinpoint specific gene regions as many genes are involved. Early efforts by Straub et al. (1998) and Wang et al (2003) implicated regions on chromosomes 2, 4, 10, 16, 17, and 18. A subsequent study using transcriptional profiling to analyze 30,000 genes from DNA samples from smokers and non-smokers found 579 more activated genes and 584 less activated genes in smokers (Philibert, 2008).

Focusing further in on specific genes, Stevens et al. have found two separate groups of single nucleotide polymorphisms (SNP) in the CHRNA5-CHRNA3-CHRNB4 gene cluster associated with common variants in nicotinic receptor subunit genes that are significantly correlated with heavy smoking (2008). One group of eight SNPs was strongly associated with increased risk of heavy smoking, and a second group of SNPs was associated with decreased risk (Stevens et al., 2008). These findings of risk and protective SNP
genotype combinations define a gradient of genetic predisposition for nicotine dependence and smoking severity. In particular, the statistically significant correlation with the first SNP group and heavy smoking behaviors implicates the α5 receptor subunit and the rs16969968 SNP, where reduced activity of this receptor appears to diminish response to nicotine and may shed light on specific biological factors relating to dependence at the receptor level (Stevens et al., 2008).

Genetic variation in the mesolimbic dopamine pathway has also been implicated in mediating nicotine dependence by influencing the degree to which individuals receive greater reward from nicotine’s effects on dopamine (Audrain-McGovern et al., 2004; Hall et al., 2002). Persistent smoking behavior has been linked to the rarer A1 and B1 alleles of the dopamine 2 receptor and the 10-repeat allele of the dopamine transporter gene SLC6A3. Individuals carrying the 9-repeat allele of SLC6A3 are associated with a 22% reduction in dopamine transporter protein, resulting in less clearance and greater bioavailability of dopamine; thus, they may experience less reward from nicotine and less susceptibility to dependence (Audrain-McGovern et al., 2004; Hall et al., 2002). In a study of adolescents with previous smoking experience, the presence of each additional dopamine 2 A1 allele translated to a twofold increase in likelihood to progressing to a higher level of smoking (Audrain-McGovern et al., 2004). Genetic variation in receptor structure and availability of dopamine may facilitate nicotine dependence by moderating how much nicotine affects the brain’s reward system and how much behavioral reinforcement occurs upon consumption.

**Implementation of Genetic Predisposition into Educational Interventions**

Given advances in understanding genetic susceptibility towards nicotine addiction, interventions targeting prevention and cessation should integrate awareness of heritability of dependence liability into existing messaging. Although some policymakers have expressed concerns about diverting funding from traditional public health approaches, acknowledging how genetic predispositions can influence an individual's path to recovery can help target, individualize, and increase efficacy of existing interventions (Hall et al., 2002; Hall et al., 2008; Dingel et al., 2012).

Rather than redistributing existing funds allocated for addressing tobacco use and nicotine addiction, more additional funding should be allocated for research and interventions focusing on genetic susceptibility for at-risk populations.

**Countering the “Won’t Happen to Me” Mentality: Prevention of Nicotine Use Initiation**

From a preventative standpoint, it is imperative to target deterrence interventions towards children and adolescents to promote nicotine abstinence and prevent dependence from becoming an issue (Dingel et al., 2012; Lantz et al., 2000; Russell, 1990). In addition to genetic and environmental factors, age is particularly important in determining nicotine use initiation. 90% of adult smokers began smoking before the age of 18, and numerous longitudinal studies have linked smoking initiation in early adolescence to life-long dependence (US Department of Health & Human Services).

The proposed educational intervention builds on existing programs at elementary, middle, and high schools and incorporates discussion of genetic susceptibility to nicotine dependence, opportunities for individualized information about risk, and framing social influence resistance skills as empowerment (Lantz et al., 2000). Current models of educational interventions have been found to have modest short-term and minimal long-term effects on smoking prevention, in part because youth do not perceive health risks of smoking to be personally relevant or a cause of immediate concern (Lantz et al., 2000; Wright et al., 2003; Hawkins et al., 1992; Docherty, 2011). Though programs focusing on social influence resistance have reported modestly significant short-term reductions in smoking initiation, the efficacy of this intervention is contingent upon students recognizing that tobacco use is harmful and personally resolving to avoid it (Russell, 1990; Sullivan et al., 1999; Lantz et al., 2000). Teaching students practical skills on how to resist negative social influences, such as harmful behaviors promoted by peers, is useful but will be complemented by an improved informative component about individualized risk incurred by smoking. The goal of incorporating discussions of genetic predisposition into existing interventions is to address the shortcomings of existing educational
interventions by increasing perceptions of personal relevance, understanding of specific health risks incurred by smoking, and incentive to resist negative social influences by providing individualized information on risk of dependence.

As the intervention is to be incorporated into existing health programs to strengthen existing messaging, facilitators will be current health instructors at each school. During the informative phase of the program where students learn about the associated health risks of smoking, health class instructors will discuss how nicotine is incredibly addictive for anyone regardless of genetic predisposition - on average, people who experiment with smoking one to three times will progress to becoming regular smokers (US Department of Health & Human Services). However, they will emphasize that individuals with a genetic predisposition will face even steeper statistical odds of dependence and addiction. Measures of genetic predisposition for nicotine dependence will be modeled upon empirical methods, including an informal tracing of family history and opportunities for subsidized genetic testing. After learning about the mechanisms of genetic heritability, students will be asked to complete a worksheet about their family’s health history including smoking and nicotine addiction. Pilot testing of interventions on genetic predisposition using simple methods of tracing family health histories has produced higher rates of smoking abstinence in addition to more negative attitudes towards smoking (Gartner, 2008). In addition, they have the choice of opting in to a subsidized direct-to-consumer genetic test of nicotine dependence from 23andMe, Decode, Gene Planet, Biomarker pharmaceuticals, or Lumigenix to learn about their own genetic susceptibility and potential subsequent health risks. Students will not be mandated to complete the genetic test to respect their privacy, autonomy, and financial capacities, but will be required to complete the family history activity which has been demonstrated to be an effective way to raise awareness about personal risk (Hall et al., 2012; Gartner et al., 2008). Previous research has found strong adolescent interest in testing for nicotine addiction susceptibility (Tercyak et al. 2006), and one meta-analysis has found that learning about genetic risk leads to an immediate motivational effect, greater perception of risk, and greater desire to quit smoking (Smercenik et al., 2011).

Marteau’s research on the impact of informing people about genetic risk has found that positive behavioral change is most likely when they are given the opportunity to participate in effective interventions (Marteau, 2001). Although several studies incorporating genetic susceptibility testing have found that informing can lead to a decrease in motivation due to a perception of fatalism, these studies did not offer interventions that gave individuals agency to reduce harm through behavior change (Wright et al., 2003; Senior et al., 1999).

In order for interventions to be most impactful, Marteau recommends that genetic risk information be complemented by provision of concrete strategies for individuals to reduce risks of adverse health outcomes (Marteau, 2001). To empower students’ sense of self-efficacy, reduce risk of increased fatalism, and increase perceptions of agency over one’s health and future, students will learn strategies from current ‘social influence resistance’ interventions for smoking prevention (Lantz et al., 2000; Hawkins et al., 1992; Docherty, 2011). These include strategies on how to “say no” to others who may encourage smoking initiation, affirm individual values and decisions, and avoid environmental risk factors. Avoidance strategies can include brainstorming how to exit harmful environments with minimal negative social consequences (i.e, pretending to take an important phone call, saying that one has allergic reactions towards smoking/cigarette content). Value affirmation exercises that have been found to improve smoking abstinence outcomes involve asking students to brainstorm, plan, and write about why their health matters to them and why they personally choose not to smoke. Students will be more informed about their individualized health considerations and predispositions, while encouraged to maintain agency and control over environmental risk factors.

Improving Treatment Efficacy: Using Genetic Information to Optimize Cessation Strategies

Like other drugs of abuse, abstinence from smoking can be extremely difficult to achieve and maintain (Russell, 1990). Two primary factors that interact to determine smoking cessation outcomes are de-
pendence and motivation (Russell, 1990; Benowitz, 2002). Sufficient motivation is essential for permanent cessation to be achieved for all smokers, but what is ‘sufficient’ depends on the degree of dependence (Russell, 1990; Quaak et al., 2009). Light smokers with low dependence may stop easily once they feel motivated, but heavy smokers with high dependence may not be able to stop even with strong motivation. Research on heritability of liability has found that genetic susceptibility predicts for more severe dependence (Stevens et al., 2008; Audrain-McGovern et al., 2004; Hall et al., 2002). Having a family history of predisposition for nicotine dependence can make it more difficult for a smoker to stop once they have started. However, clinical advances in understanding the effects of different pharmacological therapies for nicotine addiction on different genetic makeups have the potential to inform, individualize, and improve the efficacy of treatment. Given that different cessation strategies (i.e., nicotine patches, bupropion administration, e-cigarettes) exhibit varying levels of efficacy for different people, analysis correlates between individuals with certain genetic markers and their most effective cessation aids can be used to streamline selection of cessation strategies for other smokers.

In translating research into practical interventions to help individuals living with nicotine addiction, Lerman et al. conducted a study on how functional genetic variants of the dopamine 2 receptor influenced the efficacy of bupropion administration and nicotine replacement therapy. The Zyban brand of bupropion is a pharmacological smoking cessation aid, acting as a nicotinic antagonist and reducing the severity of nicotine cravings and withdrawal symptoms. Nicotine replacement therapy administers nicotine without the other harmful chemicals of tobacco in the form of gum, patches, sprays, and inhalers to relieve physical withdrawal symptoms. Examining a different allele on the dopamine 2 receptor, the Ins/Del C genotype, researchers found that bupropion treatment was more effective for individuals homozygous for the Ins C allele and that nicotine-replacement therapy was more effective for carriers of the Del C allele. Quaak et al.’s study highlights the potential for assessment of genetic background to guide selection of the most effective cessation treatment for individual smokers (2009). Although these findings have yet to be widely replicated and isolate one of the many genes involved in nicotine dependence, they point towards a future where individualized pharmacotherapy could potentially identify the most effective treatments based on an individual’s genetic makeup.

On a socioemotional level, utilization of genetic testing to facilitate cessation aid selection can also serve to increase smokers’ perceptions of self-efficacy and motivation to quit. Many smokers have already expressed an interest in receiving genetic testing, with 60-80% reporting a desire to learn about their genetic predispositions (Smercenik, 2011). The same study found that administering genetic tests led to promising, significantly positive attitude changes and behavioral outcomes. Smokers who received genetic tests felt higher personal relevance of risk perception and expressed stronger motivation to quit (Smercenik, 2011). These results were also translated to higher cessation rates and longer periods of smoking abstinence; a proposed potential mechanism for this change is that greater belief in the specificity of treatment aid selection can result in greater belief that the treatment will work. Similarly, Wright et al. found that learning of a genetic predisposition to nicotine dependence increased motivation to overcome their illness, higher personal relevance of risk assessment, and greater interest in pursuing cessation methods (2000). Although some researchers and policymakers have expressed concern that testing negative on a risk-increasing gene can result in more negative outcomes such as decreased motivation to pursue treatment, no adverse effects were found. As in the intervention for smoking prevention, informing individuals of genetic risk must be accompanied by provision of concrete strategies for changing behavior, such as effective medical treatment options and plans to remove environmental context cues from smoking from one’s life.

Conclusion

Addressing nicotine addiction is a critical public health priority, as millions of individuals continue to lose their lives to tobacco-related diseases despite many wanting to quit. As a substance with high addictive power, nicotine makes it difficult for absti-
nence to be attained and sustained. Because smoking can harm nearly every organ in the body and impact the health of others secondhand, improving and optimizing prevention and cessation interventions is imperative. Given compelling evidence substantiating the heritability of genetic predispositions toward nicotine dependence and growing understanding of how genetic makeups can influence behavioral outcomes, discussion of genetic susceptibility should be integrated into existing programs on prevention and cessation. Current prevention programs fail to elicit sufficient personal relevance for adolescents – giving them opportunities to learn highly individualized, specific information about their personal risk for nicotine dependence can increase perceptions of relevance and motivation to not smoke. In addition, advances in neurophysiological and biological understanding of the interaction of genetic variants with nicotine dependence can help optimize cessation and treatment plans with increased specificity. Though nicotine has the power to addict any individual in this world, some people are born with a “bullet in their blood”, a natural genetic predisposition that may bring them harm if allowed to manifest. By using every tool that science has produced to optimize strategic interventions to prevent and treat nicotine addiction, many more will have the opportunity to live fuller, healthier lives.

References


EXPERIENCE

The experience section presents public health challenges that students have encountered personally, highlighting the relevance of such issues to student life on a day-to-day basis.
As I stepped off of the plane onto foreign land for the first time in my life, I was overwhelmed.

I wasn’t overwhelmed by the overcrowded streets attempting to accommodate for both the impatient cars and restless crowds. Nor by the abundance of barefooted, dirt-covered children desperately selling lottery tickets and shining shoes around the city as a source of income. Not even by the hundreds of shack-like shops that bordered the streets, topped off with metal scraps for roofs. I was instead overwhelmed by the vibrancy and liveliness of the country and its people. The playful children, offering their service in exchange for an innocent dollar. The beautiful, ebony skinned people.

My people.

I was sixteen and in Ethiopia for the first time in my life. As the birthplace of my mother, father, and the rich culture they brought with them to America, Ethiopia was a mystery I had long been waiting to explore. She was the beginnings of existence, the home of a proud and resilient people, and the land of God-promised success. The potential of the country was apparent. Unfortunately, so was the poverty.

While the United States of America has 1 doctor for every 400 people, Ethiopia has 1 doctor for every 33,000 people.

I remember the stories my parents used to tell me when I was younger. About how in the large families that existed during their time, a few siblings passing away was normal, almost expected. Three of my mother’s nine siblings have passed away from illnesses and conditions we consider easily curable here in the states. A quick prick of a needle, a simple procedure could have saved their lives: a sad reality that demonstrates the devastation that lack of access causes in developing nations.

What does exist of the inadequate health care system in the country was and still is insufficient to provide for the extensive needs of its people. With few major hospitals prepared to provide decent care for their patients, the wealthy are the priority. Observing the countless sick and homeless individuals bordering the streets, the endless lines protruding from clinics as the weak and weary lay in one another’s filth for hours awaiting care was a torture beyond explanation.

Over the next few weeks, I decided to investigate more about the health disparities that plagued the impoverished, but beautiful, country I was in. The statistics were no longer sentences and bullet points I read on a CNN or WHO article. As I met more and more members of my family (which by nature of Ethiopian culture is expansive), I could associate a name and face with each statistic.

“...the overall under-five mortality rate is 88 per 1000 live births. A total of 67% of [these] deaths... take place before a child’s first birthday” (2).

One of my aunts recently had a son born with severe conditions that the country did not have the means to adequately treat. It was predicted he would pass away within the next year. He is one of the 88.

“Only 4% of births that take place in rural Ethiopia have a skilled attendant or clinician present at the time of the birth” (3).

My father cannot name any relatives of his generation from his time living in Ethiopia (some 25 years ago) that were born in the presence of a skilled attendant. Only after his generation did clinics and hospitals begin to appear in Nekemte, the village he grew up in. The mothers of Nekemte are a part of that 4%.

“...more than half of the Ethiopian population (52.1%) still used unimproved sanitation facilities in 2014. The majority (35.6%) practiced open defecation...” (4).

My father, again, cannot think of anyone in his
small town at the time that had consistent access to clean water, and recounts that many used a pit toilet and/or practiced open defecation. My mother, who also grew up in Nekemte, agrees. Only the major hotels, they tell me, had better toilet situations. “Better” being a cemented square platform atop an open pit to “fancify” the experience. Water was also a scarcity during their time. Washing hands was not as simple as running to the bathroom and using a sink, and bathing was nowhere near as simple as stepping into a shower. Their situations would become even more difficult when the wells outside their homes would dry up. A lack of basic necessities brings challenges to several important components of a healthy life: sanitation, proper hydration and nutrition, and countless other practices that are key to an individual’s health and welfare.

Such disheartening situations result in countless more unfair and unfortunate statistics:

*The capital city, Addis Ababa, contains an unbelievably underwhelming 9.01% coverage of adequate handwashing facilities in the city (5).*

*1 in 36 women in Sub-Saharan African countries, like Ethiopia, are at risk of maternal death (6).*

*Between 30 and 40% of children under-five in Ethiopia were stunted due to malnutrition (7).*

My trip helped me understand that these statistics are not just statistics; they’re people. They are people facing real situations, grappling with real hardships, and fighting real battles every day in order to survive.

I love Ethiopia. I’ve only visited once for a month, but still never hesitate to call her my country. My dad is always quick to remind me that a country one sleeps in for 30 days is not their country, but I beg to differ. The culture raised me, the country awakened me—Ethiopia is my country. Every time I sat with my cousins, I would think about how by simply being born in America, a land of exponentially greater access and opportunity than their home, my chance of living a long, healthy life was automatically higher. My heart would ache for them, because a simple difference in geographical location—one none of us could control—decided the quality of our situation.

Witnessing the unforgiving circumstances that the country’s people—my own family—had to endure was extremely difficult, but also crafted my dedication to a medical career full of change, real change, for the people who need it the most. That is the beauty of global health: saving lives that otherwise would not have been saved, reaching people that otherwise would not have been reached, offering opportunities to those who, although equally deserving as any one of us, would have otherwise remained deprived of them. And global health is not only a field for doctors; the field is for innovators, engineers, statisticians, journalists, investigators, educators, activists, entrepreneurs, leaders—anybody who is willing to contribute to the cause. The more diverse the workers involved, the more able and equipped we are to tackle the greatest healthcare concerns facing our world and our people, offering second chances and instantaneously changing lives in the process.

References


7. “Undernutrition contributes to nearly half of all deaths in children under 5 and is widespread in Asia and Africa.” UNICEF Data: Monitoring the Situation of Children and Women, United Nations International Children's Emergency Fund, data.unicef.org/topic/nutrition/malnutrition/.
I got out of my Uber at the intersection of Carey and West Baltimore Street. Hiding from the chilly October breeze, I wrapped my scarf tightly around my neck and rolled down the sleeves of my Johns Hopkins sweatshirt. Before me was a three-story brick building with “Western Grocery” scrawled across the wall in blue spray paint, and an arrow directing me to turn the corner. I followed it to the store entrance on Carey Street, which was covered in wire mesh, and stepped through the bulletproof glass door. I found myself confined in a locked vestibule with a tall, bulky African American man in a baggy T-shirt and jeans. He leaned against the menu taped to the window, waiting for his sandwich.

“Jojo, you’ve got company,” yelled the man.

I heard a shuffle come from behind a thick glass window—that separated the Chinese store owner, Jojo, from her customers. Before I saw her, I saw her display case, featuring a rainbow of candy and tobacco products. A no-smoking sign in capital letters and bold font hung ironically above the cigarette display. As she leaned over a small revolving window, through which the tall man placed $3.50 to pay for his sandwich, she saw me and immediately buzzed me through.

The door unlocked and I was allowed into her store, leaving the man still waiting for his food in the vestibule.

Welcome to food shopping in a typical Baltimore corner store.

Western Grocery and Carryout is one of 450 small groceries and corner stores in the city, most of them in “food deserts” – low-income neighborhoods that are over a quarter mile from a supermarket, in which at least 30% of residents live without access to a vehicle, forcing them to shop locally in an environment with limited healthy food sources. Some are set up like Jojo’s, with windows and walls reinforced by wire mesh and locked doors that prevent customers from freely entering the store. Shopkeepers take customers’ orders through bulletproof glass and push their requested items through a rotating window post payment. Unlike traditional grocery stores and supermarkets, corner stores and small groceries have limited food options, which are most often processed and calorie-dense, like chips and soda. Fresh and frozen produce are rarely available due to the lack of proper infrastructure, such as refrigerators, freezers, and ample shelf space.

Corner stores and small groceries represent 78% of food sources for residents in food deserts. One in four Baltimore residents live in such food deserts, according to the Baltimore City’s Food Environment 2015 Report. Food deserts tend to be in the city’s poorest neighborhoods, which are predominantly African American. These neighborhoods have more liquor stores, criminal activity and violence. People living in food deserts suffer the worst health outcomes in the city, including obesity, diabetes, and cardiovascular diseases, which lead to an increased mortality rate.

For good reason, city officials and public health...
experts are trying to see if they can use these corner stores to improve health outcomes for food desert residents by replacing nutrient-poor processed foods with fresh nutrient-rich produce. I worked for two years on a Johns Hopkins obesity-prevention research study called B’more Healthy Communities for Kids, which ended this past June. We cooperated with corner stores and carryouts in low-income, food desert neighborhoods. The study randomly assigned 28 geographic zones to serve as either controls or areas for intervention. In intervention zones, we worked to improve access and demand for healthy foods in corner stores by paying them to stock certain products, like fresh fruits, and to use educational displays and shelf labels to encourage customers to buy the healthier offerings. We also conducted taste tests, passed out giveaways, and educated customers on nutrition.

By the end of the program, my team found that, in comparison to control stores, more healthy foods were purchased in our intervention stores where they were made available and promoted. These kinds of positive results were also seen in previous healthy corner store programs, including Baltimore Healthy Stores and Shop Healthy NYC.

I had helped recruit corner store owners to participate in the program and learned that many were immigrants; most were Korean-American, but many came from China, where I was raised. I was one of the only Chinese speakers on my research team, so I did most of the interviews and data collection for the stocking and sales of products. I never had the chance, however, to learn about the Chinese store owners themselves or ask about their relationship with the predominantly black community they served. That was outside the scope of our study.

Out of curiosity, and to fulfill a recent class requirement, I decided to explore this by visiting Western Grocery & Carryout, one of our experimental control stores that had not received any intervention. The store is relatively large and also operates as a carry-out that sells hot foods.

Western Grocery & Carryout is located in Sandtown-Winchester, a low-income African American neighborhood that many people know as Freddie Gray’s home.1 In 2011, almost one-third of families lived below the federal poverty line. Average life expectancy at birth was 65.3 years, compared to the national average of 79. Out of the 55 Baltimore neighborhoods, Sandtown ranked in the top five amongst those with the highest density of liquor stores, tobacco retailers and vacant lots and buildings.1 For every 1,000 residents, 4.53 were murdered annually in Sandtown, a homicide incidence rate over twice that of Baltimore city. Sandtown also has more people in Maryland’s prison system than any other neighborhood in the state.1 “Behind Glass” corner stores, like Jojo’s, are common in these high-crime neighborhoods.

After getting buzzed into the store, I waited for store owner Shi Jin Zhou, nicknamed Jojo by her customers. There I stood, by yet another door that separated her and her cash register from the store’s interior. Recognizing me from previous visits, Jojo unlocked the door and welcomed me in. As I stepped behind the bulletproof glass, I entered Jojo’s world.

She greeted with me with a warm smile. Jojo kept her space hot, so I had to peel off my layers while I walked across the narrow hallway behind the glass display. The space was larger than it appeared from the outside and led to a small kitchen, where slices of bacon were sizzling on top of a black iron griddle. Through the glass, I spotted the man on the other side, still waiting in the vestibule. I wondered if he knew an entire kitchen existed behind the menu wall.
Jojo is a petite woman in her early 30s, with a heart-shaped face and large dark brown eyes. After graduating from college in the Fujian province, she immigrated to New York City to be with her family in 2010. Jojo worked long hours studying English and civics to become a U.S. citizen last year. Chuckling, she told me in Mandarin, “Bei le yi hou, kao wan yi hou, da gai jiu wan ji le.” After memorizing, after taking the exam, I basically forgot everything.

Jojo met her husband in New York almost as soon as she moved there. They got married and moved to Baltimore, where most of her husband’s relatives live. Jojo’s parents, who had also previously lived in Baltimore, owned Western Grocery & Carryout. They let Jojo take over the two-story property, and it has been hers ever since. The store is on the first floor, and she lives upstairs with her husband, one-year-old son, three-year-old daughter, and a nanny she brought over from China to help take care of her kids.

Jojo’s day begins at 8am. She gets ready and cooks breakfast for her family before opening the store. Every day, she works from 9am to 10pm. Once or twice a week, she takes her family to visit her parents, who moved back to Baltimore to help her older brother and his family of five. Like Jojo, her brother emigrated from Fujian and manages a similar store in Baltimore about 15 minutes away by car. Jojo described her life here as fairly good and roughly the same as how it was in China. “Zhi shi huan ge di fang shen huo,” she said. It’s just switching a location to live.

Besides continuing her lifestyle, Jojo and her family have also maintained good health after emigration. “Zhi shi man man bian da le.” Just slowly getting older, she joked.

While Jojo regarded her eating habits as healthy, she felt differently about her customers. In Mandarin, she said, They drink and eat soda and chips every day – which were the most popular items that Jojo sold. At most, they’ll eat a healthier option of a sandwich. If they have money, they’ll order a hot food, like a sandwich or fried chicken. During the interview, Jojo prepared a bacon, egg and cheese sandwich for a customer. She spread butter and jelly on two slices of toast, before adding the rest. “You’re putting jelly on the sandwich?” I asked, wrinkling my forehead out of confusion. She grinned and said that she found the combination weird too. Sweet and salty. They like it. I tried it before, and it’s actually not bad.

“Would you eat the food you sell?” I asked her. “Mei you chi,” Jojo replied. I don’t eat it. She commented that she rarely eats what she sells, not because she finds the food unhealthy, but because she doesn’t want to eat the same foods that she handles every day. I’m also not used to it. I prefer Chinese food. Jojo prepares Chinese-style cooking. We have rice, meat, vegetables, and soup sometimes. It varies! To convince me, she pointed to her rice cooker, which sat next to a big tub of mayonnaise that she used for her customers. She also commented that Chinese restaurants were easy to find, because so many Chinese people lived in the city.

Jojo lives in a food desert because that’s where her business is. However, Jojo owns a car, so she shops at least once a week at the large wholesalers B Green and Sam’s Club, and a specialized Asian supermarket about 20 minutes away called GreatWall.
stock for the store, I also pick up groceries at Great-Wall. Many of her customers have no such option. At least 1 in 3 people in her neighborhood don’t own a car or the economic flexibility to travel for groceries; so they eat Jojo’s food.

I grew up in China, where I ate mostly fresh produce. Eating according to season was part of the Chinese culture. I could see that Jojo had a similar approach to food. I wondered why she was not selling the food she bought for herself. So I asked Jojo if selling fresh produce was important to her. She told me that it was and that they had tried, unsuccessfully, to sell fruits in the past. “Zui jian dan de ping guo, orang-es, dou jing chang fang huai diao.” Even the simplest kind of fruits, like apples and oranges, are often left until they’re spoiled. Jojo said that her customers had poor diets. The healthier the food, the more unlikely they’ll eat it. Items like vegetables and fruits, they eat very little of these items. Even if we provide it, they won’t buy it, and it’ll go to waste.

Halfway through our interview, her one-year-old son wandered back into the store with his nanny tagging behind. Jojo told me that they had been walking around outside the store. “Do you think that’s safe?” I asked, as my research coordinator had always advised me to visit these neighborhoods in pairs. Not that safe, Jojo replied. But the people here, how it’s like in America is that…they’ll respect old people and kids more. Do you know that? Us young people, if we go out, they’re more likely to harass us. But the elderly and kids are safer; they won’t bully them, so it’s alright. Jojo confessed that she’s afraid to walk around outside, and if she did go out, it was for only short stretches close to the store.

She described her relationship with her clientele as pretty good, but said she found their character and behaviors improper. “Bi jiao huai,” she commented. Quite dishonest. Jojo said that if she doesn’t watch her customers, they will steal her things. There’s poor public security. That’s why we need to fence up the door and windows. “But they know your name!” I protested, struggling to imagine myself stealing from an acquaintance. They know my name because they live close by and come regularly. But they’ll still steal from me. Of course, there are exceptions. Some are good. There’re just less of them.

Although both Jojo and I moved from China to Baltimore, our experiences with the city differ drastically. Living in the “Hopkins Bubble,” I realized how privileged I was and am to never have to worry about food and physical security. Within half a mile from where I live, I could grab an apple from Charles Market whenever I craved one. Jojo had to drive miles. Yet, she is one of the lucky ones in her community.

Jojo and her neighbors face a flawed built environment, with limited parks and green spaces, dirty streets and vacant homes. This restricts their opportunities for physical activity and social interactions. They also share a fear of community violence and crime, which are results of a poor education system, lack of job opportunities and enduring poverty. But unlike many of her neighbors, Jojo’s food environment is not limited to Sandtown; she has access to affordable and fresh food options. As a result, Jojo and her family’s health conditions have not deteriorated from living in a food desert. Even though she knows the same cannot be said for most of her customers, she feels there’s very little she can do about it.

But Jojo can contribute to her community’s health, even if she’s powerless to change the built environment. Based on my team’s research, corner store owners can affect their customers’ shopping and eating habits. These changes are difficult, but not impossible over time and with education. Hopkins and the city health department are hoping to work through community members to change the food environment in these nutrition deserts. They are not only encouraging store owners to stock healthier items, but also guiding them on how to promote these new offerings. Stepping back into the vestibule, I thought about the candy and tobacco that greeted me and hoped that soon they could be replaced with a rainbow of fruits and vegetables instead. Although substantial reforms have yet to reach Jojo and her customers, I have a feeling that she will cooperate, probably enthusiastically. She has a stake in the city just as much as her neighbors do. While holding her son, who was recently born in Baltimore, Jojo said, “Wo men zhu zai zhe li.”

We live here now.
References


I looked down at the surgical area as he changed the dressing, expecting it to look like the ravaged and pitted battlefield of some major catastrophic war. But all I saw was my same soft brown skin… (Lorde, 1997, p. 44)

Audre Lorde, acclaimed Black lesbian poet and author, wrote these words in her memoir The Cancer Journals, reflecting on the first time her eyes met her skin after her mastectomy in 1978. Her journal entries were published in 1997, five years after her death from breast cancer. The imagery of the body as a battlefield and fighting cancer as though it is war is neither new to the United States nor unfamiliar to most of us. Starting with a diagnosis, it is not uncommon to hear of patients “battling” cancer, treatments becoming “ammunition,” and successful treatments resulting in the label “survivor” (Ness, 2014). Lorde’s expectation that her post-operative body resemble a battleground more than herself points to the normalization of the war metaphor in describing breast cancer – and the possible disconnect between medical discourse and patient narrative.

While the war metaphor is used to describe patient experiences with cancer’s many forms, many are focusing on its use in breast cancer, a disease which mostly affects females. As Lorde’s words suggest, the war metaphor, which is typically associated with violence and masculinity, may be antithetical to some patients’ genuine expression of their experiences with disease. Growing linguistic evidence points to the idea that metaphor is not simply a rhetorical device but also a way in which we conceptualize our experiences. Given that the metaphors that we use inherently affect how patients view their experiences, reevaluating the war metaphor is more important now than ever. As part of this reevaluation, the medical community and charities – the two largest stakeholders in the advancement of the metaphor – can address the connotations and pitfalls of the metaphor in the formation of patient narrative.

The Roots of Survivorship

In order to understand the current usage of the war metaphor in describing cancer, it is important to look at its history. As cancer cases grew in number, charities like the American Society for the Control of Cancer (ASCC) were founded in the 1910s to combat the disease. These charities created a type of rhetoric and propaganda that would advance their mission (Garrison, 2007). As the ASCC sought to mobilize the public to “Fight Cancer with Knowledge,” public reactions to cancer within the United States largely shifted from stigma and silencing to concerted public efforts to find a cure. Feeding off of this public fear, the ASCC mobilized women “to raise awareness about cancer and its curability” through its Women’s Field Army (WFA). The ASCC and WFA deliberately used references to the “ruthless killer” and “trench warfare” to provide “cancer patients and their families with the inspiration they wanted and needed” (Garrison, 2007). President Richard Nixon’s signing of the 1971 National Cancer Act and call for the “conquest of cancer” further validated the perception of cancer as the “enemy” and the effort against it as “war” (McLean, 2014). Through the hegemonic rhetoric of the early to mid-1900s, the militarization of patient’s bodies ensued: patients now “battled” cancer, treatments were “ammunition,” successful treatments resulted in the label “survivor,” and researchers searched for the treatment to finally end cancer – the “magic bullet” (Ness, 2014).

Metaphor has become an integral part of patient-physician communication as it allows patients to comprehend complex medical processes and practices in simpler terms. Vyjeyanthi Periyakoil (2008), associate professor of medicine at Stanford University, explains that “by using a metaphor to connect the relational pattern of new experience with that of a familiar, emotional-laden one, [physicians and patients] can create a contextual roadmap to understand and process a complex pattern of feelings” (p. 842). According to her statement, the use of metaphor in the context of cancer may clearly be benefi-
cial. Speaking to the war metaphor specifically, Paul Hodgkin (1985), a practicing physician, notes that the war metaphor and its associated imagery “encourages the virtues required to survive the long hours and intense hierarchies of hospital life” (p. 1820). Moreover, the war metaphor’s presentation of cancer as the “enemy” may decrease the physician’s sense of responsibility when cancer treatment falls short or goes awry (Hodgkin, 1985). Given that 2008 cancer deaths approached 2.5 million in the U.S. alone, the diversion of responsibility conferred by the war metaphor remains relevant to the medical community (U.S. breast cancer statistics, 2017).

In conjunction with the medical community, breast cancer charities have also popularized the use of the war metaphor. Since its inception in 1982, the Susan G Komen Foundation has become the largest charity in the “war” against breast cancer; in the 2011 fiscal year alone, the foundation raised over $472 million (Orenstein, 2013). Much of this success can be attributed to the Foundation’s impressive advertising campaigns which rely, in part, on the use of the war metaphor. In addition to its iconic pink ribbon that has now become synonymous with breast cancer, the Susan G Komen Foundation has adopted the war metaphor as a means to raise public support. On their pink-flooded website, the Foundation uses the terms “treat” and “fight” interchangeably and provides four definitions surrounding “survivors” and “survivorship.” Contrasting the traditional definition of survivor, in which an individual lives past a life-threatening situation, the organization defines “breast cancer survivor” as “a person living with breast cancer (from the time of diagnosis)” (“Breast Cancer Glossary,” 2017). Although the organization does not state why it includes the parenthetical addition, one can infer that it is meant to foster inclusivity among all of those affected by breast cancer. This theory is supported by the inclusion of the definition for “co-survivors,” which refers to the individuals supporting breast cancer patients starting with their diagnosis (“Breast Cancer Glossary, 2017). Regardless of the reasoning for these distinct definitions, the Foundation illustrates profound intentionality when discussing disease.

In addition to creating their own interpretations of the war metaphor, the Susan G Komen Foundation makes abundant use of the war metaphor in reaching the general public. As illustrated in Figure 1, T-shirts, laptop cases, mugs, phone cases – among a multitude of other merchandise available for purchase on their website – are laden with words related to fighting and battle. Regardless of who dons the t-shirts or uses the mugs, the Foundation’s merchandise has two main effects. First, it further perpetuates the war metaphor as the main rhetorical framework through which to discuss breast cancer. Second, and more importantly, it generates profit from the language used to describe disease. Given that the Foundation only spent 16% of its profits in 2011 on research[1] (despite its slogan “for the cure”), this raises questions regarding whether breast cancer charities should be directing the language that is used to describe patient experience. At the very least, the power that charities such as the Susan G Komen Foundation yield over the language used to discuss breast cancer begs evaluation of the rhetoric they perpetuate.

**Metaphor: A Paradigm Shift**

Before evaluating the war metaphor’s efficacy and appropriateness in breast cancer patient narratives, it is important to alter the lens through which we view metaphors themselves. Critical in this paradigm shift were linguists George Lakoff and Mark Johnson, whose work suggested that metaphor pervades not only language but also perception. They offer the example of the common metaphor that “argument is war.” Through this metaphor, claims can be “indefensible,” “opponents” are “demolished,” and arguments are “won.” So ingrained is this metaphor in our own culture that arguments can be won, ground can be gained or lost, and claims can be defended; in essence, the use of the war metaphor in the context of argument shapes not only the language we use to describe argument but also how we approach argument itself (Lakoff, Johnson, 1980). Through this single metaphor, the inherent entanglement of metaphor in our conceptual systems is elucidated. Adding to the accepted definition of metaphor, Lakoff and Johnson suggest that “the essence of metaphor is understanding and experiencing one kind of thing or experience in terms of another.” Key to this definition is the emphasis of the role that metaphor plays in shaping our experiences (Lakoff, Johnson, 1980, p. 158).
While metaphors may be used to comprehend something in simpler terms, they may also have unintended and potentially negative consequences. Lakoff and Johnson note that “the very systematicity that allows us to comprehend one aspect of a concept in terms of another will necessarily hide other aspects of the concept” (1980, p. 10). Within the context of argument, the war metaphor may, on the one hand, encourage well-substantiated claims; on the other hand, it may be un conducive to collaboration. Because of this duality, medical professionals and charities should reevaluate the use of the war metaphor in the context of breast cancer. Although war metaphors – in the context of either argument or cancer – may illuminate particular processes, they may fall short in other regards. In the latter case, alternative metaphors may prove beneficial to patients.

**Patient Narrative as a Looking Glass**

Narrative serves as a powerful looking glass into personal experience and identity. Within the context of medicine, the power of the patient narrative is manifold. While disease presents “a disruption, a discontinuance of an ongoing life,” narrative provides an opportunity “to fit the illness disruption into a temporal framework” (Hydén, 1997, p. 52). While x-rays are ordered, prognoses are delivered, and drug cocktails are concocted, narrative allows patients to have some control in an otherwise powerless experience. By returning autonomy to the patient, narrative has healing qualities. Narrative offers a medium through which patients can connect the concrete past to the uncertain present and keep “pre-illness lifestyle and identity intact” (Bury, 2001, p. 272). Clinical studies have shown a correlation between the catharsis associated with narrative and healing effects; one study cites a “decline of disease activity in patients with rheumatic arthritis due to writing about personal stressful experiences” (Kalitzkus, Matthiessen, 2009, p. 84). Narrative may also have healing qualities for people listening to the stories, as the permanence of written words can create a sense of unity and belonging between patients. These healing qualities and the ensuing importance that narrative holds within patient experiences should not be overlooked by charities and the medical community.

Given that the war metaphor has largely become the hegemonic framework within which doctors and patients alike have viewed breast cancer, one can assume that it must confer some benefits – and academics agree (Ness, 2014). As English professor Kristen Garrison (2013) notes, the war metaphor “offers hope, optimism — an absolute necessity for the kind of life-death experience cancer threatens, even if it does not immediately deliver.” In emphasizing the collective effort against cancer that includes doctors and family, “survivor rhetoric is very empowering and can be a potent—and potentially valuable—antidote to the demoralizing effects of the disease” (Ness, 2014). Sociologist Dragusin (2014) confirms the war metaphor’s empowering quality, arguing that the war metaphor and its “images of power and aggression” help counter the debilitating “powerlessness and passivity” characteristic of life-threatening diseases (p. 1229). Through these different linguistic and sociological perspectives, the reason the war metaphor has become the hegemonic rhetorical framework in the context of cancer becomes clear.

Perhaps the strongest testament to the war metaphor’s efficacy comes from reading breast cancer patient narratives. In the war metaphor, breast cancer patients find a sense of agency, community, and identity. As BC Becky, one of many breast cancer patient blogs, writes, “I can fight this, because I am a warrior and one day I want to be a survivor!” (2014, July 7). Grounded in the survivor identity, this quotation speaks to the war metaphor’s ability to give patients the agency to see beyond the bleakness of day-to-day hospital life. Much like an actual war, the war metaphor also allows patients to ground themselves and their identities in the chronology of their “battles.” Fighting Fancy, another breast cancer blog, notes, “Even though Corrie and I are at different stages of our battle, we have remained friends throughout the past year and a half” (2013, December 19). Beyond a sense of agency and control over their illness, the war metaphor confers a sense of camaraderie in an otherwise-isolating experience. My Journey with IBC (Inflammatory Breast Cancer) shares her experience meeting other IBC survivors and how “encouraging [it was] to see that there can be life after IBC” (2014, September 1). Whether by grounding themselves in the stages of their “battles” or by connecting with others who were in their positions not long
Where Language Falls Short

While the war metaphor may provide women a sense of clarity and community, some patient narratives point to a sense of disillusionment with the current rhetorical framework prescribed to breast cancer patients. Some breast cancer patients have pointed to a disconnect between the masculinity associated with war and their own feminine identity. While the war metaphor has become the hegemonic rhetorical framework through which discussion of most types of cancer is framed, breast cancer offers an interesting case study. Unlike most other cancers, breast cancer affects a predominantly female-bodied and feminine-identifying population. It should therefore be no surprise that some patients who identify with their femininity are at odds with the masculinity perpetuated by Western conceptions of war. Some patients point out problems with the reinforcement of masculinity in medicine beyond the individual case. In a journey entry, Audre Lorde shares:

Women have been programmed to view our bodies only in terms of how they look and feel to others...I must consider what my body means to me...The raped wife is accused of enticing the rapist. The battered wife is accused of having angered her husband (Lorde, 1997, p. 65).

Lorde’s words strike a chord that is still relevant today. In the growing conversation surrounding women’s rights, Lorde’s words extend the conversation to the female breast cancer patient. Her words force her readers to consider the irony in the continued situating female illness within a male-centric framework. Although many are able to look past this aspect of the metaphor and rightly use it to their benefit, issues of gender cannot be overlooked by the medical community and breast cancer charities.

While some patients have found the war metaphor to masculinize their disease, others find that it encourages an extreme sense of individual responsibility. Even before their diagnosis, women are endowed with the personal responsibility of detecting cancer early through routine mammograms (Garrison, 2007). If a tumor is found, this individual responsibility only intensifies: breast cancer patients must keep up with complex medical lexicon, potential prognoses, the latest breast cancer treatments, among other information. Among this slew of information, the war metaphor insinuates that, like any battle, “fighting” bravely will inherently lead to desired results. To this individualism purported by the war metaphor, some patients have responded by viewing their experiences with illness not as a battle, but rather as parts of the natural progression of life. Jesse Gruman, a patient treated for five different cancer diagnoses ranging from gastric cancer to Hodgkin’s lymphoma, notes that while “some could call [her] a cancer survivor,” she calls herself “lucky” (Gruman, 2013). Gruman draws the connection between cancer patients and victims of natural disasters. Just as one cannot control being involved in a flood or an earthquake, cancer patients cannot control tumor formation or how their bodies will respond to novel treatments; simply put, cancer patients should consider themselves lucky “if the stochastic spin of the mutation roulette wheel gives them tumors that respond [to treatment]” (Gruman, 2013). Audre Lorde echoes Gruman’s sentiments when her own doctor suggests that “no truly happy person ever gets cancer” (Lorde, 1997, p. 64). To Lorde, the blanket individualism in part supported by the war metaphor represents a “monstrous distortion of the idea that we can use our psychic strength to heal ourselves” (Lorde, 1997, 64). Although perhaps unintentional, this burden of individual responsibility placed on cancer patients is worthy of consideration.

The last concern patients have voiced with the war metaphor concerns those whose breast cancer treatment is unsuccessful. While the war metaphor acknowledges the struggle that breast cancer “survivors” and current breast cancer patients have overcome and are overcoming, patients and doctors alike are concerned about what the war metaphor insinuates about those that don’t live to hear the label “survivor.” Barbara Ehrenreich (2000) famous author and former breast cancer patient, writes,

...the mindless triumphalism of ‘survivorhood’ denigrates the dead and the dying. Did we who live ‘fight’ harder than those who’ve died? Can we claim to be ‘braver,’ better people than the dead? (p. 53).
Ehrenreich’s poignant words raise an important point about the way in which we treat not only those that are currently facing breast cancer, but also the many who have had unsuccessful breast cancer treatment.[2] Through the desirable end-goal of the survivor label, patients may be burdened with feelings of failure and inadequacy. This is especially true when patients are facing a terminal diagnosis and no longer have the survivor identity to look forward to. Referring to these cases in which there is not yet a cure, Caroline’s Breast Cancer Blog questions “if there is no cure, how do you survive it?” (2013, December 6). This question makes the war metaphor’s shortcomings apparent: while it may be effective at evoking a sense of strength and motivation, the metaphor ignores a large subset of patients. This provides an excellent opportunity for medical professionals and breast cancer charities to intervene and better accommodate the people they exist to serve.

**After the Gunpowder has Settled**

The patient voice is gaining ground in the medical field. This comes as a result of a burgeoning realization that patient narrative may point physicians to better, patient-specific treatments. The growing philosophy is coined Narrative-Based Medicine (NBM), aptly named to counter Evidence-Based Medicine. Rather than relying on the facts and figures on which “modern” medicine is based, NBM views patient narrative as a tool with which physicians can tailor treatments. Through this view, NBM “[brings] the patient as a subject back into medicine” (Kalitzkus, Matthiessen, 2009, p. 81). Breast cancer poses a unique opportunity for physicians to apply this growing tool for multiple reasons. The first reason is that it affects a relatively homogeneous population, which consists of female-bodied patients over the age of 30. Second, the large number of breast cancer patients provides a large sample population to analyze; this large population also makes a timely intervention even more crucial. Third, and perhaps most importantly, the astonishing public awareness of breast cancer, due in part to charities such as the Susan G. Komen Foundation and their control over public discourse, offers a unique platform through which real change can be made.

In systematically changing how disease is discussed, we must consider alternative rhetorical frameworks. In the case of breast cancer (and other cancers), it is important to note first that disease is discussed differently depending on the culture in which it is rooted and, second, that war is not the only way in which to discuss disease. Khalid (2008) makes the important distinction that “the language (not to mention the conclusions) of any science reflects the particular society within which it exists” (p. 698). While war may seem like the “natural” way to discuss disease, it is very much a Western way of framing illness. Khalid contrasts the Western, war-rooted concept of disease with the Traditional Chinese Medicine emphasis on “balance.” She notes that, in Traditional Chinese Medicine, “referring to the experience of disease as warfare would be completely foreign” (Khalid, 2008, 698). This distinction poses the exciting possibility of using alternative rhetorical frameworks to frame disease, as there clearly is no one “natural” way to discuss illness.

In rejecting the war metaphor, some alternative rhetorical frameworks have started to gain momentum. Some patients have begun viewing their experience with breast cancer as a journey, as opposed to a “war” (Ness, 2014). As with any road trip, patients may have passengers (family members, doctors, etc.) alongside them and experience “high points” and “low points.” This metaphor also encourages viewing cancer not as an “enemy” within the body but rather as another passenger on the journey. In turn, this metaphor confers a sense of agency over the disease back to the patient and lacks the intensely individual aspect of the war metaphor. Others have started to view their bodies as cities (Khalid, 2008). Just as a city has buildings and “good” and “bad” people that inhabit these buildings, so too can patients. In facing cancer, patients have “good” (i.e. immune) and “bad” (cancerous) cells which respectively reside in different organs – or “buildings” within the context of this metaphor. These frameworks are just two examples of metaphors patients have integrated in telling their stories and by no means are right for everyone. However, conversation regarding new ways in which to discuss disease, as well as concerted efforts by the medical community and breast cancer charities, proposes the exciting possibility of ushering in novel, patient-centered ways of discussing illness.
Where You and I Fit In

In 2000, my father came home from a business trip to find my mother distressed and holding her bruised and fatigued three-year-old son. Consultations with four different physicians all yielded a likely-flu diagnosis. Upon the fifth, bloodwork was ordered; I was diagnosed with Acute Lymphoblastic Leukemia, a common childhood blood cancer. After three years of drinking crushed-up chemotherapy regimens mixed with condensed milk, begging the nurses to stop pricking my finger in a three-year-old’s Spanish, and slowly piecing together that I, along with the other kids dressed in gowns at the hospital, were different from my friends at pre-school, I was declared in remission. I was a survivor. For my parents, the survivor label stood and continues to stand as a testament to our family’s strength in its most difficult time. As for myself, I have just started to consider the role the war metaphor has played in shaping my own identity.

The war metaphor has become the hegemonic framework with which diseases ranging from childhood leukemia to prostate cancer to HIV/AIDS are discussed within the United States. The human stories and voices presented in this essay speak to something much larger than breast cancer patient blogs or journal entries. If reading these intensely human experiences is important, learning from and acting on them is paramount. Breast cancer poses an interesting case study in that it is a disease with great public awareness and whose cure has significant financial support. Changes to how it is discussed may serve as an important paradigm shift in how the language regarding disease is determined. Especially in cases where patient language does not align with those of doctors and charities, it is our collective responsibility to evaluate and act on the language used to describe the experiences of our parents, our children, our aunts, our uncles, our friends, our loved ones, and ourselves.

[1] In that same fiscal year, the Foundation spent more on “administrative costs” and “fundraising” combined than on breast cancer research (Orenstein, 2013).


References


RESEARCH

The research section invites the members of the Stanford community to share their essays, perspectives, and research with a broader audience interested in public health.
In 2005, Target pharmacies reinvented the classic orange pill bottle with a new design that boasted color-coded rings, a relocated cap, and most importantly a larger, easy-to-read label. Bottles became easier to open, and medication became easier to identify and consume correctly.

Surprisingly, this innovation did not come from a pharmacist or a pharmaceutical company, but from an art student. Deborah Adler, a master’s student at New York’s School of Visual Arts, was inspired by an incident where her grandmother accidentally ingested her husband’s medication (Adler). While her grandmother did not suffer any serious medical complications from the incident, Adler became aware of how easy it was for medication information on pill bottles to be misread or misinterpreted.

For example, warfarin is a common over-the-counter blood thinner taken by over 2 million Americans. However, when taken with aspirin, another common over-the-counter medication, it can drastically increase the risk of hemorrhaging and internal bleeding (Ho). Though they are benign when taken apart, mistakenly mixing them can cause adverse drug interactions and increase the risk of serious and sometimes fatal side-effects, decrease the effectiveness of other medications, and can lead to overdose. Unfortunately, errors like these are common. In 2007, a report from the American Institute of Medicine reported that “1.5 million patients are injured each year by medication errors, of which more than one-third occur at home,” where patients must read and interpret prescription information on their own (Jeetu).

Even with recent innovations like Adler’s, there are still massive shortcomings in communicating important health information to the consumer. From a design standpoint, one of the biggest issues with prescription labels is readability—specifically, the font size, placement of the text, and the consistency of the overall label design. For example, a 2011 publication from Consumer Reports found that the average font size on a pill bottle is less than 14 point font, which is approximately 0.5cm tall, for a drug name, and can be as small as 8 point for important drug warning and dosage information (Consumer Reports). Both between different labels and within a single label, the typeface, capitalization, and bolding used are often inconsistent, as are the orientation and placement of text. In one extreme example, a warning label for internal bleeding was placed crookedly and read perpendicularly from the rest of the dosage information.
limited or low vision.

Additionally, when pharmacies incorporate techniques like highlighting or underlining to separate information, they often do so excessively. CVS pharmacies, for instance, use blue highlight over black text for multiple sections. This “overwarning” does not prioritize information effectively and actually causes the brain to disengage with information due to overstimulation (Robinson).

The content on drug labels is also often unclear. For instance, vague dosage interval instructions like “take orally twice a day” may be interpreted differently by each consumer (Jeetu). Some may interpret this strictly as “once every twelve hours,” while others may assume their medication can be taken anytime during their daily routines. This lack of clarity can result in improper dosage intervals, leading to a patient having too much or too little of the medication in their system at one time and increasing the risk of negative side-effects.

Another underlying issue is the ambiguity around the intended audience for drug labels. According to the FDA, the purpose of the prescription label is to “give healthcare professionals the information they need to prescribe drugs appropriately” (“An Introduction”). This contradicts insights from local pharmacist Frances J. Cheng, gathered in a recent interview. According to Cheng, most of the information on prescription medication labels is for the consumer, not the pharmacist, who can obtain all the necessary information from the small barcode on the side of the bottle instead of from the actual text (Macias). On both the federal and local levels, there is ambiguity with regards to the intended audience and purpose of the label. As a result, individual pharmacies are given control to invent their own systems of labeling, often at user expense.

The best example of this is perhaps Deborah Adler’s new bottles for Target pharmacies in 2005. The new design increased readability and the user response was overwhelmingly positive. However, when CVS bought the Target franchise in 2015, the administration immediately discontinued the bottles, citing the high production cost of reproducing this bottle design across their 9000 pharmacies nationwide (Taylor). The decision was met with immediate consumer backlash; for instance, one woman recalled digging through her trash to retrieve old Target bottles and another reported saving and reusing her old bottles at the risk of not remembering the expiration dates of her new medications (Taylor). Because of how easily companies can change their labeling standards, the user experience was once again neglected in the design process.

This is not the first time the public has expressed their desire for change. In an extensive survey administered by the California State Board of Pharmacy in May 2008 it was revealed that a majority of consumers felt drug labels should be easy to read and clearly indicate the purpose of the drug, and that neither of these needs were being met by current designs (Prescription Drugs). Therefore, any future design, whether an overhaul of the entire bottle or a simple label revision, must prioritize user experience via readability, organization, and content.

One way to accomplish this is to bring in user-experience designers who can reach out to consumers as well as pharmacists and doctors before implementing a new design (Babich). Pharmacists would be able to provide input on bottle and label design from a functional standpoint, and doctors would be able to offer valuable feedback and inform user experience designers of the most common medication errors among patients historically. Much of the current user interaction and user experience research is done retroactively, after the label’s release; being proactive in the design process allows critical feedback from the user to drive product design.

Nonetheless, even if changes to the FDA’s loose requirements are made, it can take years for the standard to be mandated across the United States (“An Introduction”). As a result, labels are variable, and even positive changes are not standardized within a reasonable length of time.

Label effectiveness has been well-researched, yet little has changed, implying that the problem stretches beyond physical design and may include societal and institutional factors. As mentioned previously, slow-moving FDA regulations make changes to label design difficult to standardize and detracts
from any incentive companies may have to alter labels. Even if the problem is well-researched, drastic changes, like less content on bottles, may not be an option for these nationally regulated (or semi-regulated) pharmaceutical industries. Health literacy is another contributor. Defined by the American Medical Association as “the ability to perform basic reading and numerical tasks required to function in the healthcare environment” (Weiss), health literacy can affect user interaction with prescription medication across different demographics. A study conducted by Northwestern University in five different cities across the United States found that adult patients who had completed less education had over twenty percent higher rates of misunderstanding label instructions compared to those who had completed more or higher levels of education (Davis). This study illustrates both how inaccessible design disproportionately harms vulnerable segments of the patient population and how difficult it is to convey health information to a wide range of consumers, all possessing different levels of health literacy.

In response, some institutions have proposed plans for a universal, human-centered design standard. In the same Northwestern study, researchers were able to improve comprehension of the most misunderstood label by over thirty percent by simply incorporating more explicit dosage instructions (Davis). The U.S. Pharmacopeia, the authority that sets voluntary standards for prescription medication, and the Institute for Safe Medicine Practices have also both proposed methods of improving and standardizing drug labels. These include the use of 12-point type, including the patient’s name, drug name, and drug instructions on the label, and resolving ambiguity about drug and dosage ambiguity including images or descriptions of drug appearance and by eliminating leading zeros or confusing time periods for dosage intervals (Consumer Reports). However, the lack of enforcement mechanisms for these proposals means that pharmaceutical companies often treat them as suggestions, and ignore them in favor of our current design system.

Clearly, there is both a flawed system in place and a high demand for a better product from its user base. Future labels must change, but how might these changes actually occur?

Firstly, the purpose and function of the label must be well defined. A consensus must be reached at both the federal and local levels so that the purpose and intended audience of the label is understood. This could take the form of implementing a long-term plan for a universal pharmaceutical standard that reduces variability and therefore lessens the likelihood of misinterpretation. In the short term, reform at the federal level may be difficult and time consuming. However, in the long term, shortening the turnaround for new standards and permanently setting timelines for standard reform would ultimately increase user safety. Many reputable organizations like U.S. Pharmacopeia and the Institute for Safe Medicine Practices have already developed and proposed standards; these existing proposals can save time and money for the FDA and have the potential to be adapted and implemented at the federal level.

Finally, because labels are ultimately a communication issue, the pharmaceutical industry must find new ways to communicate important health information. Many pharmacies now have websites where consumers can learn more information about their prescription. However, with the addition of new technologies like QR codes and intelligent expiration dates, information can be delivered to the patient like never before. IDenticard security badges, for instance, are manufactured to develop a large red “X” twenty-four hours after they are activated (TEMP-badge). The development of intelligent expiration dates on bottles has the potential to be a valuable method of protecting consumers from expired medications. Although largely untested in other applications, using this material would not require the label or bottle to be redesigned. Instead, it incorporates technology into the physical label material, making the design more human-centered. While still in the research and development stages, intelligent expirations labels may also be an important stepping stone for incorporating other new technologies on prescription drug labels.

QR codes or “Quick Response” codes are a type of matrix barcode that, when printed, look like small, pixelated squares. QR codes were originally used to
scan and identify car parts but have since evolved from their original form and application (Uzun). Now, anyone with a smartphone can access this information. To obtain the encoded data, the user must download an app, many of which are free, and take a picture of the code. Then the code links the user to websites, stored texts, or sends an SMS message to their phone.

QR codes can store a considerable amount of data and are more versatile than traditional barcodes. For example, one QR code can store one hundred times more information than a barcode and can be read or scanned in any orientation (“QR”). It also has the potential to be printed in smaller formats than the barcode because it is a “two-dimensional” square that takes up less horizontal space.

QR codes could have vast implications in providing medical information to the consumer. On the bottle, or even on the lid, a small QR code could be printed and include all the information previously provided by the label. Imagine a patient walking into the pharmacy and scanning all their new medications with their smartphone. Immediately, they receive an SMS message with a warning for a possible adverse drug interaction, saving them from a possible deadly misstep. While human errors still would not be eliminated entirely, this new system would greatly reduce them.

QR codes can also be applied to assist populations with different accessibility needs or levels of health literacy. After one scan, an SMS message can be sent to the phone each time the user needs to take their next dosage of medication, thus eliminating vague dosage instructions for people with cognitive or memory issues. In other applications, this information can be scanned and then automatically read aloud for those who are visually impaired. Synthesizing these technologies gives users access to the most relevant information and decrease the probability of adverse drug interactions.

While a grandiose overhaul of the prescription medication label may be in order, other more practical and immediate solutions are also available. In the immediate future, revisions to labels must be designed with the user in mind and pharmaceutical companies must prioritize user experience across all levels of health literacy. Moving forward, the purpose of the label must be defined so that a safer standard can implemented at the federal level. Finally, the label must be free to evolve and find innovative new ways to convey information to the user. Unfortunately, today adverse drug events are commonplace, but moving forward with smart, human-centered design they are ultimately preventable.

References


Introduction

Around 8:00pm on August 31st, 2017, Ma Rongrong, a parturient soon to give birth at First Hospital of Yulin City, Shaanxi Province, China, ended her own life by jumping out of the hospital window. The hospital released two screenshots of the security footage on Sept. 6th, which showed that two hours before, Ma twice appeared to be kneeling in front of her husband Yan Zhuangzhuang and her mother-in-law. According to the hospital, the security footage screenshots evinced a story of pain: Ma begged for a Cesarean section, which could relieve her labor pain, but was turned down by her conjugal family.1 Driven to desperation by labor pain, she committed suicide.2
The family agreed to the pain narrative—they also believed that Ma committed suicide to relieve herself from labor pain. However, they claimed that the hospital prevented Ma from having a C-section.3 Yan explained that Ma did not kneel to beg for a c-section; she fell to the ground because she could not bear the pain. To those of us who do not know Ma personally, her entire story is captured in two images: one in which she kneeled on the hospital floor, painful; one in which she lied on the ground, painless. In the Chinese dichotomy of Qian (heaven) and Kun (earth), the feminine energy belongs to the earth, the fertile provider of life. Ma’s fate seemed to be constantly pulled by a downward motion: the unbearable heaviness of birth brings this young parturient again and again to the ground. Earth, gravity, fertility, weight—these entangled symbols weave a story of femininity and pain.

One False Dichotomy, Two Groups of Articles

Ma’s story sparked two waves of discussion on the Chinese Internet: first, people debated whether women should have a right to elective Cesarean sections to avoid labor pain; then, people questioned whether the concept of pain relief was conflated with C-sections, and whether labor pain should be addressed as an issue of its own. If pain relief measures during labor, such as epidural anesthesia, provides painless vaginal birth as an option, why is the Chinese public not exposed to such information?
In this essay, I aim to look into one false dichotomy deeply rooted in Chinese society: the dichotomy between a painful vaginal birth and a painless C-section (referred to as “false dichotomy” below). I will analyze this false dichotomy by examining media influence, specifically magazines on family life and reproduction. Two groups of magazine articles are considered to be written about the false dichotomy: the first group is written within the false dichotomy on choosing between a C-section and a vaginal birth; the second group tries to bridge the dichotomy by addressing pain in parturition. I will conduct quantitative analysis on these articles, analyze the result and demonstrate the existence of this false dichotomy. Then, I will propose reasons on three levels why the false dichotomy continues to exist: (1) on the surface level, few discussions are present in magazines; (2) articles within the dichotomy, specifically those against painless C-sections, suppress further conversation about pain; (3) lastly and most subtly, these articles create a culture around parturition, casting an implicit judgement on certain values. These underlying values prevent the emergence of conversations about pain relief.

**Definition**

In this section, I will state the definitions for crucial terms in this paper. Commonly used in magazine articles are Chinese words fen mian 分娩 and chan fu 產婦, both of which are formal vocabularies widely used by both the medical community and the media. 分娩 is the process of birth giving. 產婦 means “laboring woman”—a woman defined by the process of labor, whether she is in it or about to enter it. To best capture both the meaning and the tone of these words, I will regularly refer to the corresponding English terms parturition and parturient. Parturition is “the action or process of giving birth to offspring.” A parturient is a pregnant woman who is entering or about to enter parturition.

In this article, I will not focus on C-sections performed out of medical necessity. I will use the term “elective C-sections” to encapsulate C-sections performed out of not medical need but the parturients’ will. One common form of painless delivery, epidural anesthesia, also referred to as epidural, is the “injection of an anesthetic into the lumbar area of the spine in the space between the spinal cord and the dura, which eliminates sensation from the point of insertion downward, used especially in childbirth.” Having clarified my definitions for parturition, parturients, elective C-sections and epidural anesthesia, I will move on to my research methodology.

**Methodology**

Magazine resources for this paper come from the Chinese Knowledge Resource Integrated Database (CNKI)—one of the most comprehensive and prestigious platform in China for digitalized knowledge resource, initiated by Tsinghua University in 1999.

Open to the public, this database charges 0.5-1 CNY (0.07-0.15 USD) per page for both online reading and download of articles. I am able to gain access to CNKI through Stanford Libraries.

From the magazine section of CNKI, five Chinese magazines most pertinent to reproduction or family life were selected. Then a preliminary search of the following keywords is conducted: fen mian 分娩 (partuition), pou fu chan 剖腹產 (Cesarean section), shun chan 順產 (vaginal birth), wu tong 無痛 (painless) etc.

<table>
<thead>
<tr>
<th>Name</th>
<th>Name in Chinese</th>
<th>Location</th>
<th>Year</th>
<th>Focus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenting Science</td>
<td>《父母必讀》</td>
<td>Beijing</td>
<td>1980-2017</td>
<td>Parenting</td>
</tr>
<tr>
<td>Love and Health</td>
<td>《婚育與健康》</td>
<td>Henan</td>
<td>1996-2014</td>
<td>Sex, reproduction</td>
</tr>
<tr>
<td>Marriage and Family</td>
<td>《婚姻與家庭· 社會紀實》</td>
<td>Beijing</td>
<td>2003-2017</td>
<td>Family</td>
</tr>
<tr>
<td>Fashion Baby</td>
<td>《時尚與兒》</td>
<td>Zhejiang</td>
<td>2007-2017</td>
<td>Parenting</td>
</tr>
<tr>
<td>Chinese Baby</td>
<td>《母嬰世界》</td>
<td>Shanxi</td>
<td>2001-2010</td>
<td>Pregnancy, parenting</td>
</tr>
</tbody>
</table>

Table 1. Five Chinese Women’s Magazines about Parturition.

A first reading of all the articles with the above key words determines whether they surround any of the two themes: (1) the choice of vaginal birth or the choice of Cesarean section, or (2) parturition and pain. A second reading of the selected articles poll them on concepts such as attitudes towards C-section, attitudes towards pain etc. Results are recorded for quantitative analysis; simultaneously quotes are collected for a qualitative analysis.
Results

In results section, quantitative analysis on magazine articles reveals the following: 1) the false dichotomy between a painful vaginal birth and a painless C-section exists; 2) few articles are written about the false dichotomy; 3) attitudes towards C-section were largely negative compared to those towards vaginal birth; 4) standard biomedical procedures such as epidural hardly dominate the conversation about pain relief and 5) attitudes towards pain were mostly negative.

1) The False Dichotomy Exists

Magazine articles about parturition attest to the existence of the false dichotomy. Six articles, published in different magazines in different years, share titles similar to “Vaginal Birth vs. C-Section.” Four articles open with the question: “vaginal birth or C-section,” which three claim is a question that every parturient has to face. Several articles buttress that one important aspect of this dichotomy is pain.

2) Lack of Media Attention

To put it simply, the false dichotomy between a painful vaginal birth and a painless C-section exists because magazines do not address it enough. Graph 1 to Graph 5 show the numbers of articles on 1) choosing C-section or vaginal birth, and 2) parturition and pain, compared to the overall number of articles for the five magazines over the years.

Graph 1. Parenting Science, a Beijing-based publication which prides itself as a “science magazine,” is the most prestigious and authoritative of the five. Even though the number of all articles written each year fluctuate between 600-963, the number of articles on false dichotomy each year has never exceeded 3.

Graph 2. A small, sensational local tabloid from Henan, Love and Health publishes 36 issues per year in some years and 12 issues per year in others. No articles from 2002, 2005 or 2006 are found on CNKI—not unreasonable to assume that the magazine did not publish in those years. The magazine stopped publishing after two issues in 2014, hence the great variation in number of all articles each year. Even though it publishes as many as 1801 articles per year, articles on the false dichotomy has never exceeded 1.2% of all articles written that year.

Graph 3. Marriage and Family is a Beijing-based magazine, publishing around 500 articles per year. No more than five articles on the false dichotomy are written in a year. No article on the false dichotomy was published in the past three years.

Graph 4. Fashion Baby is a Zhejiang-based magazine catered to younger audience. Each year, of the 501-977 articles its publishes, around three are about the false dichotomy. Interestingly, from 2011 to 2017, exactly two articles are written each year on choosing C-sections or vaginal birth. From 2010 to 2012, two articles are written each year on pain and parturition. From 2013 to 2017, this number decreases by half and one article is written each year on pain and parturition. Compared to other magazines, Fashion Baby's bar graph follows a clear pattern, which may suggest that the magazine has a quota on the number of articles on each topic.
As Graph 6, a composite graph of all five magazines show, the two groups of articles of interest remain small in number over the years. Every year from 1988 to 2007, less than 5 in every 1000 articles are written about the two topics combined across the five magazines—an undeniably low number.

3) Attitudes Toward Vaginal Birth and C-Sections

Graph 7-9 collect the first group of articles’ (choosing vaginal birth or C-section) opinion on Cesarean section and vaginal birth. Attitude towards C-section in these magazine articles have been consistently mixed or negative over the years. In the debate between vaginal birth and C-section, articles lean towards vaginal birth to a considerable degree. It is not difficult to fathom which method of birth a parturient who has been reading these magazines would choose.

4) What We Talk About When We Talk About Pain Relief

The second group of articles on the false dichotomy are those about parturition and pain, many touching on the subject of pain relief. One might assume that by pain relief, these articles are referring to standard biomedical procedures, like epidural. However, as Graph 10 and Graph 11 show, this is not the case. Two thirds of articles on pain relief never mention epidural, but instead describe other methods like Lamaze, family accompany and water birth. Granted, epidural has gained public awareness rapidly, since the first article on epidural appeared on the five magazines in 2001, but even in recent years, no decline is observed in other methods like Lamaze either.
5) Attitudes Toward Pain

Graph 12-13 study the second group of articles’ understanding of pain. According to graph 12, of those pain and parturition articles that do convey a value judgement on pain (either explicating stating or implying that pain is good or bad), an absolute majority associate pain with negative attitude. About 1/3 of the articles discuss pain’s negative impact on parturient’s mental state, such as fear and anxiety.

The Lost Case about Pain

In order to resolve the false dichotomy, I want to see how two groups of magazine articles interact with each other. According to graph 12, most articles in the pain and parturition category agree that pain is negative, which gives parturients an incentive to seek painless methods of delivery. In the first group of articles (choosing between vaginal birth or C-section) however, a painless elective C-section is constantly cast as a false option: an option nonetheless, but not the one that should be chosen.

As graph 7 and graph 8 show, the first group of articles disapproves of elective C-section as an answer to the pain issue. Curious what other answers they propose, I studied what magazines against elective C-section say about pain. Half of the articles (27 out of 57) never bring up pain in their discussion. A quarter (15 out of 57) identify pain as an issue but provide no solution. Only 2 out of 57 articles suggest epidural as a pain relief measure.

When some of these articles attempt to provide an answer to the pain question, these attempts can be grossly misguided and self-contradictory. On one hand, some articles claim that pain is inevitable and good. Despite evidence on the efficacy of painless delivery, many recent articles still argue that pain is “surely there,” “unavoidable,” and “a hurdle that can’t be avoided.” Not only can pain not be avoided, but also it must be glorified: pain “[opens] a woman’s strength,” “makes people mature and strong,” and turns the parturient into a real mother.

On the other hand, other articles depict pain as bad but trivial. Using the phrase “Tong Bing Kuai Le Zhe (in pain but happy),” this group of arguments see pain as an unpleasant, but temporary state before immense pleasure. Many claim that seeing the baby dispels the pain instantly: “when I saw my baby, all pain went away;” “but when the baby cried, I forgot about the pain immediately;” “it was painful, but as soon as I saw you come out, it did not hurt at all.”

These arguments emphasize that birth is a positive experience despite pain, while the previous ones emphasize that birth is a positive experience because of pain. Pain cannot be both positive and negative, both essential and trivial. Thus, these two groups of arguments contradict each other.

This section shows that articles against C-sections fail to provide a consistent or satisfactory answer to the pain issue. Attempting to answer the pain question, articles simultaneously justify, fetishize and trivialize pain. These failed attempts are both the products and the perpetuators of the false dichotomy—they are the products because their support for vaginal birth determines their stance on pain; they are the perpetuators because appearing to solve the pain issue suppresses further discussion for pain relief.

A Culture of Parturition

In “Results,” I have illustrated that magazines write little on the two topics of interest: 1) choice of vaginal birth or C-section, and 2) parturition and pain. Why are these topics so rarely written about? I argue that on an even more subtle level, these magazines construct a “culture” surrounding parturition—a tapestry of social norms and moral values that they create, conform to, and justify. Like a membrane, this culture allows for only contents that reflect certain values to infiltrate. In the ensuing sections, I will list three elements I have discovered in this “culture of parturition,” analyze their underlying values, and extrapolate their impacts on lack of conversation on pain relief.
“Gua Shu Di Luo (When the Melon is Ripe, the Pedicel Falls Off)"

Recurrent in these magazine articles are “nature arguments” that label birth as an “instinct” or a process of nature. Analyzing common expressions within this category, this section will show how nature arguments deprive the parturient of her subjective experience of birth by taking away her presence, active efforts and sentience in labor.

A signature of these arguments is the expression that parturition is “a natural/normal physiological process.” Inspired by anthropologist Emily Martin’s book The Woman in the Body, I question how parturition can be “a” physiological process without indicating whose physiological process it is, as if a physiological process is objective, impersonal and existing outside of living organisms. The attempt to appeal to a natural or biological framework creates a false sense of objectivity that separates childbirth from the parturient and erases the parturient’s presence.

One idiom repeatedly appears in these magazine articles: “Gua Shu Di Luo”—when the melon is ripe, the pedicel falls off. The idiom is generally used to justify that birth naturally happens when the right time arrives. This analogy reveals jarring fact: the melon refers to the fetus; the pedicel possibly refers to the placenta; the falling of the pedicel refers to parturition. The parturient is nowhere to be found in this analogy: no one conducts the maturity of the melon; the melon carries itself to term. The subject does not “do” anything. Instead, the objects automatically come to “be.” The shift of focus from doing to being obliterates the parturient’s active effort in birth.

Other than the maturity of a melon, vaginal birth has been compared to the selection of organic vegetables and rice, the yielding of fruit for trees, the process where “melted snow off the ice-covered mountain flows towards the sea,” and the fact that when the boat gets to the bridge, it naturally goes straight with the current. None of these analogies have a sentient subject: trees, melted snow and a boat are not sentient beings that can feel, but parturients are. Cloaked in the myth of nature, without a sentient subject, we can only observe on the macroscopic level that birth happens. We cannot identify on an individual level how birth happens: birth can happen easily, joyfully or painfully. It can happen so excruciatingly that it drives women like Ma Rongrong to death—the feeling aspect of birth is lost. How can we have a productive conversation focused on the parturient’s comfort and well-being if the culture of parturition constantly diminishes her presence, active efforts and sentience in parturition?

“Da Han Da Jiao (Screaming and Shouting)"

After Ma Rongrong’s death, the public, torn between the hospital’s and the family’s opposing accounts, struggled to choose which one to believe. The missing piece of the puzzle is what each party said in the security footage two hours before Ma’s death, when she either voluntarily or involuntarily kneeled. Ironically, the security footage does not record sound. In this chaos where all parties fight to establish their narratives, Ma Rongrong’s voice is forever silenced, both metaphorically and literally.

To my surprise, the amount of content linking parturients with silence is astonishing. A good parturient is a quiet one. On the receiving side, many authors write that doctors scold them for screaming. One the giving side, some authors advise parturients to be silent: “mothers-to-be have to remember, you must not scream or shout. That affects the work of medical professionals, wastes your energy and causes anoxia for the fetus.” A bad parturient is a screaming and shouting one. One repeatedly appearing phrase is “Da Han Da Jiao”—to scream and shout. The image of “screaming parturient” becomes a classic caricature: she “[squirms] around,” “[tosses] and [turns]” and “[makes] a scene.” She is a laughing stock, and one does not want to be like her.

I argue that the focus on screaming is a classic case of medicalization. Medicalization refers to the process of converting a non-issue, or an issue of other nature, into a medical issue. To avoid screams that are out of pain, the rational measure to take would be to tackle pain instead of the screams. The medicalizing brush takes a picture of institutional injustice—women’s lack of access to pain relief, and repaints it into a picture of individual deviance—the insanity of the screaming parturient. The unquiet parturient is often associated with madness, a concept suggest-
ing deviance and stigma. One author of “Embarrassment during Parturition” writes: “at the time I was like a madman… the pain and discomfort made me lose my ladylike demeanor, not to mention screams and cries.”  

Screaming as a response to pain can be censured or forgiven. Some justify medical professional’s censure of screaming by arguing that their “impatience” is “not without reasons,” because if every parturient is “emotionally-stable,” they “would not be in such bad mood.” Others normalize the screaming: the parturient in “Embarrassment during Parturition” was forgiven, both by her nurse and the editor of the magazine. Both regard screaming to be normal. The editor writes “even if you do have some insane behaviors, do not blame yourself. The doctors and nurses are used to these screaming parturients.” While I believe most readers will share my outrage for the censure of screaming, it is worth noticing that the toleration of screaming is far from the optimal response. In the “Nervoso” chapter of the book Death Without Weeping, anthropologist Nancy Scheper-Hughes studies the medicalization of hunger in the Brazilian municipality of Bom Jesus: hunger, a sociopolitical problem, is medicalized into nervousness, a medical problem. Through drug prescription, nervousness is “treated” and the sociopolitical problem is forgotten. The toleration of screaming may create a similar false sense of complacency—first, systematic injustice becomes individual pathology. Then by normalizing individual pathology, the systematic injustice is wiped clean. Normalizing screams is not conducive to conversations about pain relief during childbirth.

“Jiao Qi (Finicky)” and “Ren Xing (Self-Willed)”

When I first conceived the idea for this project, I asked my mother back in China, who gave birth to me vaginally, what kind of people opt for C-sections. She gave me a crisp response: “the finicky ones.” The adjective she used is Jiao Qi (嬌氣)—fragile, spoiled or finicky. Paradoxically, to be Jiao Qi is to be both incompetent and demanding. With a radical that is the character for women (女), Jiao Qi is a highly gendered adjective used almost exclusively on women and children.

A concern against Jiao Qi is present in magazine articles. One article titled “Parturition Experience of My Spicy Finicky [Jiao] Wife” ridicules the wife from the husband’s perspective for being demanding and having “irrational” fears about pain. Jiao Qi is not only a gendered criticism men imposes on women, but also a deeply internalized insult that parturients themselves want to avoid. In “Mothers Talk About Natural Births,” one mother claims that she thinks hospitals that do not allow family to accompany are better: “If the family is beside, the parturient will perhaps be more finicky [Jiao Qi].” For her, family company should be sacrificed in order to avoid Jiao Qi, even though she never pinpoints why Jiao Qi is wrong and what negative consequences it brings. In another article, another mother believes that she was able to give birth quickly because she exercises and does housework during pregnancy. “I did not think I was a delicate [Jiao] princess just because I was pregnant,” she said. With a sarcastic and critical tone, she assumes that other pregnant women are Jiao Qi, and she is easy to distinguish herself from these other women. For a culture that constantly conflates individual acts of demand with a long-term, persistent demanding personality, demands for pain relief can be under constant attack of ad hominem, and the question of whether these demands are justified or not is neglected.

The demanding aspect of Jiao Qi is captured in another adjective: Ren Xing (任性), which literally means to let one’s will rule. If women are discouraged to be self-willed, whose will should they comply to? Textual evidence suggests a strong link between respect for medical authority and criticism against Ren Xing: “the most important thing is for mothers-to-be to…actively cooperate with the doctor. Must not be self-willed (Ren Xing).” Interestingly, the tone of that sentence already establishes a sense of authority in itself. In self-deprecating humor, one parturient in another article says that she was “stupefied” by labor pain and unable to comply with birth instructions of the doctors. Losing her sanity, she banged her head on her bed, ran around and asked to go home. Having gone through a turbulent parturition, she addressed her child in the end of the article: “I felt the fear afterwards. You mom was too self-willed.” Granted, she did not comply with the medical authority, but her account suggests that she was irrational in that mo-
ment and not under control of her own will either. If parturients are put on trial for being Ren Xing, this author ironically pleads guilty by reason of insanity.

This discrepancy raises an important issue: the parturient takes on the dual roles as a laborer and a patient. American sociologist Talcott Parsons coined the term “sick role” in 1951, arguing that being sick allows the patient to bear certain responsibilities, such as compliance, but also receive certain benefits, such as being cared for and absolved of responsibilities. Too often the parturient is asked to bear the responsibilities of the sick role without receiving the benefits: if Jiao Qi—to be both incompetence and demanding—is a negative trait, then the opposite is to be both competent and compliant: competent as a laborer, compliant as a patient. A good laborer knows how to push. A good patient follows instructions. Society expects the parturient to be both, but exploits the fact that she is fully neither: not fully a laborer, the parturient is not entitled to adequate work conditions, such as a painless delivery; not fully a patient, the parturient is not absolved of responsibility when she is perceived to have done something wrong. Rules about compliance require her to relinquish her agency, but constant criticisms of her behavior suggest the presence of her agency.

Conclusion

In this essay, I have briefly introduced my research project on magazine media influence on the false dichotomy between a painless C-section and a painful vaginal birth in China. Quantitative analysis shows the following: 1) relatively few magazine articles are written on choosing between a C-section and a vaginal birth or on pain in parturition. 2) Magazine articles’ attitude severely lean towards vaginal birth in the choice between vaginal birth and C-section. 3) Standard biomedical procedures such as epidural hardly dominate the conversation about pain relief. 4) Most articles on pain and parturition view pain as a negative experience. Then, I have demonstrated why articles against elective C-sections inadequately answer the pain question and suppress further conversation about pain. Finally, I have discussed the “culture around parturition” created by magazine articles on parturition—nature analogies, the emphasis against screaming and shouting and the stigma of being finicky and self-willed subtly prevent further conversations about pain relief, which can bridge the dichotomy.

This paper is developed from final projects for History 203C: History of Ignorance and Anthro 82: Medical Anthropology. I thank the instructors for both classes, Professor Robert Proctor and Professor Angela Garcia, as well as Teaching Assistant Aaron Neiman for insights and comments that shaped and greatly improved this paper. I would like to express my gratitude to Professor Matthew Kohrmann, for proposing media influence as a major tenet of the study and suggesting the methodology of examining magazine articles. I am appreciative of Professor Suzanne Gottschang, Professor Helen Longino, Professor Angela Garcia, Professor Londa Schiebinger and Professor Marcia Stefanick for referring me to readings, people and ideas that substantially shaped and assisted the research behind this paper.

References

1. The standard practice of the hospital is to obtain both the consent of the patient and the assent of the family before surgeries or treatments, according to Clause 33 of the Management Ordinance of Medical Institutions. On Sept 6th, the hospital released Ma’s Notification and Consent Form, where Ma’s and Yan’s signatures are seen on the day of admission (Aug 30th), but only Yan’s signature appears on the day Ma enters the delivery room (Aug 31st). This form proves that the consent and assent obtaining process is in accordance with Clause 33. Further to prove that Yan has decision over Ma’s treatment is another form signed by Ma that delegates Yan as her power of attorney, which Ma theoretically can recant at any point.


Fleeing from Terror: 
Considering Safety When Designing Public Spaces 
in the Age of Mass Murder 
Nic Fishman

Sometimes, the safest thing people can do is flee from danger. However, what if they are in a room with dozens, or hundreds, of other people when that danger arises? How do they get out? And when architects designed the room—whether an intimate theater, concert hall, or sprawling convention center—did they think about how to optimally allow people to exit in an emergency?

In the following paper we establish a standard for evaluating a given room's safeness: We use a model-predicted evacuation time resulting from a simulated terror crisis as our safety metric. Then, we develop algorithmic methodologies to optimize room design, and propose a regulatory framework for ensuring future construction projects protect building occupants.

Our safety-assessment algorithm first takes in a prospective floor-plan design. Then, we computationally run a series of randomized terror scenario simulations, keeping record of the amount of “time”—represented with a conceptual, particle physics-based proxy—that it takes for the population (e.g. a group of theater-goers) to get out. This “time” is averaged across 8 simulations to minimize variance, producing a metric we term “Time to Exit” (TTE). This TTE is then inputted into an iterative statistical process which adjusts the parameters of the floor-plan (e.g. exit-door placement) in order to create a modified design that better minimizes the room's TTE score. By evaluating and creating rooms that ensure short evacuation times, we address a societally relevant public health issue: Terror crisis response.

1 Introduction

In the modern era, it is rare for a theater in the United States to catch fire and cause hundreds of people to die. One hundred years ago, this particular tragedy was all too common, but after decades of legislation, updated fire codes, and improved building materials, we have largely put a stop to theater fires. All of this regulation has directly translated into huge public health gains: After all, designing better buildings makes people safer.

Today, we face a tragedy of similar scale: Mass shootings motivated by individuals who can do extraordinary damage. Hundreds of Americans die each year in gun-fueled rampages, an increasing proportion of them children when accounting for recent school-centered shootings [Cha17]. As this public health issue continues to escalate, it becomes clear that we need a policy solution that keeps people safe. Perhaps, the most obvious answer is gun control, but this is a highly contentious issue in the United States and is politically intractable. The next logical step may be to think about establishing mental health screening, identifying potentially unstable individuals, and providing them therapy to help them become more mentally healthy, thereby stunting atrocities at the perpetrator-level. This seems sensible, but experts have concluded “the sorts of individuals who commit mass murder often are either not mentally ill or do not recognize themselves as such.” [Cha17]. Most budding, bloodthirsty killers would be resistant to therapy and other such interventions, because they see the outside world as the root of all their problems [Kha17]. In other words, while such a therapy-based approach is beneficial for the general public good—improving national mental health is always a great objective—it does not feasibly mitigate harms from terror-based events specifically.

A more practical solution is to think about how we design our public spaces, and to consider how we can — moving forward — design rooms that are intrinsically safer. Hence, we propose an objective framework for evaluating a theater’s “Time to Exit.” Note that in this analysis, we use the word “theater” to represent generalized enclosed places where people congregate, from convention centers to stadiums to movie theaters to classrooms. Directly defined, “Time to Exit” (TTE) is the time it would take everyone to evacuate a room in response to a sudden attack. If, after evaluating the TTE for a user-submitted theater design, we generate an improved room schematic that is modified with computationally optimized exit-placements and possesses a separate (hopefully lower) TTE, then we can evaluate how safe a theater currently is, and compare this to how safe it could be. The core of this algorithmic framework is establishing an effective model to simulate how people would flee a theater when a terrifying actor appears. To accomplish this simulation task, we take inspiration from chemistry, using a heavily modified version of the Metropolis algorithm used by chemists to simulate fluid dynamics. Our framework can model TTEs for any size of theater, any number of people, and any number of barriers (e.g. benches or tables) in the room. This framework can then be applied in a legislative setting, allowing regulatory bodies to set an acceptable threshold on how much a proposed theater design's safety score can deviate from its respective optimized design safety score, and subsequently, we can make more informed decisions when approving new construction projects.
2 Modeling Crowd Dynamics

Given the set up of a theater, its dimensions, location of obstacles, location of exits, the initial position of the people in the theater, and the position of the terror (e.g. a weapon-wielding terrorist, a bomb device, a fire, or any other stimuli that people would be repulsed from), how long does it take everyone to get out of the theater?

2.1 The Metropolis Method

Human behavior is notoriously multifaceted and difficult to predict, so to make this problem more approachable, we need a model: A system that will represent complicated crowd dynamics in a more computationally manageable way. At this point, we turn to chemistry for inspiration, invoking a model that predicts how randomized particles might move toward a lower potential equilibria along a potential field. A highly relevant topic in molecular-simulation sectors is fluid dynamics: How can we simulate the behavior of liquids at various temperatures, pressures, and volumes? The solution to this issue is called “Hard Sphere Simulation”, where every molecule is assumed to be a sphere (or, in two dimensions, a circle), and all spheres are considered “hard” in that they are not allowed to overlap. Spheres are assumed to have no interaction unless they’re overlapping, in which case they have infinite potential. The simulation permutes all the particles in one time-step, via a symmetrical distribution on every axis. We will call this a “move.” To make these simulations accurately simulate reality, an acceptance criterion is applied to decide whether to accept a “move.” The acceptance criterion is the probability that the system moves from the old state \( o \) to the new state \( n \). This is calculated using the Maxwell-Boltzmann distribution, which takes a change in potential energy for a system, and returns a probability of that change:

\[
x \sim \text{Uni}(0, 1)
\]

\[
\text{acc}(o \rightarrow n) = e^{-\frac{U(n) - U(o)}{kT}} > x
\]

The acceptance criterion is a Bernoulli random variable that will accept a new state \( n \), with potential energy \( U(n) \), according to the PDF of the Maxwell-Boltzmann distribution, at temperature \( T \) (mathematically, temperature is multiplied by the Boltzmann constant \( k \), so in this paper, we will treat \( kT \) as one parameter).

Combining all these components, the Metropolis algorithm is born [FS01]. See Algorithm 1.

Algorithm 1 This simple set of algorithms gives a high level appreciation for how simple the Metropolis algorithm can be. All that happens is \( X \), the initial position of the particles, is moved \( n \) times, each particle in \( X \) given a random displacement according to a normal distribution with \( \mu = 0 \) and \( \sigma = \sigma_x \). A move is accepted if the particles do not overlap, otherwise it is rejected.

```plaintext
1: procedure METROPOLIS(n, X, kT, \sigma_x)
2:     \( U \leftarrow \infty \)
3:     for \( i=1:n \) do
4:         \( X, U \leftarrow \text{move}(X, en, kT, \sigma_x) \)
5:     return \( X, U \)
6: procedure MOVE(X, en, kT, \sigma_x)
7:     \( X_n \leftarrow \text{normrand}(\mu = 0, \sigma = \sigma_x, n = \text{len}(X)) \)
8:     \( U_n \leftarrow \text{energy}(X) \)
9:     if \( \exp(-U_n - U)/kT) > \text{rand} \) then
10:        return \( X_n, U_n \)
11:     return \( X, U \)
12: procedure ENERGY(X)
13:     for \( x_i \) in \( X \) do
14:         for \( x_j \) in \( X \) do
15:             if \( \text{overlap}(x_i, x_j) \) then
16:                 return \( \infty \)
17:     return \( 0 \)
```

2.2 Extending to the Human Case

How do we connect the movement of particles in a flowing liquid to people in a movie theater? The key insight is that humans
are like particles. The $kT$ value can be thought of as the level of panic in the theater: How likely people are to be confused and go the wrong way. The $\sigma_x$ value is the distance people can move in a single time-step: The larger it is, the closer the simulation is to real time. There is, of course, a major item missing from the model we have so far described: There is no motivating force. Thus, the essential leap in logic is to conceive all the particles as being negatively charged. With this modification, the model prods the people to move towards the exit. Elaborating further, the exit will be simulated by a positive point charge and the terror by a negative point charge. Accordingly, the negatively charged people will have lower potential (i.e. be in a more favorable state) when they are closer to the exit and farther away from the terror object. A negatively charged particle will be at its lowest potential when closest to the positively charged particle.

This requires some minimal modification to the algorithms above. Namely, the energy function will now perform the following calculation— if $e$ is the vector position of the exit and $t$ is the vector position of the terror:

$$U = \sum_{x \in X} \frac{kQ_t}{||x - t||} - \frac{kQ_e}{||x - e||}$$

With this substitution, the Maxwell-Boltzmann acceptance criterion (Equation 2) will over time force the simulation to its lowest potential equilibria. In layman’s terms, the people will leave the theater. To make this model more realistic, we can account for in-room barriers like seats, railings, walls, and columns with some further modifications. Thus, we have an system that can effectively simulate any theater set-up.

### 2.3 Extending to Multiple Exits

Our model can be extended one step further. So far, it only allows for a theater to have one exit. If we added a second or a third exit, there is a logical incongruity: There would be an optimal point in-between the two exits, where moving in either direction would cause an increase in potential (i.e. be unfavorable) that the acceptance criterion is unlikely to accept. Think about how if an electron had a proton on either side of it at equal distances away, the electron (here, the theoretical person) would be immobile. Thus, our model system would likely achieve a steady state equilibrium without everyone evacuating the theater. Some theoretical people would be paralyzed between the two exits. This is not realistic. The simplest, most efficient solution to this problem is to say that people are "smart": They will know what exit is closest to them, and only experience the attractive force of that exit. This greatly simplifies the calculation for multiple exits, and elegantly solves the steady-state equilibria reality incongruity. To incorporate this adaption, we make a slight modification to the energy function. See Algorithm 2.

---

**Algorithm 2** This iteration of the energy algorithm takes $X$, the current position of the people, $B$, the position of all barriers, $E$ the position of all exits, $t$, the position of the terror, and $l$ and $w$, the dimensions of the theater. The overlap functions are in reality specific to the shapes being compared and involve a bit of interesting geometry, but have been excluded here for succinctness.

```plaintext
1: procedure ENERGY(X, B, E, t, l, w)
2:    ▷ Check if any people are out of the bounds of the simulation
3:    if any.out.of.bounds(X, l, w) then
4:        return ∞
5:    for i ← 1 : len(X) do
6:        ▷ Check if person overlaps any barriers
7:        if any.overlap(X[i], B) then
8:            return ∞
9:        ▷ Check if person overlaps any people
10:       if any.overlap(X[i], X[i + 1 : end]) then
11:          return ∞
12:    U_n ← 0
13:    for x in X do
14:        ▷ Get closest exit, do potential calculation, and add to summation
15:        e ← get.closest.exit(x, E)
16:        U_n ← U_n + \frac{1}{||x - t||} - \frac{1}{||x - e||}
17:    return U_n
```
2.4 Summary

In summary, to establish the safety-evaluation framework presented in this paper, we need the ability to simulate how people would flee a theater in response to a terrifying actor. To do so, we take inspiration from chemistry by using a heavily modified version of the Metropolis fluid dynamics algorithm. We arrive at a model that estimates TTE for a theater of any size, any number of people, and any amount of interior barriers.

3 Runtime Optimization

Even though this algorithm is theoretically fast, there are some factors that can create extensively prolonged computational run-times. Currently, our algorithm runs in about 13 seconds for our test theater design (described later). For industry and government usage, a shorter runtime would be optimal. The improved algorithm is for the number of people in the theater, as the energy calculation checks whether all people are in overlap with all other people. Runtime optimizations were implemented, specifically cell lists and parallelization, outlined within the supplemental appendix Section 8 at sub-header 8.3.

As Table 1 shows, these optimizations cut the runtime of a simulation by 37%.

<table>
<thead>
<tr>
<th>Algorithm 2</th>
<th>Algorithm 3</th>
<th>Parallelized Algorithm 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.35 s</td>
<td>10.04 s</td>
<td>7.78 s</td>
</tr>
</tbody>
</table>

Table 1: These are the average runtime calculated after 100 simulations using each algorithm.

4 Score Functions

4.1 Minimum Simulations for Accurate Approximations

At this point, we have two more major problems to solve. These issues are parallel to each other, and the solution to the first is necessary to solve the second:

1. First: How to set the number of iterations \( n \) and the other simulation parameters, \( kT \) and \( \sigma_x \), for optimal runtime.
2. Second: How to find the optimal exit position given a theater (dimensions, barriers, initial position of people).

On a deeper level, these problems are conceptually parallel. In the following two subsections, “Runtime Score” and “Exit Score,” one will notice many similarities. After all, both problems involve running the simulation and getting an accurate, stable value (i.e. the runtime for problem 1, and the number of accepted iterations it takes for the theater to empty out for problem 2) from the output. Because the simulation is a Monte Carlo algorithm, the values it produces will vary as random variables. So the task is to figure out how few times the simulation can be run to get a result with at least a 95% certainty of being within 99% of the true expected value of the value of interest. We can apply a method developed by Psutka and Psutka [PP15] (the co-authors share the same last name) to test the accuracy of sampling from a function like this to see that an average of 8 samples will give the 95% certainty of being within 99% of the true expected value. The mathematical derivation of this “8” value is elucidated in our supplemental appendix Section 8 at sub-header 8.2.

4.2 Runtime Score

We must start by optimizing the amount of time the program itself takes to run. Having the minimum simulations, 8, for an accurate estimate allows us to write our objective function for runtime. This function is incredibly simple: Given a \( kT \) and \( \sigma_x \), it will hold all other aspects of the simulation constant, run the simulation 8 times (each time collecting the runtime), fit a distribution with the maximum likelihood estimators, and finally, return the expected runtime from that distribution.

4.3 Exit Score

Similar to above, we can write an objective function for an exit vector. This is the most important part of the framework, as here, we determine how to best position the exits to minimize evacuation time, so that people can safely flee in an emergency. The public health benefits are self-explanatory: Saving lives is the ultimate good. Given a vector of exit positions \( e \), the function will hold all other aspects of the simulation constant, run the simulation 8 times (each time collecting the number of frames until the theater is empty), then fit a distribution with the maximum likelihood estimators, and finally, return the expected number from
that distribution. The output of this function is the Time To Exit (TTE) metric.

5 Optimization

Everything described up to this point has been independent of the theater being examined. Now, the theoretical algorithms described above will have to be run for each theater to optimize the \( n, kT \) and \( \sigma_x \) for the given theater, and then, we will use these parameters to minimize the runtime. Subsequently, we optimize the exit positions and get the ideal TTE for a given theater. The main complication surrounding this real-life application is actually performing these optimizations. Unlike the above theoretical scenarios in Section 4 where it was relatively simple to derive a likelihood function, the objective functions defined in Sections 4.2 and 4.3 for runtime and exit score seem impossible to elucidate in this more reality-centric scenario. This means the framework requires a different type of optimization, gradient free optimization, which can work without being able to take the derivative of the factor being optimized. The framework utilizes two different forms of gradient free optimization, the Nelder-Mead method and Bayesian Optimization, which are used to optimize runtime and exit position, respectively. To delve into the heavy mathematics of this method, see supplement Section 8.4.

6 Results

To understand how our framework could be used in a regulatory setting to determine a theater design’s safety rating (in terms of optimal exit placements to minimize TTE), we examine a simple theater as an example.

The theater shown in Figure 1 contains all the information the framework needs to evaluate the exit position: The dimensions of the theater, the positioning of all interior barriers, and an initial exit position (assumed to be the “reasonable” exit position necessary for the runtime optimization).

6.1 Runtime Optimization

The framework starts by setting the maximum number of iterations for each simulation \( n \). It does this by simulating the initial exit position 8 times, fitting a distribution, and selecting a minimum number of iterations that will mean 95% of good simulations will complete. For this theater, that \( n=346055 \).

Using this value of \( n \), the framework then optimizes runtime by running the simplex algorithm on the runtime score function. The initial simplex is set with \( kT = 0.05 \) and \( \sigma_x = 0.05 \). These initialization values were determined experimentally to promote good simplex convergence for this problem. The process of optimization takes approximately one hour, and cuts the simulation runtime by 57%.

<table>
<thead>
<tr>
<th>Pre-optimization</th>
<th>Post-optimization</th>
</tr>
</thead>
<tbody>
<tr>
<td>( kT = 0.05, \sigma_x = 0.05 )</td>
<td>( kT = 0.0033, \sigma_x = 0.04 )</td>
</tr>
<tr>
<td>7.78 s</td>
<td>3.36 s</td>
</tr>
</tbody>
</table>

Table 2: These are the runtime scores with the initial and optimized values of \( kT = 0.05 \) and \( \sigma_x = 0.05 \).

6.2 Exit Position Optimization

The framework then moves on to optimizing the exit position. For an in-depth mathematical view of how this process works and how the Bayesian Optimization algorithm explores the space of possible exit positions, see supplemental Section 8.3. The final exit position the Bayesian process achieves is illustrated in Figure 2.

7 Conclusion

In conclusion, we examine how this framework can be integrated into a legislative setting, utilizing it to create regulations that address one of the greatest public health harms currently faced by the United States: Mass shootings and other similar terror events. Given the exit score function and the optimal exit position, we can use a easily understandable comparison fraction (below) to
evaluate the original design’s exit positioning with respect to the optimal design’s exit positioning, and subsequently, we can decide whether to proceed with construction. For our comparison fraction, we have:

$$\frac{TTE_i - TTE_o}{TTE_o} \leq \Delta$$

(4)

Where $TTE_i$ is the TTE for the initially submitted plan, and $TTE_o$ is the TTE for the optimal solution derived through the Bayesian Optimization. $\Delta$ is the acceptability threshold set by a regulatory body. A reasonable $\Delta$ might be 0.50, which would allow construction companies to at most reduce the safety score of a theater by 50% of the ideal (perhaps for cost-cutting or aesthetic reasons) and still move forwards with the project. In this case, the $TTE_i = 2730$, and the $TTE_o = 1261$, so the fraction evaluates to 1.165, which would likely be deemed an unacceptably high level of divergence from the room’s optimally safe exit-placement design. Accordingly, we would give the architects this feedback, along with the optimal, computationally-derived exit positions. Subsequently, they could reevaluate their design to be better at keeping people safe from terror events.

Thus far, we have very specifically examined the case of optimizing exit position to minimize evacuation time, but the beauty of this framework is that it could be extended to adjust every quantifiable aspect about the design of the theater: The spacing of the seats, the angle of the rows of seats, the number and spacing of aisles, etc. These all can be evaluated, modeled, optimized, and re-evaluated to generate a TTE-based safety-score evaluation. Obviously, in this paper, we do not intend to belittle the training and expertise of professional architects: There are many economic, aesthetic, and safety factors that go into the design of buildings. However, now we have the ability to specifically and quantitatively assess whether a room is easy-to-exit in the case of danger, and perhaps more importantly, generate a modified room design that minimizes the “Time to Exit” using a rigorous, mathematics-based model. Considering the clear-cut nature of this TTE score regulatory test, incorporating our threshold into the construction-focused legislative branches seems like a rational step in building safer new buildings. By saving lives in crisis scenarios, the ultimate goal of any harm mitigation initiative, our TTE-based optimization of room construction is a great boon for the field of design-based public health.

8 Supplemental Mathematical Appendix

8.1 Runtime Optimization

8.1.1 Cell Lists

Cell lists are a way of breaking up the simulated space into equally sized blocks, and then only computing interactions between particles in adjacent cells. This means that especially for simulations with many particles, the number of required calculations is significantly lower. See Figure 3. The framework can make use of this idea, even though the situation is not exactly the same as the one Allen describes.[AT89]

The framework will similarly use cell lists to break up the simulated theater, but because our methodology assumes particles have no interaction with each other, it doesn’t go as far the molecular dynamics cell list implementations. All our cell list strategy has to account for is a given particle’s interactions with other “hard” objects in the cell(s)—noting that particles can be in multiple cells—that the given particle is occupying.

There’s a lot that can be pre-computed using this implementation. First, note that the barriers in the respective cells will not change: After all, barriers are intrinsically in a fixed position for a given room. Secondly, the cells that neighbor any given cell will be constant, so this can also be pre-computed. Finally, we can use pre-computation with regards to the static perimeter cells. The only variables within cell lists that will change are what people are occupying what cells. Refer to Algorithm 3 to see the implementation of the energy function using the framework’s modified cell list strategy.
8.2 Minimum Simulations for Accurate Approximations

8.2.1 Determining Appropriate Distributions

The two variables of interest here are the runtime and the number of frames until the theater is empty. The first step to providing the accuracy above is understanding how these two variables vary.

From Figure 4, it is clear that both of these values vary as Log-Normal distributions.

8.2.2 MLE for the Log-Normal Distribution

The way the framework is going to get these proven bounds on the value of interest is by fitting the Log-Normal distribution for some number of samples. The next step is to derive the $\mu$ and $\sigma^2$ that maximize the log-likelihood function of the Log-Normal distribution

$$X_i \sim \text{LogNormal}(\mu, \sigma^2)$$  \hspace{1cm} (5)

$$f_{X_i}(x|\mu, \sigma^2) = \frac{1}{x\sqrt{2\pi}\sigma^2} e^{-\frac{(\log(x) - \mu)^2}{2\sigma^2}}$$ \hspace{1cm} (6)

First, the likelihood function, given $X=\{X_1, X_2, ..., X_n\}$, is the product of the probability densities of each $X_i$:

$$L(\mu, \sigma^2 | X) = \prod_{i=1}^{n} f(X_i|\mu, \sigma^2)$$  \hspace{1cm} (7)

$$= \prod_{i=1}^{n} \frac{1}{X_i\sqrt{2\pi}\sigma^2} e^{-\frac{(\log(X_i) - \mu)^2}{2\sigma^2}}$$ \hspace{1cm} (8)

$$= (2\pi\sigma^2)^{-\frac{n}{2}} \prod_{i=1}^{n} \frac{1}{X_i} e^{-\frac{(\log(X_i) - \mu)^2}{2\sigma^2}}$$ \hspace{1cm} (9)
Next, take the log of the Eq. (8) to get $L(\mu, \sigma^2 | X)$:

\[
L(\mu, \sigma^2 | X) = \log \left( 2\pi \sigma^2 \right)^{-\frac{n}{2}} \prod_{i=1}^{n} \frac{1}{X_i} e^{-\frac{(\log(X_i) - \mu)^2}{2\sigma^2}}
\]

\[= -\frac{n}{2} \log(2\pi \sigma^2) - \sum_{i=1}^{n} \left[ \log(X_i) + \frac{(\log(X_i) - \mu)^2}{2\sigma^2} \right] \tag{10}\]

\[= -\frac{n}{2} \log(2\pi \sigma^2) - \sum_{i=1}^{n} \left[ \log(X_i) + \frac{\log(X_i)^2}{2\sigma^2} - \frac{2\log(X_i) \mu}{\sigma^2} + \frac{\mu^2}{2\sigma^2} \right] \tag{11}\]

\[= -\frac{n}{2} \log(2\pi \sigma^2) - \frac{n\mu^2}{2\sigma^2} - \sum_{i=1}^{n} \left[ \log(X_i) + \frac{\log(X_i)^2}{2\sigma^2} - \frac{\log(X_i) \mu}{\sigma^2} \right] \tag{12}\]

Now taking the partials, first with respect to $\mu$:

\[\frac{\partial L}{\partial \mu} = -\frac{n\mu}{\sigma^2} \sum_{i=1}^{n} \frac{\log(X_i) \mu}{\sigma^2} \tag{15}\]

Setting this to zero and solving, then:

\[0 = -\frac{n\hat{\mu}}{\sigma^2} + \sum_{i=1}^{n} \frac{\log(X_i)}{\sigma^2} \tag{16}\]

\[n\hat{\mu} = \sum_{i=1}^{n} \log(X_i) \tag{17}\]

\[\hat{\mu} = \frac{\sum_{i=1}^{n} \log(X_i)}{n} \tag{18}\]

Next taking the partial with respect to $\sigma^2$:

\[\frac{\partial L}{\partial \sigma^2} = -\frac{n}{2\sigma^2} - \sum_{i=1}^{n} \frac{(\log(X_i) - \mu)^2}{2(\sigma^2)^2} \tag{19}\]

Setting this to zero and solving, then:

\[0 = -\frac{n}{2\hat{\sigma}^2} + \sum_{i=1}^{n} \frac{(\log(X_i) - \hat{\mu})^2}{2(\hat{\sigma}^2)^2} \tag{20}\]

\[\frac{n}{2\hat{\sigma}^2} = \sum_{i=1}^{n} \frac{(\log(X_i) - \hat{\mu})^2}{2(\hat{\sigma}^2)^2} \tag{21}\]

\[\hat{\sigma}^2 = \frac{\sum_{i=1}^{n} (\log(X_i) - \hat{\mu})^2}{n} \tag{22}\]

\[\hat{\sigma}^2 = \frac{\sum_{i=1}^{n} (\log(X_i) - \frac{\sum_{i=1}^{n} \log(X_i)}{n})^2}{n} \tag{23}\]
So the maximum likelihood estimators for the Log-Normal distribution are:

\[
\hat{\mu} = \frac{\sum_{i=1}^{n} \log(X_i)}{n} \\
\hat{\sigma}^2 = \frac{\sum_{i=1}^{n} (\log(X_i) - \frac{\sum_{i=1}^{n} \log(X_i)}{n})^2}{n}
\]  

(24)  

(25)

### 8.2.3 Minimum Samples for Accurate Log-Normal MLE

Using the methodology developed by Psutka and Psutka [PP15] for the normal distribution, lower bounds can be derived for the number of samples for a given certainty of a given confidence of accurate maximum likelihood estimates. It is relatively easy to adapt their methods to the Log-Normal distribution.

**Expected Log-Likelihood**

First, we need a way to evaluate the accuracy of a likelihood estimate. The best way to evaluate this accuracy would be to ask: Given the true parameters of \( \mu \) and \( \sigma \), what would the value of the log-likelihood function be? In short, the answer is the expected log-likelihood function. The expected log-likelihood function is defined as:

\[
E[L] = \lim_{N \to \infty} \left( \frac{1}{N} \sum_{i=1}^{N} L(\mu, \sigma^2 | X_i) \right)
\]

(26)

\[
= \lim_{N \to \infty} \left( \frac{1}{N} \sum_{i=1}^{N} \left( -\frac{n}{2} \log(2\pi \sigma^2) - \frac{\mu^2}{2\sigma^2} - \frac{1}{2} \sum_{i=1}^{N} \left[ \log(X_i) + \frac{\log(X_i)^2}{2\sigma^2} - \frac{\log(X_i)\mu}{\sigma^2} \right] \right) \right)
\]

(27)

\[
= -\frac{n}{2} \log(2\pi \sigma^2) - \frac{\mu^2}{2\sigma^2} - \lim_{N \to \infty} \left( \frac{1}{N} \sum_{i=1}^{N} \left[ \log(X_i) + \frac{\log(X_i)^2}{2\sigma^2} - \frac{\log(X_i)\mu}{\sigma^2} \right] \right)
\]

(28)

\[
= -\frac{n}{2} \log(2\pi \sigma^2) - \frac{\mu^2}{2\sigma^2} - \sum_{i=1}^{N} \left[ \lim_{N \to \infty} \frac{1}{N} \sum_{i=1}^{N} \log(X_i) + \frac{1}{2} \lim_{N \to \infty} \sum_{i=1}^{N} \frac{\log(X_i)^2}{2\sigma^2} - \frac{\log(X_i)\mu}{\sigma^2} \right]
\]

(29)

\[
= -\frac{n}{2} \log(2\pi \sigma^2) - \frac{\mu^2}{2\sigma^2} - \sum_{i=1}^{N} \left[ E[\log(X_i)] + \frac{E[\log(X_i)^2]}{2\sigma^2} - \frac{\mu E[\log(X_i)]}{\sigma^2} \right]
\]

(30)

Now with the expected log-likelihood in terms of the expectation of various functions of \( X \), those expectations must be solved. Starting with the expectation of \( \log(X) \), which is trivial, by the definition of the Log-Normal distribution:

\[
\log(X_i) = Y \\
E[\log(X_i)] = E[Y] \\
\sim N(\mu, \sigma^2)
\]

(31)  

(32)

Similar logic is applicable to the derivation of the expectation of \( \log(X)^2 \):

\[
Var(Y) = E[Y^2] - (E[Y])^2
\]

(33)

\[
E[Y^2] = Var(Y) + (E[Y])^2
\]

(34)

\[
E[Y^2] = \sigma^2 + \mu^2
\]

(35)

\[
E[\log(X_i)^2] = \sigma^2 + \mu^2
\]

(36)

Returning to the expected log-likelihood function:
Evaluating Likelihood Accuracy

Now setting aside for a moment this expected value for log-likelihood, the fraction below will motivate a means for evaluating the accuracy of any estimated $\hat{\mu}$ and $\hat{\sigma}^2$:

$$\frac{L(\hat{\mu}, \hat{\sigma}^2|X)}{E[L(\mu, \sigma^2|X)]} \geq \beta$$

(41)

This fraction puts the likelihood using the maximum likelihood estimators for the Log-Normal over the expected value of the log-likelihood function, given the true $\mu$ and $\sigma^2$. This is useful, because we now have a fraction that will range between 0 and 1, but that will asymptotically approach 1 as the number of samples $n$ used in the MLE of $\mu$ and $\sigma^2$ approaches infinity. This means the value $\beta$ is a proxy for estimation accuracy. It is this value we will set to ensure we get within 99% of the true expected value of the value of interest.

Taking the log of Eq. (40) and rearranging so that we have a less than inequality we have:

$$log\left(\frac{L(\hat{\mu}, \hat{\sigma}^2|X)}{E[L(\mu, \sigma^2|X)]}\right) \geq log(\beta)$$

(42)

$$L(\hat{\mu}, \hat{\sigma}^2|X) - E[L(\mu, \sigma^2|X)] \geq log(\beta)$$

(43)

$$E[L(\mu, \sigma^2|X)] - L(\hat{\mu}, \hat{\sigma}^2|X) \leq -log(\beta)$$

(44)

Minimum Samples for Accurate MLE

We will start by defining $\hat{\mu}$ and $\hat{\sigma}^2$ as the estimates resulting from $i$ random variables in $Y = \{Y_1, Y_2, \ldots, Y_n\}$. We will also define $Z = \{Z_1, Z_2, \ldots, Z_k\}$ where $k$ will be a large integer. $Y$ and $Z$ are drawn from the same distribution with parameters $\mu$ and $\sigma^2$.

This allows us to define:

$$i^*_\beta = \min_i \{E[L(\mu, \sigma^2|Z)] - L(\hat{\mu}_i, \hat{\sigma}^2_i|Z) \leq -log(\beta)\}$$

(45)

The estimate $i^*_\beta$ is by simulating the above procedure. This can be seen in Algorithm 4.
It is clear from Figure 5 that \( i^* - 3: \text{Geo}(p) \). This also makes sense. There is some probability that the MLE estimate fits the distribution well with only \( i \) samples: Each iteration we increase the number of samples, running the same experiment and stopping after getting a success. A geometric random variable is defined as the number of experiments before a success, so it makes sense that it would accurately capture this phenomenon. Here, too, we need to fit this distribution to get the value of \( p \). It is therefore necessary to derive the maximum likelihood estimator for the Geometric distribution:

\[
L(p|X) = \prod_{i=1}^{n} (1 - p)^{X_i-1} p 
\]

\[
L(p|X) = p^n (1 - p)^{\sum_{i=1}^{n} X_i - n} 
\]

\[
\mathcal{L}(p|X) = n\log(p) + (\sum_{i=1}^{n} X_i - n)\log(1 - p) 
\]

\[
\frac{\partial \mathcal{L}}{\partial p} = \frac{n}{p} - \frac{\sum_{i=1}^{n} X_i - n}{1 - p} 
\]
Setting the partial to zero, and solving for $\hat{p}$:

\[
0 = \frac{n}{\hat{p}} - \frac{\sum_{i=1}^{n} X_i - n}{1 - \hat{p}}
\]

\[
\hat{p} = \frac{n}{\sum_{i=1}^{n} X_i}
\]

This estimates the distribution of $i^{*}_\beta - 3$ very well, as is clear from Figure 5, meaning that $\hat{p} = 0.5719$ is a good estimation. Using this value, it is now possible to derive the minimum number of samples that will guarantee 95% certainty of being within 99% of the true expected value:

\[
P(i_{\beta} \leq i_{\text{min}}) \geq 0.95
\]
\[
1 - (1 - p)^{i_{\text{min}} - 1} \geq 0.95
\]
\[
(1 - p)^{i_{\text{min}} - 1} \geq \frac{1}{20}
\]
\[
i_{\text{min}} = \log\left(\frac{1 - p}{20} + 1 - p\right)
\]

This value is, of course, 3 short of the actual value, so adding three and rounding up, we conclude that 8 samples is the minimum required to have 95% certainty of our MLE estimates being 99% accurate to the true distribution.

8.3 Optimization

8.3.1 Runtime

There are several assumptions that underpin the optimization of runtime. First, the optimal values for $D_1$, $D_2$, and $D_3$ are at least relatively robust if not entirely independent of the exit position. Were this not true, it would be impossible to optimize these runtime variables. The second assumption is that we have a “reasonable” solution with which to do the optimization. This will likely be a human selected exit vector that does have to be completely optimal, but cannot be atrociously bad (there will always be some exit positions where people never leave, or would take so long to escape that it isn’t worth the simulation time). This is necessary, or else, it would be relatively impossible to do the runtime optimization.

Setting the number of iterations

The first value to set is $N$, because it will not require any gradient free optimization. It is, at this point, important to draw the distinction between this value, the runtime, and the frames until we have an empty theater. The runtime is the number of real-time seconds the algorithm requires to run. The frames until we have an empty theater is the number of accepted moves before all people have evacuated the theater. The number of iterations is the total number of moves attempted, both accepted and rejected. The value $i_{\text{min}}$ is the maximum number of iterations before the simulation stops. This cutoff is necessary especially when dealing with non-“reasonable” solutions.

How will the framework optimize $N$? It will use the now-familiar technique outlined throughout Section 4: Eight runs will be conducted and the total number of moves required before all people escape will be collected. The iterations vary as a Log-Normal, the same as runtime and frames. A distribution will be fit to this data using MLE.

Nelder-Mead

The Nelder-Mead method attempts to find a global minimum for some real-valued function over some number of variables. In this case, it will be minimizing the runtime score function with respect to $D_1$ and $D_2$. For higher dimensional problems Nelder-Mead never really converges, but for the simple case of 2 variable optimization (assuming a mono-modal function), it is a very efficient solution.[NM65]

8.3.2 Exit Position
For optimizing exit position, the Nelder-Mead algorithm will not work. If we are optimizing exit position for a stadium that holds thousands or tens of thousands, then there will be dozens of exits and Nelder-Mead will never converge. Even for a small number of exits, it is very unlikely exit position is a mono-modal surface: Consider a simple, symmetrical theater with two exits—the exit score for this function is at least bi-modal, as at the optimal positions, the exits can be flipped to achieve the same peak at a different input point.

This means the framework must use some other gradient-free optimization algorithm, preferably one that requires minimal iterations, as the exit score is computationally expensive to evaluate. This leads us to Bayesian Optimization.

The way Bayesian Optimization works is by treating the objective function as a random function (note: the exit score is a random function). If the objective is a random function, then we can place a prior over the domain of the random function. This prior is designed to capture our belief about the behavior of the function. The function is then evaluated for some number of initial randomly chosen points, and these points are used to update the prior in Bayesian fashion, generating a posterior distribution. This posterior distribution is then used to maximize the acquisition function in order to select the next point to evaluate.[SLA12]

References


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