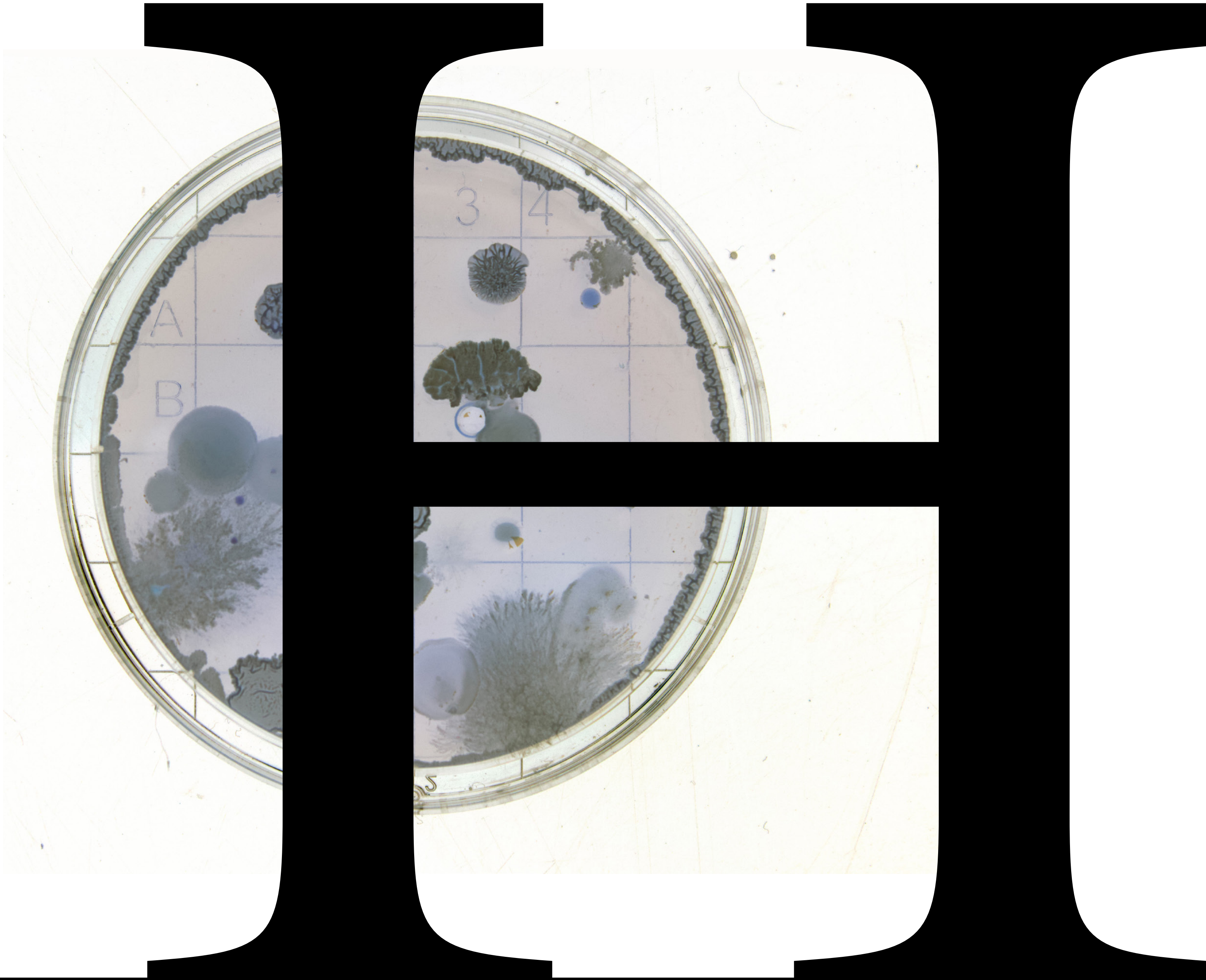
HEALTH SCIENCE INQUIRY

VOLUME 11 | 2020

DETERMINING HEALTH

Where society, environment, and human biology intersect



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CONTENTS

VOLUME 11 | 2020

NEWS

SPOTLIGHT ON CAREERS

ASK AN EXPERT

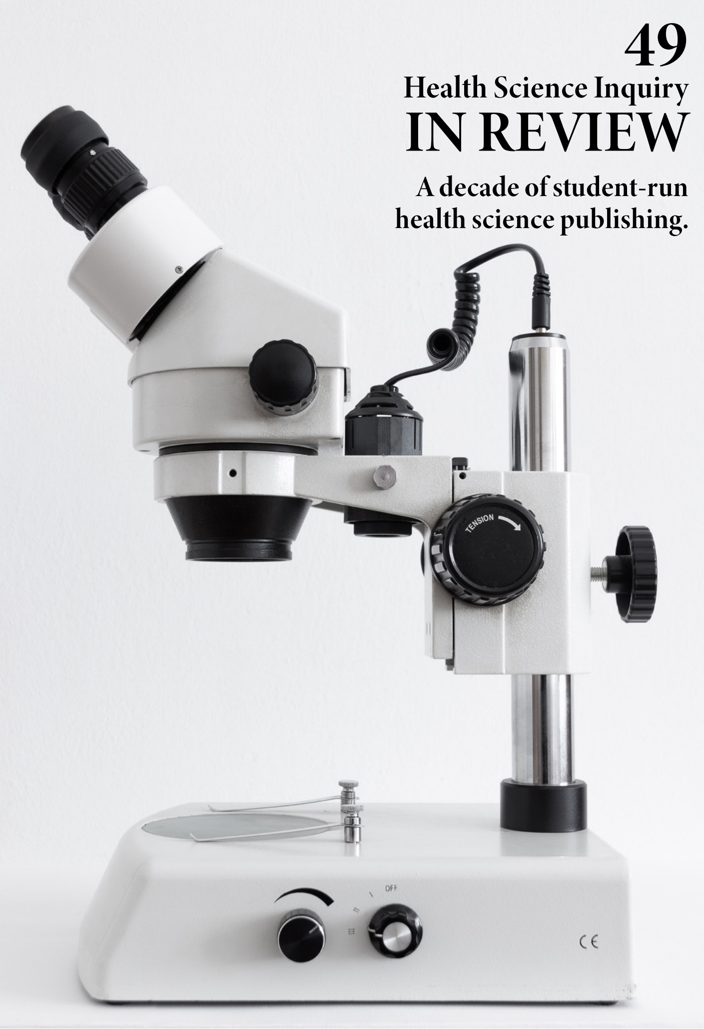
INTERVIEW

PROFILES

CONTENTS

VOLUME 11 | 2020

FEATURES

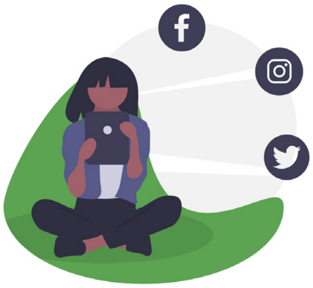


49

Health Science Inquiry

IN REVIEW

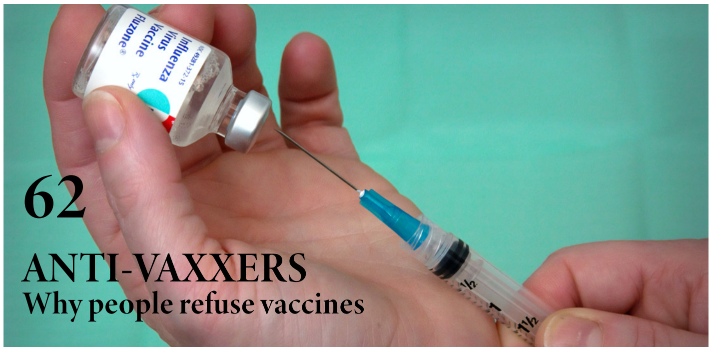
A decade of student-run health science publishing.



56

When Social Media Met Nutrition

How influencers spread misinformation, and why we believe them



62

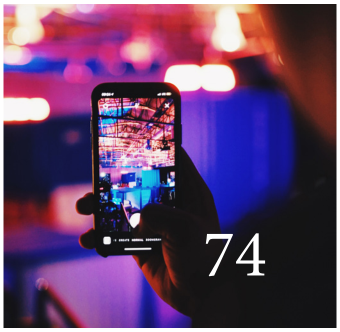
ANTI-VAXXERS

Why people refuse vaccines

68

The ART of Science Storytelling

SHORT FICTION



74

Blue Elephant

“Confused, he stared at his phone, then put it down and started looking around...”

78

Koko

“Growing up where I’m from, people didn’t dream much of anything...”

PHOTO ESSAY

82

A Week in the life of a Geneticist

CONTENTS

VOLUME 11 | 2020

ARTWORK

4

Unsustainable Development, A Confrontation
Katlyn C. Richardson

This composition — hand drawn with graphite — represents the intersection between the environment and human health. The backdrop consists of a familiar scene of skyscrapers and winding highways, which fill the lower landscape. The buildings reach towards the centre of the image surrounded by an eclipse of haze/pollution. From this haze appears nothing but six eyes. These eyes belong to some of the main classes of animals (clockwise left to right: amphibian, fish, reptile, bird, mammal) as well as humans, and represent our natural environment and human health. It is my intention that placing their fading gaze above the veneer of a dim and grey cityscape leads to unsettling imagery which confronts the viewer in hopes for a less exploitative, sustainable future.

Katlyn is currently a PhD student at the University of British Columbia where she studies the role of granzymes in skin health and disease.

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9

More than Meets the Eye
Nancy V. Wu

Healthcare professionals can use imaging techniques such as X-rays to determine a "biological" cause of illness. But what if the "other" determinants of a person's health could be revealed as well? This artwork contemplates such a possibility.

Nancy is completing her MSc in Epidemiology at McGill University and will study medicine at the University of Toronto.

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ON THE COVER

Disconnected | Michelle Ku

This digital illustration alludes to the bridges that researchers are building between three contrasting areas of daily life: healthcare, the environment, and technology. On the surface level, we only see the beauty of nature; however, below the murky water lies potentially harmful constituents surrounding the submerged Vitruvian Man, representing health and medicine. The digital nodes represent the technological efforts to connect health care and the environment.

Michelle is currently completing a MSc in Nutritional Sciences at the University of Toronto. Michelle specializes in microbiology and molecular biology and her research focuses on the effects of flaxseed components on the gut microbiome and estrous cycle. Aside from academia, Michelle is a science communicator and freelance digital illustrator. You can find her work at on social media platforms such as Instagram and Twitter @mypetcephalopod.

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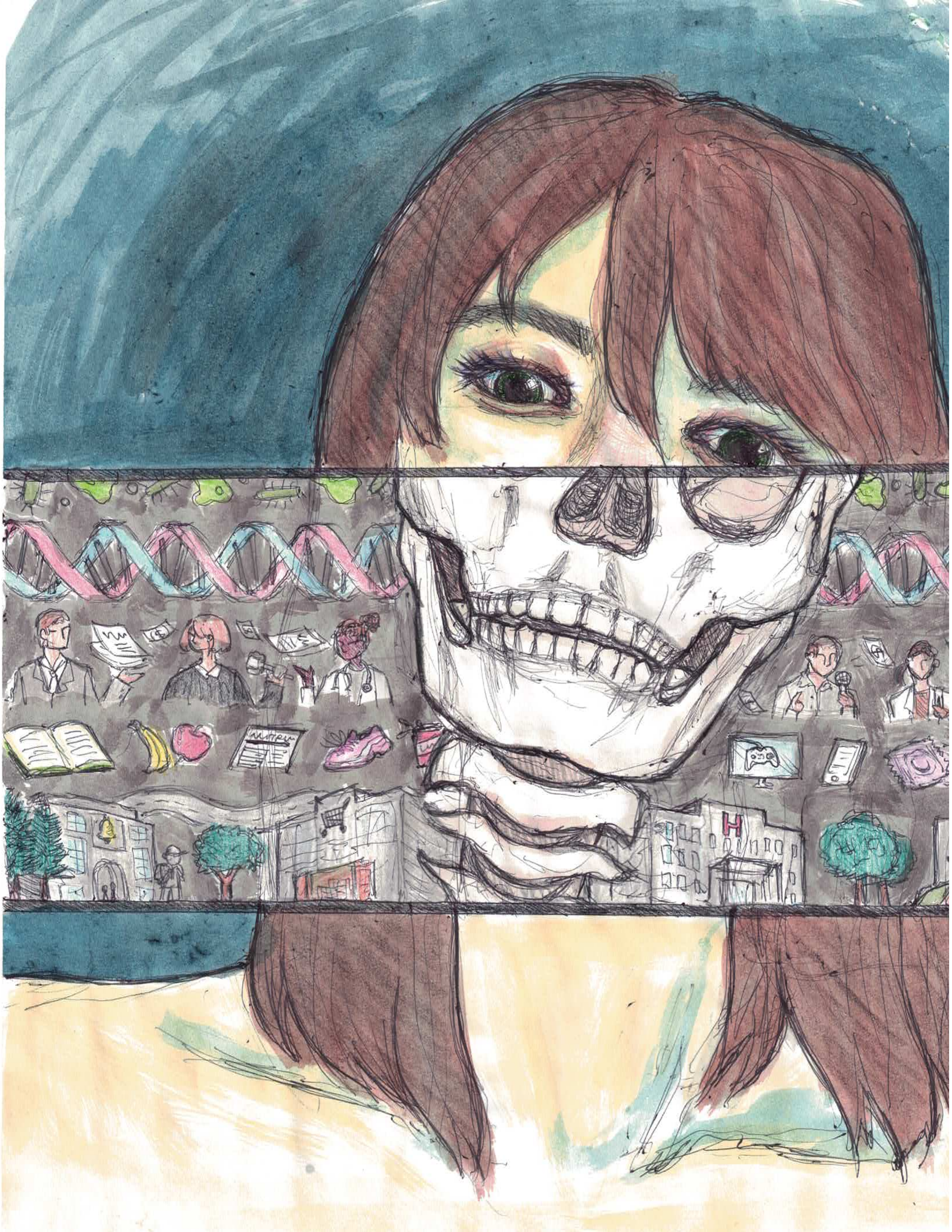
CONTENTS

RESEARCH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HEALTH

Autism spectrum disorders may be linked to air pollution

Mouse studies reveal prenatal diesel exhaust exposure can render offspring vulnerable to autism spectrum disorder-like symptoms.

BY HEATHER GERRIE

The prevalence of autism spectrum disorder (ASD) has increased dramatically, rising from a diagnostic rate of one in every 10,000 children during the 1970s to one in 66 by 2018 [1].

Rising alongside the number of ASD cases are levels of air pollution. Research from neuroscientist Staci Bilbo at Duke University suggests the two may be linked. According to Bilbo, the surge in ASD cases strongly points to an environmental factor.

ASD is characterized by impairments in communication and stereotypic, repetitive behaviours. Though genetics – and a growing recognition of the disorder – account for a portion of cases identified each year, Bilbo says there are more cases than can be accounted for.

"All the genetic studies that have been done can only explain roughly 50 per cent of the cases of ASD," Bilbo said. "There has to be some other culprit."

Air pollution is the third leading cause of mortality worldwide and can affect us even before birth [2]. Maternal exposure to high levels of air pollution during pregnancy is linked to negative health outcomes in offspring, including premature birth and childhood asthma [2]. Diesel exhaust, which is the primary toxic component of air pollution, is particularly relevant. The levels of diesel exhaust at the time and place of birth is one of the strongest and most consistent predictors of ASD [3].


photo credit - Patrick Hendry

Prenatal exposure to air pollution may increase offspring risk of developing ASD.

According to Bilbo, the intersection between air pollution and ASD can be found at the level of the brain's immune system, which functions as the interface with the environment. In the brain, the immune system consists of microglial cells. Known as the watchdogs of the brain, microglia constantly survey the health of their environment and are the first responders to disruptions such as trauma, disease, and inflammation [3].

Microglia also play a critical role in wiring the brain during development. They assist with connecting developing neurons – the messenger cells of the nervous system – and removing unnecessary or incorrect connections [4].

During pregnancy, maternal immune activation from exposure to inflammatory stimuli – such as air pollution – can cause hyperactive and abnormal immune function in developing offspring. Hyperactive microglia release neurotoxins and inflammatory mediators which affect neuron function and survival.

"The reason that we think

microglia are particularly important in autism, is that we increasingly think autism is of prenatal origins," Bilbo said. "Microglia colonize the brain very early in development, so if you had an immune perturbation during pregnancy, this would alter microglial function, and therefore brain development."

If air pollution alone could induce ASD, all babies born in urban areas with high diesel exhaust exposure would be at high risk. However, Bilbo says the reality is more complicated, likely involving multiple genetic and environmental factors interacting with pollutants to result in ASD.

> *"We need interventions that don't rely on people packing up and moving to the countryside."*

Initial research from Bilbo's lab found that offspring of pregnant mice exposed to diesel exhaust particles throughout gestation had overly activated microglia, but no apparent behavioural abnormalities [4,5]. However, Bilbo noted a growing body of literature suggesting that psychological stress during pregnancy affects offspring brain development. Both stress and exposure to pollutants act on a common biological pathway – the immune system [4].

Bilbo then combined prenatal exposure to diesel exhaust particles with a psychological stressor, such as the restriction of nesting material during the final week of pregnancy. In addition to the predicted abnormal microglia, offspring now displayed behavioural and social deficits comparable to the ASD symptoms seen in humans [5,6].

The male offspring in these studies were more susceptible to developing ASD-like symptoms than females [6] In humans, males are diagnosed with ASD four times more than females [1].

Bilbo's findings agree with the 'two-hit model' theory, where an initial 'first hit' to the immune system – such as prenatal exposure to air pollution – renders the developing immune system more reactive if a 'second hit' occurs [4]. In the case of ASD, if the first hit is an environmental toxin, the second hit is likely a social toxin.

"In humans, it's not just pollutant levels, ASD is mediated by something else as well, which we very much believe now to be socioeconomic status and social stress," Bilbo said. Meaning that a 'double hit' of air pollution and maternal exposure to psychological stressors, such as violence or poverty, increases offspring risk for ASD.

A study from the University of California investigating whether traffic-related pollution was related to ASD rates in Los Angeles found that amongst families living near highways, mothers from low socioeconomic backgrounds were more likely to have children with ASD [7]. The study reported that vulnerability, poverty and stress in mothers likely exacerbated the effects of pollution exposure during pregnancy.

"The people who are exposed to the highest levels of environmental toxins are also those that generally have the fewest resources to try and do anything about it," Bilbo said. "It becomes an environmental justice issue, and at that point we need policy change. We need interventions that don't rely on people packing up and moving to the countryside."

It is difficult to show in human studies that an effect is more than just correlative, but "if we can show causality in a mouse, then we can demonstrate to the people who are making policy decisions that there is a real, causal mechanism," Bilbo said.

Bilbo hopes that as we are forced to rely less on fossil fuels, the air quality in cities will improve. Even now, the transition to greener technology may begin to decrease risk of ASD in urban areas.

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MENTAL HEALTH

Intergenerational connection between environment and mental health

BY TAMMY LU

Mental health is a complex and stigmatized topic. While often used as an umbrella term to include any aspect affecting mental wellbeing, it also extends to more serious clinical and psychiatric conditions including depression, anxiety, and substance use disorders. A World Health Organization report in 2012 found that psychiatric disorders alone make up 13 per cent of the disease burden in the world [1,2]. While the cause of many psychiatric disorders remain difficult to define, new research suggests that many of them may have environmental and intergenerational roots.

Stephen Gilman, is the senior investigator and chief of the social and behavior sciences branch at the National Institute of Health in the U.S. His research focuses on how social determinants such as race and socioeconomic status contribute to mental disorders. Gilman has taken a developmental and life-course approach to understanding the factors in early life that can influence the onset and subsequent recurrence of psychiatric disorders in adults.

In his study of Finnish evacuees from World War II, Gilman found that parental exposure to mental disorder presents as a risk factor that can be passed onto the next generation.

The Finnish evacuation program of World War II was responsible for the evacuation of Finnish children to Sweden in order to protect them from war-time dangers such as armed conflict, malnutrition, and the deaths of family members. These evacuated children were fostered by Swedish families and were returned to Finland at the end of World War II. Using census data, hospitalization and evacuee records, Gilman compared hospitalization rates for psychiatric disorders amongst evacuated children and their non-evacuated siblings. Doing so, he found that evacuated women were 2.19 times more likely to be admitted to a hospital for a psychiatric disorder than their non-evacuated siblings [3,4].

In a follow up study, Gilman compared the children of the female evacuees to the children of their non-evacuated siblings. He found that daughters of previously evacuated women were 2.04 times more likely to be hospitalized for psychiatric disorders, and 4.68 times more likely to be hospitalized for mood disorders compared to their cousins, whose mothers were not evacuated. Surprisingly, Gilman found no correlation between evacuated fathers and their children [5].

Findings from these two studies suggest that children who face parental separation, and other stressors of war, may be at an increased risk for the development of psychiatric disorders, with that risk carrying onto the next generation, particularly in younger females. Gilman's results also highlight the protective effects of foster care programs on depression, particularly for younger boys. But it's not yet clear whether risks for psychiatric disorders were inherited biologically or whether these risks were due to nurture and the environment in which these children grew up. There's undoubtedly much more research needed to understand how environmental risk factors for psychiatric disorders may be passed down through generations, but the risks themselves are clear.

Stephen Gilman **@GilmanStephenE**

Gilman has also studied the effects of economic hardships on mental health. By comparing states and neighborhoods with high- and low-income inequality, Gilman found that women and girls were more likely to experience depressive symptoms in areas with high income inequality than those in other areas [6, 7]. Although it has not been studied whether these risks are heritable, income inequality, much like parental separation, can be viewed as a form of hardship that has the potential to impact the mental health of subsequent generations. With the large number of exposures affecting mental health outcomes and likely affecting more than one generation, it is important to reduce mental health risk exposure as much as possible, especially in children whose brains are still developing. Why girls are at a higher risk of developing mental disorders than boys from exposure to hardships such as parental separation and low socioeconomic status is not known. Ongoing research will study the gender differences in developing mental health disorders.

“It has been shown that even though treatments for mental disorders aren’t perfect, they can still be very effective for many individuals.”

Research will always yield more questions to be answered, but Gilman says, “There is a lot we know already that we can implement, such as increasing the access to resources for treatment of mental health problems.” This is not a surprise as a report by the WHO in 2011 outlines that less than two dollars per person is spent on mental health world-wide [2]. According to Gilman, studies increasingly show large populations of individuals suffering from psychiatric disorders that are not being treated. Even within high-income countries, 30-50 per cent of people are not receiving treatment for psychiatric disorders, with that number increasing to 76 and 85 per cent in low- and middle- income countries, respectively [2].

“[There’s] a lot to be said for screening and recognizing mental health problems,” Gilman added, particularly with suicide and depression. In a study that examined individuals who completed suicide in the U.S., 83 per cent sought health care, but almost half (approximately 41.5 per cent) did not receive a mental health diagnosis, and only 24 per cent received a diagnosis four weeks prior to death [8]. With better diagnostic methods and tools, interventions can be taken to prevent unfortunate consequences of psychiatric disorders, such as suicide. In discussing the importance of research into the development of psychiatric disorders, Gilman highlights “the importance of asking about access to care.”

“Population studies of psychiatric disorders show that a substantial proportion of individuals who have a psychiatric disorder have not been treated,” Gilman said. “It has also been shown that even though treatments for mental disorders aren’t perfect, they can still be very effective for many individuals; therefore, increasing access to treatment is important.”

Gilman explained that issues of diagnosis and access to mental health treatment becomes even more complex when it comes to children, because they are dependent on parents to “initiate treatment.” Exposure to risk factors during “sensitive periods” of childhood are particularly impactful to a child’s development as their brain is still plastic. Gilman argues that protecting a child from these risks is more efficacious than changing behavior later in life, as interventions are also likely to be more effective in early childhood.

Environmental factors such as parental separation and economic inequality represent a small fraction of the factors that can increase the risk of developing a psychiatric disorder. Exposure to a risk factor during childhood has the potential to increase the risk of psychiatric disorders later in life, and can potentially be passed on to the next generation. Although how this occurs is not yet clear.

Nonetheless, a point Gilman frequently reiterates is the importance of “reducing exposure of children to very economically adverse situations, and strengthening or providing resources for identifying mental health problems early and improving access to treatment.”

When it comes to the treatment and management of psychiatric disorders, Gilman says he hopes for a cure to be “on the horizon.”

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Protecting the placenta

How your environment may negatively impact the lifeline of your baby.

BY MARIYAN J. JEYARAJAH
STEPHEN J. RENAUD
DANIEL B. HARDY
GENEVIEVE EASTABROOK
PEEYUSH K. LALA

Pregnancy outcomes can be influenced by numerous factors including drug use, viral infection, and socioeconomic status.

photo credit - Nynne Schroder

Pregnancy can alter practically everything about an expectant mother's life – from what they wear, to what they eat, to even physiological changes in the shape and size of their brain. All these exciting changes are simply the pregnant mother's response to welcome their new child.

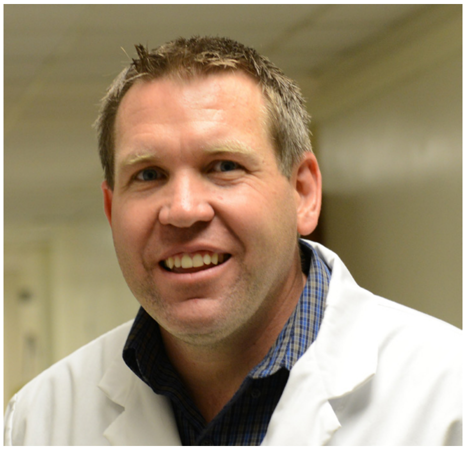
In addition to their baby, another incredible aspect to pregnancy is the growth of a completely new organ: the placenta. The placenta acts as the baby's lifeline and provides the baby with all necessary nutrients and oxygen. The placenta is responsive to its surrounding environment and can serve as a living barrier, adapting and responding to negative environmental factors that can jeopardize the health of the baby [1]. However, there are limits to the placenta's ability to adapt, and therefore, understanding the everyday environmental risks that can harm both placenta and baby can help ensure the proper development of the child.

One of the leading environmental factors resulting in poor pregnancy outcomes is drug use. Currently in Canada, one in five women report marijuana use as a common activity during pregnancy [2]. With the recent legalization of marijuana in Canada, this is a troubling statistic, as not much is known about the effects of cannabis on pregnancy. Daniel Hardy, an associate professor of physiology and pharmacology at Western University advises against marijuana intake during pregnancy. A recent study from his lab found that exposure to Δ9-THC, the psychoactive component of cannabis, can result in poor placental outcomes [2]. Pregnant rats given Δ9-THC showed greatly reduced placental function and transfer of nutrients and oxygen to the baby. Moreover, Δ9-THC resulted in the rats giving birth to low-weight, or growth-restricted babies, an outcome often associated with an increased risk of cardiovascular and metabolic disorders in humans [2,3].

Another key environmental factor that can negatively impact the health of a baby is poor nutrition. In Canada, approximately 2.5 million women are classified as low socioeconomic status [4]. These individuals often face greater challenges in obtaining nutritious foods and frequently find themselves consuming high carb, high fat diets. This can have damaging effects on the placenta and can cause the placenta to mature too quickly [5]. When placentas mature rapidly, they age prematurely, and produce an unusually low oxygen atmosphere. This environment can result in fetal growth restriction.

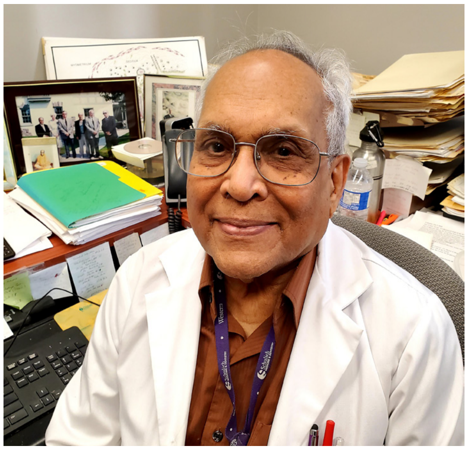
There are other environmental factors that can harm the placenta and baby that lie outside the control of the mother, for example, viral infection. Zika virus is most prevalent in countries with warm climates. However, due to warming temperatures associated with climate change, the range of this virus has vastly expanded. Mosquitos carrying Zika have traveled from Africa and have infected pregnant mothers living all over the world, including the Americas and Europe. In the instance of Zika infection, after being bit by a mosquito carrying Zika, the virus has been shown to cross the placental barrier, alter oxygen transport activity, and result in children with microcephaly, a condition in which the brain is not correctly developed [6]. Influenza, or the yearly flu is another virus that may be damaging to pregnancy. Pregnant mothers who contract influenza in their third trimester are more susceptible to respiratory defects and have an increased risk of fatality [7]. Viral infections such as influenza may for the most part seem out of our control, but obstetrician and gynecologist, Dr. Genevieve Eastabrook suggests that expectant mothers and the public can take matters into their own hands by receiving yearly vaccinations.

Lastly, one of the major environmental concerns faced by pregnant mothers is misinformation from social



Daniel Hardy

Genevieve Eastabrook



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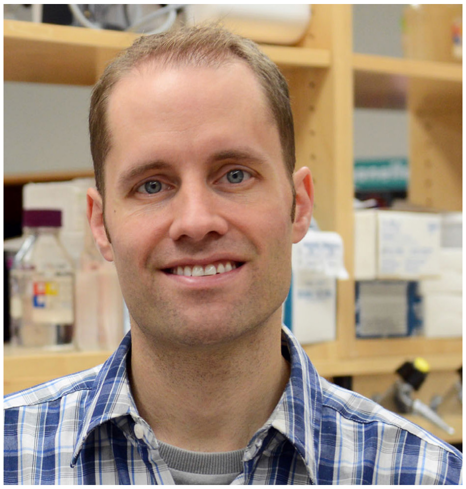

Stephen Renaud

media and popular culture. In today's society, some celebrities feel entitled to provide information to their followers, and this advice is often taken at face value without scientific rigor. This creates disparity in the quality of information and consequently, women can be exposed to a lot of misinformation. This ranges from fads promoting lotus births — where the umbilical cord is left to naturally detach from the fetus — to even consuming the placenta. There is no scientific evidence indicating any benefit to these practices [8,9]. Lotus births and consumption of the placenta will more likely lead to negative side effects such as an increased risk of infection [8,9]. To combat misinformation, Dr. Jen Gunter, a Canadian obstetrician and gynaecologist advocates for women's health through social media. Gunter recently published the book, "the Vagina Bible", where she utilizes pop culture tactics to dispel incorrect information [10]. She provides information to expectant mothers, creating opportunities for them to implement good practices and give their babies a chance for a healthy start.

It is evident that many factors can influence the outcome of pregnancy. Specifically, an expectant parent's surrounding environment can create significant challenges to the placenta and place both mother and baby in harm's way. However, clinician and scientist, Dr. Peeyush Lala from Western University says there's not too much reason for concern. The placenta is a resilient organ that can take care of all the baby's needs. In today's world, most individuals undergo pregnancy with little to no complications. Lala's advice to any pregnant mother is to follow the instructions of their doctor, eat balanced meals, not partake in risky behaviours such as drugs and alcohol, and to simply "cherish the moment." To provide even more support for pregnant mothers, researchers such as Stephen Renaud, an assistant professor of anatomy and cell biology at Western University, aims to understand how the placenta develops to safeguard growth of the baby. Renaud's lab focuses on understanding the genetic and immune regulation of the placenta, trying to comprehend how it develops and functions during pregnancy. He believes that by unraveling the mysteries of the organ, we can best support and nurture it, so that it may do its job to serve as the baby's lifeline.

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POPULATION MEDICINE

Northern Canadian Indigenous and the environment

A relationship compromised by colonization and climate change.

BY COLIN JAMIESON

The environment is a complex system comprised of social, cultural, and natural forces that can regularly influence one's health and wellbeing. It has power over both opportunity and behavior and has historically led to human adaptation. This is particularly true among Indigenous populations of Canada. Canadian Indigenous peoples share a strong, longstanding relationship with the natural environment and have been driven to adapt as a result of colonialism, systemic oppression and exclusion, forced displacement, and climate change [1-3]. Harmony between humans and the natural world is highly revered among Indigenous communities. Indigenous peoples often rely on the natural environment for sustenance and in return they cherish and respect it [4-5]. This harmonious relationship is often seen as a fundamental component of Indigenous culture; in fact, many Indigenous peoples integrate environmental health into their sense of wellness or personal well-being [6]. Andrew Papadopoulos, an associate professor in population medicine at the University of Guelph, explained that Indigenous peoples often "look at the absence of caribou, the rising of temperatures, the melting of ice, the presence of trichinella in walruses, and the absence of other traditional food sources" when expressing their wellbeing.

As a result of colonization, Indigenous populations have been distanced from their traditional lands – thereby compromising traditional food practices and the pertinence of local knowledge [5]. Despite contributing little to climate change, these communities have been displaced to regions experiencing the most rapid environmental changes. Rising environmental temperatures at the Canadian Arctic has led to unstable ice conditions and has altered animal migration patterns [7-9]. Traditional Inuit peoples rely on the conditions of the sea ice to enable safe travel to hunting and fishing grounds, and thus, unstable ice conditions have hindered access to traditional food sources. This has led to a growing prevalence of food insecurity among Inuit households increasing the risk of hunger and malnutrition among these individuals. In fact, a study from McGill University found that food insecurity was three times more prevalent among Inuit compared to off-reserve Indigenous households [1]. A Canadian study also found that increasing sea ice instability has restricted Inuit peoples' freedom of movement, increased physical dangers associated with hunting and fishing, and has significantly disturbed traditional ways of living [5]. Ice trips are associated with social bonding and the transference of traditional knowledge, as climate change has made these trips more dangerous and less practical it has disconnected Inuit peoples from their environment – causing a significant loss of place [5]. Cultural disruption compounded with social isolation and endangered personal safety has resulted in increased levels of stress and worsened mental health among these populations.

When providing Indigenous communities with support, it is vital to build relationships and work in consultation. Papadopoulos stressed the importance of providing "care, treatment, or services in a culturally appropriate manner." In the context of Indigenous communities, it is important to recognize their desire for self-governance and autonomy as well as the importance of tradition within their culture [10-11]. When pathogenic growth occurred in

photo credit - Jordan Ostapiuk

The Bow River in Alberta, Canada - called Makhabn in the Blackfoot language - was used by Indigenous people for travel, hunting, and fishing, long before European colonization.

Northern Canadian water sources due to rising temperatures, water treatment systems were put in to provide potable tap water to Indigenous homes without consultation. However, members of the community continued to rely on contaminated water sources because that was where the community obtained drinking water for generations past. Not only was the government assistance a failure, for Papadopoulos, introducing the water treatment systems without consultation “represents further colonialism,” as it may be interpreted as an attempt at assimilation, further distancing these populations from traditional practices.

“It’s the balance of how you respect the culture, the desires, and the determinations of the population, without adding to further colonialism and greater repression of these communities,” Papadopoulos said.

Canadian researchers, including Papadopoulos, have been attempting to develop culturally appropriate strategies to aid in Indigenous adaptation to climate change. These approaches have tended to utilize some form of collaborative, community-based monitoring, where members of Indigenous communities were actively involved in the monitoring of environmental change [2]. Firstly, traditional knowledge can help contextualize scientific observations and better scientific understanding of the local impacts of climate change. Secondly, actively working with Indigenous members in climate research and its dissemination has been shown to significantly improve the translation of research findings into practical action [12]. Through collaboration both public health researchers and Indigenous communities can learn from one another and generate culturally appropriate strategies.

When providing Indigenous communities with support, it is vital to build relationships and work in consultation.

“Indigenous communities prefer to communicate orally, face to face, primarily through elders and more knowledgeable individuals within the community down to younger members,” Papadopoulos said. In line with this preferred means of communication Papadopoulos and his colleagues have established several means of public health transmission including digital story telling for Canadian Inuit communities [14,15]. Younger members of the community would record elders explaining a message about healthy behaviors and how they interpret health and wellbeing. This video can than be uploaded to a website and shared among other Northern communities across Canada relieving the barrier of travel.

“[This created spaces for] elders to express what wellness means to them and what others can learn from the message that they are presenting,” Papadopoulos said. “It was community-driven and supported by researchers.”

Digital story telling parallels traditional word of mouth transmission and is an example of a collaborative, culturally appropriate strategy in which Indigenous community members and public health researchers can effectively disseminate information. This platform can be used to disseminate information regarding adaptations to climate change or other public health issues while upholding Indigenous voice and perspectives [14]. The most essential aspect was that the Indigenous partners were able to lead these projects and present these messages in a way that best matches the needs of their cultural environment. For not only can one’s environment have a direct influence on health in terms of mental stresses, access to food or clean water, but also indirectly through the transmission of health knowledge and awareness of healthy behaviors.


Andrew Papadopoulos

The environment can greatly impact one’s health and wellbeing. This can occur directly through the disruption of healthy behaviors or indirectly through communication of these behaviors. However, these effects are extremely culturally dependent. Different cultures possess different values and priorities; therefore, it is essential to address impacts through a culturally dependent lens [2,3,6,12]. Papadopoulos explained that it’s important for researchers, public health officials, or members of the government to recognize the specific values of communities and provide support in an appropriate manner. A lot can be learned from Indigenous tradition and local knowledge especially in the context of environmental change [12].

“A better understanding of cultural traditions and Indigenous values and allowing Indigenous communities to work with us or guide us in helping them, is going to be an area where we see some great benefits long-term,” Papadopoulos said.

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ENVIRONMENTAL HEALTH

Climate change and human health

The choice between surviving and thriving.

BY LING WU & HUGH MONTGOMERY

Protestor holds up a sign during the 2019 Global Climate Strike in Eriangen, Germany

photo credit - Markus Spiske

Climate change is the greatest and most unprecedented challenge we are facing in the 21st century: one that threatens every facet of life upon which we rely. There is increasing evidence of the profound impact of climate change on human health including consequences of extreme weather events, and most pressingly, newly emerging patterns of infectious disease. The severe impacts of global climate change on public health requires the sustainable action of individuals, businesses, and governments to shoulder the responsibility of preventing a rise in global temperatures. Most importantly, this involves reaching the societal targets of the Paris Agreement – keeping average temperatures below two degrees Celsius above pre-industrial levels [1].

In Geneva, the first World Health Organization [WHO] Global Conference on Air Pollution and Health was held in 2018. The chief aim of which was to catalyze a global response against air pollution, associated disease exposures, and overall cost to society [2]. This same objective is echoed by the Lancet Countdown on Health and Climate Change [LCHCC], an annual, international, and multidisciplinary report that highlights and monitors the evolving landscape of health in the era of climate change [3]. In its 2019 report, the LHCC addressed our pressing fight with climate change as "an unprecedented challenge" that "demands an unprecedented response."

Surviving

Present day populations are fighting against extreme weather, insecurity of food and water, volatile patterns of infectious disease, and the exacerbation of existing health threats [3]. Of note are the adverse effects of climate change on maternal and children's health. Unsurprisingly, mothers and children in low- and middle-income countries face greater risk of malnutrition due to food insecurity, challenges to affordability of food, and lack of adequate healthcare [4,5]. Stunted growth, severe wasting, and restricted intrauterine growth cause 2.2 million deaths globally, and 21 per cent of disability-adjusted life-years [DALYs] among children younger than five years [4].

The 2019 LCHCC highlights the importance of child health against the backdrop of an increasingly changing climate. It emphasizes how our response to climate change today can shape the health profile of the future, creating one of extremes and uncertainty, or one in which population health, especially that of children, is not defined by a changing climate [3].

Children born today are projected to experience terrestrial temperatures four degrees Celsius higher than the pre-industrial average [3]. Air pollution is anticipated to accumulate to dangerously high levels in over 90 per cent of cities [3]. Food shortages and insecurity are predicted to rise due to shortened crop growth seasons and reduced crop yield, increasing risks of malnutrition amongst susceptible populations [3,5]. Simultaneously, the world is facing changes to disease transmission, notably, increased transmission of lethal viral diseases such as dengue, for which incidence has increased over 15 fold in the last 20 years [6]. Children across the globe, specifically those living in African and coastal areas will experience greater disease burdens from infectious diseases, especially dengue, malaria, diarrhea, gastroenteritis, wound infections, septicemia, and cholera [3]. As they age, organs such as the lungs and heart of children born today, will be damaged principally by fossil fuel-driven air pollution; it is predicted that these effects will accumulate over the span of their entire life [3]. Global deaths due to air pollution approached seven million in 2012, whilst global premature deaths due to fine particulate matter reached 2.9 million in 2016 [7]. On the other hand, the livelihoods of the aging families of children born today are threatened by worsening changes in weather patterns and conditions, causing higher incidences of heatwaves, stronger droughts, floods, and storms [3]. Specifically, increased cases of annual daily human exposure to wildfires were recorded globally in 78 per cent of countries between 2015 and 2018, with the largest being at nearly 21 million person-days in India and 17 million person-days in China [3].

> *"Our response to climate change today, will determine the world we live in tomorrow."*
>
> *- The Lancet Countdown*

Climate change will have impacts on us all. At present, humanity is experiencing the effects of climate change: such as delayed spring, advanced summer, and intensive storms. To a large extent, the ecological system is disrupted by the overwhelming energy gain, especially fossil fuel consumption [8]. Consequently, generations are witnessing ice melting, rising sea levels, and weather becoming more and more extreme. Indeed, the increased production and trapping of greenhouse gases through the fossil-fuels emissions have led to global temperature fluctuations, and the disruption of ecosystems through greater incidences of natural disasters, most notably the bush fires of Australia in 2019 [9].

Fortunately, the outlook of our future does not have to be defined by current projections. Should considerable actions be taken, scientists believe that limiting the rise of global average temperatures to "well below two degrees Celsius" is possible, and would ultimately reshape the health of a child born today [3].

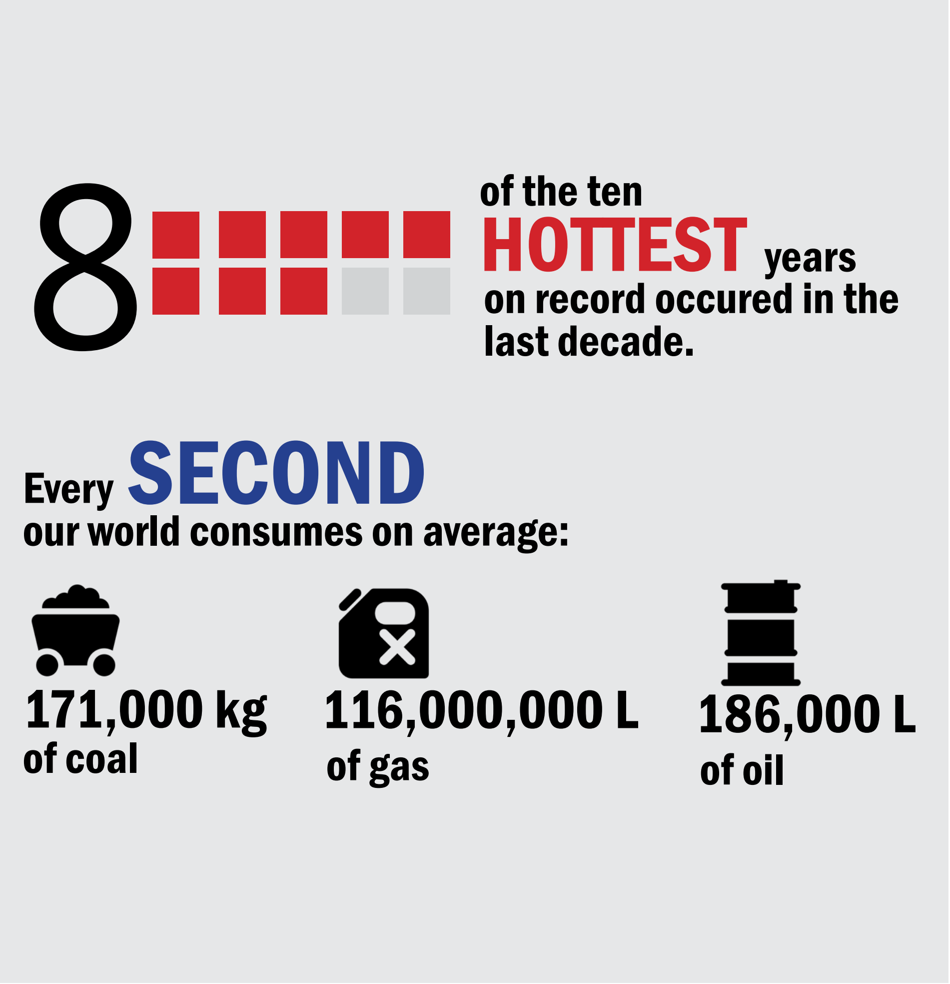
Thriving

Ambitious action, global adaptation and mitigation efforts should be enforced for the prosperity of our planet and future generations. Countries are becoming more resilient to the effects of climate change through the implementation of climate services to the health sector after recognition of the importance of national climate change risk assessments. 54 per cent of cities throughout the world carried out climate change risk surveys in 2018, and 109 countries have medium to high levels of infrastructure to mitigate consequences from health emergencies such as pandemics and changes in weather patterns such as air pollution and floods [3].

Increased media coverage of climate change and its effects on human health have raised global awareness and catalyzed individual initiatives to lead low-carbon lifestyles. Global action and engagement by governments has also increased in recent years, with even small island developing states such as Fiji, Palau, and Samoa, placing greater attention to health and climate change [3]. In 2017, France committed to ban the sales of petrol and diesel vehicles by 2040 and to become a carbon-neutral country by 2050 to meet its targets under the Paris Agreement [10]. In 2018, Canada committed to phase-out traditional coal-fired electricity and improve greenhouse gas regulations for natural gas-fired electricity by 2030 [11] In 2020, the United Kingdom announced plans to close coal-fired power stations by 2024 and ban the sale of new diesel and gas cars [12,13]. Should targets such as these be reached, children born in the UK and Canada today would see the phase-out of coal by their fourth and tenth birthdays, followed by the rollout of solar and wind energy [3,11–13]. Children born in France would witness the replacement of petrol with renewable energy vehicles by the age of 20 [10]. In 2050, generations would witness net-zero emissions all over the world.

Fortunately, climate change is gradually arising to the consciousness of individuals, catalyzing the modification of lifestyles and patterns of consumption. Indeed, a strong and sustainable response to climate change requires an unprecedented level of global participation. This begins with dedicated and sustained individual action: buying plant-based foods that are seasonal and local; reducing ruminant meat and dairy consumption; lowering thermostat temperature [each degree reduction can save on average 1000 pounds of greenhouse gas emissions a year]; switching to 100 per cent renewable energy sources; increasing cycling, walking, and public transit usage; reducing flights; and lastly, increasing economic reinvestment in the renewable energy sector [3,14,15].

In reality, societies have yet to do enough. Despite the efforts of governments to promote renewable energy, the allocated budgets are much less than those used in the expansion of fossil fuel use. Moreover, engagement and cooperation by all sectors from individuals, businesses, and governments are essential to the success of ambitious and sustained responses to climate change that can incite a global commitment to lasting reductions in emissions. Consequently, the interactions of energy gain, global climate change, public health, massive migration, extreme poverty, social unrest, and mental illness will affect not only children but people of every age and on every continent.



8 of the ten **HOTTEST** years on record occured in the last decade.

Every **SECOND** our world consumes on average:

171,000 kg of coal

116,000,000 L of gas

186,000 L of oil

Numbers from the 2019 Lancet Countdown . Icons by Adrien Coquet, Desainer Kanan, and Vectors Market.

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SPOTLIGHT
ON CAREERS

EPIDEMIOLOGY

Tackling environmental health: from research to government

Q&A with Elaina MacIntyre, an epidemiologist with Public Health Ontario and a University of Toronto adjunct professor.

BY ALISON HOWIE

Elaina MacIntyre is an epidemiologist specialist at Public Health Ontario and an adjunct professor at the Dalla Lana School of Public Health at the University of Toronto. MacIntyre acquired a B.Sc. in microbiology and immunology at Dalhousie University in Halifax, Nova Scotia where she was raised. After working for a year, MacIntyre decided to pursue an M.Sc. in occupational and environmental hygiene at the University of British Columbia. Upon completing one year of coursework for her M.Sc., MacIntyre transitioned into a PhD program where she researched the association between air pollution and childhood ear infections in a cohort of 60,000 babies in British Columbia. She subsequently completed a postdoctoral fellowship at the University of British Columbia while living in Munich, Germany. MacIntyre worked as an environmental epidemiologist at the German Research Center for Environmental Health before returning to Canada, and has been in her current role for seven years.

What led you to pursue a career as an epidemiologist specialist and as a professor of environmental health, and what path did you take to get here?

I've always felt a close connection to the environment, and I've always been quite passionate about environmental causes. In terms of how my career unfolded, I really had no intention of working in this field. I did my undergraduate degree in microbiology and business because I had planned to go into pharmaceutical and disease research. I happened to take an elective environmental health course in the final year of my undergraduate degree, and the course brought up aspects of epidemiology, population health, and preventative medicine, and introduced me to this field of science that really brings together my passion for the environment, and links it to human health and disease. I worked for an epidemiologist for a year and that's when I really got the bug. Once I discovered that there was this world of research that bridged everything together, I was sold. It was just a matter of finding a supervisor who I would want to work with for a number of years doing research that I cared about. It started as an M.Sc. and then evolved into a PhD. I was very lucky to have consistent funding during my PhD, and one of my fellowships required me to work, so I chose to go to Munich, Germany. I really wanted to get experience in a very different environment, and luckily they were doing similar research to the research I had already done with my PhD. When that work placement wrapped up, I found myself really loving the institute and the people I worked with, and that's when I decided to do a post-doctoral fellowship and later decided to stay on as an environmental epidemiologist. My decision to move back was more for my family, rather than a career move. I had been keeping my eyes and ears open for potential opportunities available in Canada for a year before my current job brought me to Toronto.

Elaina MacIntyre

What does your average day look like?

It definitely changes every day. Most days are ones where I'll sit down at my desk and discover that there are new and last-minute things to respond to, and my day doesn't go nearly as planned. I don't like doing the same thing every day, so for me this is perfect. My day usually starts with reading up on new and emerging research in areas where we know there are some misinformation or misunderstanding. In collaboration with a small but diverse team, we decide if we should dig a little deeper and learn more about certain issues. Since Public Health Ontario is a technical and scientific body that provides advice and support to the Ontario government on any topic related to public health, there's really no limit to the kind of topics that I might look at on any given day. Air pollution and water quality are two topics that often come up. Another part of my job involves managing a number of environmental health surveillance projects. This often involves identifying data from outside the health sector, and interpreting them in a way that makes it useful for public health decision making. I'm also an adjunct professor at the University of Toronto, where I co-lead an occupational and environmental health seminar series and present guest lectures.

You had a significant role in the Public Health Ontario report, "Environmental burden of Cancer in Ontario." Can you talk a bit about the relationship between the environment and cancer?

What's often not well recognized is that we're connected to the environment around us every second of our life. We're breathing air, drinking water, eating food and walking outside in the sun – these exposures never end, and we often don't give them a lot of thought. Decision makers often come to us and say, "we recognize that environmental health is increasingly important, but we want to know what aspect of the environment is most important for the health of our population." What we set out to do with the report was to address this question and to identify the carcinogens in our environment that we think cause the most cancer. One of the key findings was that the top two causes of environmental cancer, at least those that are most significant in Ontario, are not things that are man-made. Sunlight and radon are both entirely natural, and there are many good, well-documented ways to protect yourself from them. We often identify man-made sources, such as factory emissions, as top environmental concerns, so I think the findings from this report were really eye-opening for many.

Do you feel that enough is being done in Canada to mitigate the health effects of common environmental risk factors?

I think our real strength right now is that we are improving our understanding of how the environment impacts our health. The decisions that have to be made in terms of protecting population health are not always clear, but the first step is to just understand what's going on. Going back to the burden of cancer report, one of the reasons why the man-made carcinogens may not have been as significant could be that in the last few decades, we've done a good job at controlling some of those things. We've gotten really good at developing controls and engineering technologies that have improved our environment where we traditionally had been concerned. In part, the findings from the burden of cancer report might actually demonstrate that, while there's always going to be more that can be done, we've made good progress already.

Do you have any advice for graduate students interested in pursuing a similar career path?

I would encourage anyone who has a real passion and curiosity about this field to pursue it. A few decades ago, we thought that the health impacts associated with air pollution were only a problem in certain regions of the world. What we've learned in the last 10 or 20 years is that even in regions like Vancouver, with some of the best air quality in Canada, we see associations between air pollution and poor health. As this knowledge continues, and as we build a greater understanding, I think the field is going to change a lot. But for people like me, that's what makes it so exciting. If you're interested at all, definitely pursue the field. It can be discouraging at times, and it can be hard to get into, but reach out to people who you think are doing exciting work and ask them to mentor you. Part of why I moved from Halifax to Vancouver was because I found someone through publications that I wanted to be my supervisor. I approached him and, luckily, he was willing to take me on. When I talk to colleagues and other people in my field, we all have very similar stories. We found someone we wanted to learn from, they took us under their wing, and the rest is history. Never be timid or hesitant to reach out to people, because we all remember what it was like to be in your shoes.

"Never be timid or hesitant to reach out to people, because we all remember what it was like to be in your shoes."

ENVIRONMENTAL HEALTH

Where population health meets clean energy

Q&A with Jill Baumgartner, health researcher and associate professor at McGill University.

BY ALISON HOWIE

Jill Baumgartner is a health researcher and an associate professor at the Institute for Health and Social Policy and the Department of Epidemiology, Biostatistics, and Environmental Health at McGill University in Montreal, Quebec. In her early career, Baumgartner worked for non-governmental organizations focused on global health. Realizing that advancing her career would be challenging with a B.Sc., Baumgartner decided to pursue an M.Sc. in population and international health at the Harvard University School of Public Health. The thesis component of her M.Sc. stimulated her passion for research, leading her to complete a joint PhD in population health science, and environment and resources at the University of Wisconsin-Madison. Her research there focused on the health impacts, specifically the cardiovascular disease risks, associated with exposure to air pollution in homes that burn biomass fuel for cooking. Upon completing her PhD, Baumgartner moved to McGill University where she has worked for six years. Her work today is an extension of her PhD research on the health impacts of air pollution; she is interested in evaluating the health impacts of clean energy policies and programs. She also leads work to evaluate the environmental contributors to urban health inequalities in low- and middle-income countries.


Jill Baumgartner

What does your average day look like?

One of the huge advantages of being in academia is that your day varies quite a bit, and that's something I really like about the job. But it can also be intimidating, especially early in one's career. A colleague once remarked how there are very few jobs where you can be at risk for coming into work without a clear plan for the day, so it's important to provide structure and be organized. My average day usually involves meeting with students, grant writing or brainstorming, participating in research meetings, and reviewing science done by my group or other researchers. I also teach courses in environmental epidemiology and exposure science. Another important part of most researchers' jobs is sitting on advisory committees. For example, I've advised non-governmental organizations on the least polluting household stoves and advised funding agencies on research directions to consider supporting.

What aspects of your research are unique compared to other research being done in environmental health?

Most of my work is on the health impacts of environmental risks in low- and middle-income countries. My team does a lot of primary data collection because, unfortunately, the environmental data that we need are often not available through secondary sources in low-income countries. For example, most countries in sub-Saharan Africa do not have a reference-quality air pollution monitor. One unique aspect of my research group is that we conduct large scale secondary data analyses and collate data sets that we've gathered from all over the world, but then we also work on primary data collection projects where we travel to people's homes to collect measurements.

I'm particularly interested in understanding the health and air pollution impacts of real-world environmental policies. For example, in Beijing, the government is banning coal and putting electric or gas-powered heat pumps into millions of homes. We were interested in evaluating the effect of this program on air pollution and health. What we've found is that, for the most part, villages want to make this transition from coal to electric heat pumps, but some of the poorest households may have trouble paying for the additional electricity costs.

> *"My advice to an emerging researcher in environmental health is the same advice I'd give to any researcher:*
> ***always start with a really good question."***

Climate change has been a hot topic in the world recently. How is it affecting our health?

We do have increasingly strong evidence showing the impacts of climate change on health, both directly and indirectly. I am not a climate change researcher myself, but I do work closely with climate modelers who are looking at how air pollution from different sources, including household solid fuel burning and agricultural burning in rural areas, contribute to climate change. My role is to provide some of the input data for models generated by atmospheric scientists that look at the potential climate impacts of air pollution and the potential climate benefits associated with reducing these sources of pollution.

If you could offer a piece of advice to an emerging environmental health researcher, what would it be?

My advice to an emerging researcher in environmental health is the same advice I'd give to any researcher: always start with a really good question. Once you have a good question, then you can start thinking about the tools you want to use to answer that question, including a creative study design, new data, and fancy statistical methods.

How do you envision the future of research as it pertains to environmental health?

Environmental health is a broad field and there are a lot of interesting directions that intersect with toxicology, exposure science, epidemiology, and policy. The intersection of environmental and urban health is an important area. In many cities, urban residents have, on average, better health than their rural counterparts, but the urban poor often have much worse health.

In developing countries, the health of the urban poor is often impacted by environmental risks, including lack of access to safe water, poor sanitation, low-quality housing, polluting energy, and crowding. Understanding what health looks like for the urban poor and how environmental factors contribute to health inequalities is an important research area, particularly since cities are growing and inequalities are also growing.

INFECTIOUS DISEASE

From working with animals to humans

Q&A with Nicholas Ogden, an expert on vector-borne diseases and the Director of the Public Health Risk Sciences Division.

BY SUPRIYA HOTA

Dr. Nicholas Ogden is a senior research scientist and the Director of the Public Health Risk Sciences Division for the Public Health Agency of Canada (PHAC). His work focuses on assessing the risk and impact of climate change on vector-borne diseases – including Lyme disease, West Nile, and other zoonoses – and develops tools for community adaptation to these disease risks. His team undertakes ecological and epidemiological studies, conducts systematic reviews and meta-analyses, and uses genome sequencing to understand pathogens and their ecology. Building on this knowledge, they then try to understand and predict when and where the disease risks might appear due to climate change.

Ogden received his veterinary degree from the University of Liver-

Dr. Nicholas Ogden

pool. After 10 years of clinical practice, he completed a PhD in the ecology of tick-borne disease from the University of Oxford. He was then appointed as a professor at the Faculty of Veterinary Science at University of Liverpool where he continued his research in the ecology and epidemiology of tick-borne diseases in Europe and Africa. Ogden's postdoctoral work at the Université de Montréal – in collaboration with PHAC – focused on the potential emergence of Lyme disease in Canada associated with climate change.

> “It is important to have knowledge of the scientific literature but also the spirit of critical inquiry.”

What is the most and least favourite part of your position? What are some personal attributes that make you successful at your job?

The favourite parts of my job are my research, the people that I work with, and the organization that I work for. One of the hardest parts is when we must put that research aside and help out during an outbreak – such as right now with the coronavirus. Some personal attributes that may make me better at my job include helping and encouraging others, as well as my knowledge and experience with research development. Because I am working with infectious diseases, my training in biological and veterinary sciences, my understanding of the ecology and epidemiology of emerging infectious diseases, and how to control them all help me at my job. Basically, my multiple skills and experiences help me become a more effective health practitioner.

Can you tell us about some project(s) that you are currently working on? How does your work help the community and/or the country?

We integrate climate change, field and laboratory studies, and environmental determinants to predict where and when infectious diseases may emerge in Canada. We also explore how the ecosystem could change if an outbreak were to happen. Furthermore, we assess how infectious diseases could cause risks to Canadian communities so they can be informed about the possible emergence of infectious diseases due to climate change and how they can be better prepared for them.

Why did you choose to work at the PHAC?

My wife and I moved to Canada because she had an opportunity to work here and be close to her family. Back in the UK, I was working in academia as a professor in the Faculty of Veterinary Science at the University of Liverpool. There, my research focused on the ecology and epidemiology of tick-borne diseases. At the time, tick-borne diseases were not a public health issue in Canada. But a colleague, who worked for a part of Health Canada – which became PHAC – raised the possibility that Lyme disease may move north from the US to Canada due to climate change. From this, a project developed and I got a post-doctoral position at the Université de Montréal to model potential effects of climate change on the emergence of Lyme disease in Canada. Following this work, I was fortunate enough to be offered a post at PHAC.

What is your career goal? Do you see your position evolving overtime at the PHAC?

My career goal is to contribute to the knowledge in a way that helps the communities and/or the world to become better protected from infectious diseases. I don't see my position evolving except in terms of taking on more management duties. But I really like what I do!

If you were to start all over again, would you make any changes to your career path? What changes would you make and why?

No, I wouldn't make any changes to my career path. There were times in my life when I changed jobs and felt that maybe I made a mistake in changing paths. But now when I look back, I think all of my past work experiences have given me something. There is not a part of my past career that I regret.

What inspired you to pursue a PhD after 10 years of clinical practice? Do you ever use the knowledge/ experience from your Doctor of Veterinary Medicine (DVM) degree in your current position?

I pursued a PhD for two reasons. Firstly, it was time to move on and secondly, I was looking for new intellectual challenges. The challenges that I experienced in my clinical practice had become increasingly routine. I also started to realize that more research in the area of emerging infectious diseases was needed, and I thought that understanding how diseases work in wildlife could be fundamental to understanding how diseases work in humans. A funding opportunity came up and I ended up working in the field of Lyme disease.

Yes, the basic training I received (including examining biological samples under a microscope and learning how diseases make animals sick) and the skills I have learned (such as examining healthy and diseased animals, diagnosing illnesses, and seeing first hand how epidemics occur in animal populations) gives me insights into my current work. I am working on emerging infectious diseases that originate as diseases that are transmitted from animal to human populations, for which understanding the biology and ecology of the diseases and how they affect animals are very important. My past training and experience stand me in good stead.

What is the current demand for individuals with an M.Sc. or PhD in your field? Do you see the demand for this position increasing in the future? If you could offer advice to new M.Sc. or PhD graduates and emerging researchers in your field, what would it be?

I think there is an increase in the demand for individuals with M.Sc. or PhDs, especially during infectious disease outbreaks. There is no better example than the time we are living in right now – the COVID-19 outbreak. We need individuals who have graduate degrees in ecology and epidemiology, who can understand the animal, human, and ecosystem aspects of the story, to help better control and prevent the emergence of infectious diseases. These qualified and skilled individuals can be found working for international organizations such as the World Health Organization, to national organizations such as PHAC, to educational institutions. There is always a need for people who have deep expertise in the specific fields of microbiology, bacteriology, virology, epidemiology, and genomics. But we need both specialized and generalist individuals to put the pieces together. A piece of advice that I would offer is to read widely and deeply. It is important to have knowledge of the scientific literature but also the spirit of critical inquiry. With that knowledge, you attain the position to develop hypotheses, leading to research ideas that you can explore with rigorous studies.

MENTAL HEALTH

At the intersection of mental health and drug addiction

Q&A with Jibran Khokhar, biomedical science researcher and assistant professor at the University of Guelph

BY MADISON PEREIRA

Jibran Khokhar completed his B.Sc. from Queen's University, and subsequently earned his PhD in pharmacology and toxicology under the supervision of Rachel Tyndale at the University of Toronto and the Centre for Addiction and Mental Health. After completing his degree, he pursued a post-doctoral fellowship with Dr. Alan Green in the department of psychiatry at Dartmouth College. During this time, he worked to develop new and safer therapies for co-occurring schizophrenia and alcohol use disorder. Today, Khokhar is an assistant professor in the department of biomedical sciences at the University of Guelph. His research continues to focus on the development of new medications for co-occurring schizophrenia and substance use disorder, and the effects of adolescent drug use on mental illness and addiction.

Jibran Khokhar

How has graduate school prepared you for your faculty role at the University of Guelph?

My mentor, Rachel Tyndale, allowed me to focus on the research aspect which helped me learn specific techniques, but she also helped me work on other skills including critical thinking, scientific writing and oral presentation skills. During my graduate studies, a lot of my experiments went wrong or didn't work and it's similar to being faculty and a principle investigator. Often times my grant applications are rejected and not funded. From my graduate studies, I've learned that it's important to be able to keep your chin up while taking hits and it's helped me persevere with whatever obstacles are thrown my way in terms of my career.

> *"We need to remember that our funding is coming from everyday taxpayers and improving life for them should be at the forefront of our research."*

Your research focuses on schizophrenia and drugs of abuse. What sparked your interest in these topics?

When I was a graduate student, I had to take a course called, "tobacco control from cells to society," for one of the scholarships that I received. As a basic neuroscientist, it was my first real experience into seeing all of the different aspects in tobacco control. There was a statistic from one of the presentations that stood out to me: how 80 per cent of all cigarettes sold are used by less than 5 per cent of the population - those with co-occurring mental illnesses. I found this shocking and it was something that I had never heard before, but it sparked my interest. Somehow my other post-doctoral fellowship options fell through and I ended up at Dartmouth College in a lab where co-occurring schizophrenia and substance use disorder was the focus. I ended up taking a fond liking to this research and I am continuing that in my role now.

Are there any particular drugs of abuse that your research is focused on?

In our lab, we are currently studying many drugs of abuse including cannabis, alcohol, and nicotine. We also examine different forms of drug delivery in our research, including drinks, vaporizers, and edibles.

Are there any recent discoveries/projects ongoing that you're really proud of?

All of the graduate students that are in our lab are doing a phenomenal job on their own projects. In one, we are looking at the effects of cannabis use on the brain in terms of behavior as well as changes in brain circuits. In another project, we're looking at the effects of e-cigarettes on adolescent versus adult brains, and we're seeing that adolescents are in fact more vulnerable and find the vapours to be a lot more rewarding than adults do. We've also taken some findings from genome wide association studies and brought them into animal models by using transgenic animals. In doing so, we are seeing some interesting differences in genes that have been implicated in cannabis use.

Do you get to interact with community members as part of your job?

Yes, interacting with community members is something that I try to do. I have been invited to go to various schools to talk about vaping. Being able to do this is really important to me in terms of both improving science literacy in the communities that we live in, but also giving back to our community.

Since marijuana has recently been legalized in Canada, do you think that has influenced where your research has been directed? How do you envision the future of healthcare research will go?

Going back to when I was at Dartmouth College, the reason that I started to explore cannabis was because I knew that the legalization of marijuana was coming up in Canada. I wanted to carve out a little niche for myself in this field and become a cannabis researcher in Canada. We need to remember that our funding is coming from everyday taxpayers and improving life for them should be at the forefront of our research. I think we need to move towards more translationally impactful research. There is definitely room for basic research, but I think having more defined translational outcomes can only help us scientists and researchers keep our eyes on the prize.

Is there anything that you know now that you wish you knew in graduate school?

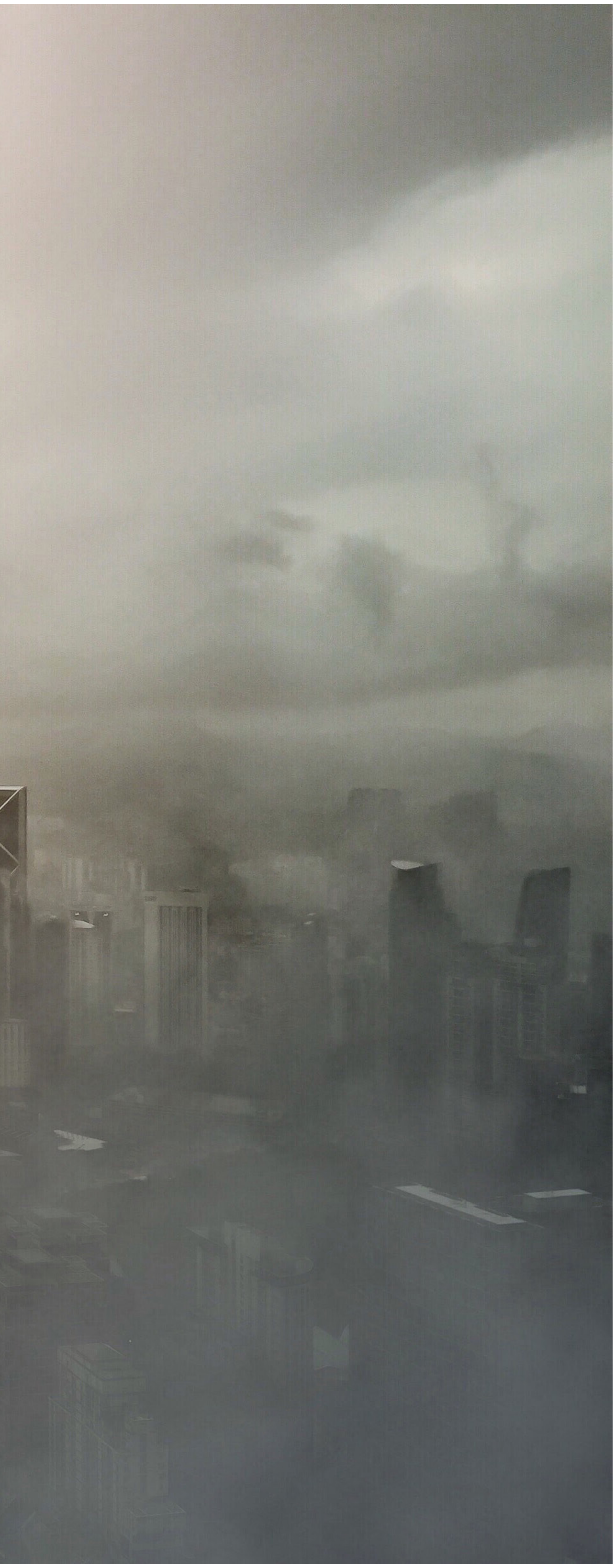
If I could go back to when my experiments weren't working during my PhD degree, I would tell myself that it will all work out. We worry and it's normal to worry, but everything works itself out in the end.

WE BUILT THIS CITY ON POLLUTION AND MOLD

How urbanization inadvertently promotes the development of asthma and allergic disease

An interview with **DR. STUART TURVEY**

text **SARA NESS** photos **HASSAN ISHAN + DAVID LEE**



Malaysia - photo HASSAN ISHAN

Asthma is often allergic in nature, primarily triggered by exposure to airborne allergens such as pollen or cat dander. Although we have long known that asthma and other allergic diseases are caused by interactions between environmental triggers and our own genetic predisposition, the complexity of these interactions has made it difficult to develop concrete disease prevention strategies. Furthermore, researchers have been faced with a great challenge in identifying and cataloging the cumulative impacts of the many environmental exposures identified to this point.

Our 'exposome' is our entire history of environmental exposures – beginning in the womb and extending to our time as adults. In recent years, it has become clear that the exposome has vast effects on overall human health [1], in large part because of the way it impacts our microbiome – the bacteria, viruses, and other microbes that live on and in our bodies producing substances that are required for our optimal health.

Research has shown that the presence or absence of specific microbes in an infant's microbiome can increase or decrease the risk of asthma and allergic disease development [2-5]. The infant microbiome is thought to be primarily affected by exposures in the first days and weeks of life, like mode of delivery (vaginal or caesarian section), infant antibiotic use, and method of feeding (breastfed or bottle-fed). While these factors have the greatest impact [6-9], the microbial colonization process is also shaped over time by other internal and external environmental exposures before eventually settling into a more stable community by the age of three [10-12].

As the global prevalence of asthma and allergic disease continues to climb at an alarming rate, some researchers argue that it's worth looking at our collective exposome, the exposures that are common to everyone living in an urbanized environment. Doing so might help us understand the detrimental effects that urbanization has on developing microbiomes [13].

With urbanization, the prenatal and infant exposome has shifted drastically from what it has been for most of human history; in general, babies have less microbial exposure than ever before. This is in part due to the over-use of cleaning products and other toxic substances that kill microbes, but it's also due to reduced exposure to naturally occurring sources of microbes, like pets and farm animals, natural greenspace, and soil. Not only does this make it difficult to establish a healthy microbiome, but it also doesn't allow our immune system to develop the tools it needs to function effectively. Furthermore, the exposome of an urban society is wrought with toxic exposures: vehicle-related pollution, smoke from solid fuel burning and tobacco, mold, household pests, and toxic components of plastics, like phthalates and bisphenol A (BPA). These toxic but common urban exposures are detrimental to our microbiome health and immune function. It also affects those with a lower socioeconomic status disproportionately; low income individuals often live in aging or poorly maintained structures with increased levels of unfavorable microbes and toxin-producing pests [14,15]. By viewing the exposome as a byproduct of our built society, we can better understand why asthma and allergic disease are on the rise in urban centers, and what we can do about it.

Dr. Stuart Turvey is the Director of Clinical Research at the British Columbia Children's Hospital and the Canada Research Chair in Pediatric Precision Health. As a clinician and immunologist, Turvey's lab is working to identify underlying microbial, cellular, molecular, and genetic differences between disease-affected and healthy children to elucidate mechanisms of disease pathogenesis and identify new targets for disease prevention and management. As co-director of the Canadian Healthy Infant Longitudinal Development (CHILD) Cohort Study, Turvey also collaborates with researchers across the nation to carry out Canada's largest population-based birth cohort study, which is quickly becoming one of the world's most informative studies of its kind.

Since 2008, CHILD study researchers have been following over 3,500 pregnant women and their children to examine how mode of delivery, infant antibiotic use, maternal diet, breastfeeding, household chemicals, stress, and other factors influence the development of chronic diseases like asthma and allergies. This work will help identify novel approaches to disease management, inform policymakers of the required preventative updates to our society's medical and urban planning standards, and inform the general public on the implications of cleaning behaviors, diet habits, and parenting strategies. We sat down with Turvey to discuss his involvement with the CHILD cohort study, and to reflect on the implications of his research on our society's status quo.

Your research on infant exposure to phthalates really struck a chord with me as a mother because it's such a difficult exposure to control. We live in a plastic society, where exposure to phthalates is inevitable. I think my phthalate-exposure concern echoes across many of the exposure risks that have been identified so far; how do you manage those inevitable, but less-than-desirable exposures within your own family?

Parents, I think, appropriately worry about their children and try to optimize their health in general. My job as a researcher is to sort of help identify risky exposures, problematic exposures, but also kind of put that in context so that people can still live their lives and not be anxious. So, I think your approach is sensible, which is to recognize that there can be exposures that are problematic.

I think you've got to live your life and encourage kids to be outside, sleep well, to eat a broad and healthy diet, to get exercise, and not to chase them around with hand sanitizer. That being said, I think these things we've researched are real exposures that do have potential health outcomes, so we try to educate families about them and also change policy. Most of us are doing a pretty good job. Things will inevitably happen, but we shouldn't, nor can we control everything.

Research from your lab also digs into prevention measures that would likely require municipal involvement, such as increasing biodiverse greenspace in cities and updating building codes. Do you expect that it will be difficult to convince policymakers to take heed and come up with the funding required for these preventative measures?

This preventative research was championed by Hind Sbihi, a post-doctoral fellow who worked with us.

Sbihi had an engineering background and I wanted her to think

Turvey Lab (left to right) – Bhavi Modi, Stuart Turvey, Kate Del Bel, Mehul Sharma, Alicia Jia, Meriam Waqas, Susan Lin.
Not pictured – Henry Lu, Darlene Dai

about the microbiome as an interactive system. When we think about the gut microbiome, we often think about it in terms of this micro level – how we might be influenced by the dog, or the antibiotics, or breastfeeding. Sbihi's push was this macro-idea, that society has, over time, become more and more industrialized, and as a consequence of that, we've lost biodiversity. We see that we've lost big charismatic fauna, like pandas and gorillas, but we've also lost lots of microbes that we as a human species evolved with. So, the idea that maybe you can be less sanitized and 'rewild' the environment, is intriguing and people have done experiments like this that seem to suggest it works.

I think city planners are really interested in making healthy environments. It may be as simple as encouraging less manicured green space with a diversity of trees and plants. I think our job is to challenge city planners to think about these things. I do think these messages are universal so that families and individuals can participate as well.

What are some manageable ways we can integrate research findings from the CHILD study into our own lives to reduce the risk of chronic disease in our own families?

What we know is that a diverse microbiome is important for health. When babies are born, they are relatively sterile and are suddenly exposed to a huge community of microbes. There are things we can do to facilitate exposure to these diverse microbes. If a baby can be born via vaginal delivery, and that's safe for the mother and the baby, that should be encouraged by the health system. Breastfeeding is also very important for modifying and establishing that microbiome, so anything that the health system can do to support mothers and successful breastfeeding is great. Another big factor is around the use of antibiotics; I think we should cherish antibiotics, but we should use them very thoughtfully because they kill off microbes that are important to maintaining our health, as well as those causing problems. Antibiotic stewardship efforts have been powerful in reducing exposure to antibiotics in young kids, but there's still more to be done.

Indianapolis - photo DAVID LEE

In the CHILD study, about 20 per cent of children were reported to have received a course of antibiotics in the first-year, which is much better than the reported statistics from 15 years ago, but it's still a lot, and it's likely too many. I think that's a message for pediatricians and family doctors, but also for parents. They shouldn't go to the doctor demanding antibiotics and feeling it's the only way that the child is going to get better, when with a bit of time, they'll get better without intervention.

If we were able to catalog the list of microbes required in a microbiome to support healthy immune development, could we wipe out asthma and allergic disease using tailored probiotic supplements?

Part of the research that we're doing considers that question: if we can identify the health promoting bacteria, are we able to start to replace them? If a child really needs antibiotics, maybe there's a way to then supplement them with a therapeutic cocktail of microbes that would help restore the lost microbial diversity that is inevitable with antibiotic use. I think we don't know that answer yet, but some of the research that we do with the CHILD study is looking to understand the microbiome structure that's linked to health and disease. Kids at highest risk for asthma and allergies seem to be missing some specific microbes, and in a couple of mouse studies, we were able to show that supplementing with those microbes protected the mice from asthma.

That's sort of my long-term hope, but there's lots of work to be done to define the missing microbes, as well as looking at how they can be grown and then proving that they can be safe in young babies. In the market there are aisles and aisles of probiotics, so there's a market for it and a sort of acceptance in the general public, but the problem is that the organisms that are being offered commercially now aren't the right ones, at least for the diseases that we are talking about. We need specific organisms that make specific metabolites that will do the job.

I think it does have the possibility of working, but in the meantime, we should just work towards the population-based interventions like minimizing the use of antibiotics.

In one way or another, many of the disease-promoting factors you identify in your work are in some way tied to socioeconomic class. Do you see any way to minimize the influence socioeconomic class has on the development of asthma and allergic disease in our society?

If, as a society, we can improve the quality of life and the support for our community, particularly the most vulnerable members of the community, I think that's where we can have the greatest impact on health. I think the message is that we should be looking to the most vulnerable, the ones experiencing these adverse exposures and really committing to support them. I don't think there's any one exposure or any one magic bullet, but poverty, low socioeconomic status, educational challenges, high stress, and poor housing all go together. So, if we can identify and support that group as a society, I think that will have huge impact on the lifelong trajectory of the kids growing up in those tough environments. It's really a package of exposures that we put under the banner of socioeconomic status, and it boils down to be our society's responsibility.

I think it'll be interesting to see how all of this plays out. BPA was a huge concern in the early 2000s and now it's quite easy to find BPA-free containers, canned food, and toys. As people become more aware of other exposure risks, it'll be interesting to see how things change.

I think that's right. I think it's our job to identify the problems, to call them out, and then to try to mitigate the exposure to these things through regulation. However, with technological advancements we'll always be exposed to new things that aren't always great, and we'll have to identify them as well. It's really a cycle of scientists identifying the problems and then regulators regulating, and the families being aware. It's a cycle of trying to do better.

EDITOR'S NOTE: This interview has been edited for length and clarity.

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PROFILE

BLURRED LINES

STUDYING CONCUSSIONS WITH A CONCUSSION

text SARAH LAFRAMBOISE
photo RENATA BASTOS GOTTGTROY

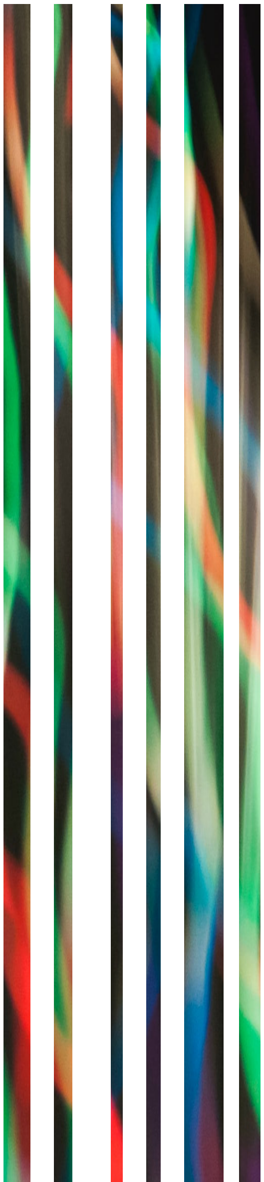
Many researchers feel an emotional connection to their work, but for Renata Bastos Gottgtroy this takes on a whole new meaning. As a PhD student at Auckland University of Technology in New Zealand, Renata both studies concussions and is afflicted by one.

On February 6, 2016, I watched Renata get checked into the boards during an ice hockey game as a member of the York University Lions Women's Hockey Team. As I sat in the stands, suffering from my own concussion, I couldn't help but feel the hit in my bones. Before I knew what was happening, I was running down to the ice. I knew that something was wrong.

She laid on the ice for a few minutes, eventually stumbled her way into the hallway and sat there. Tears in her eyes, she looked up at me and we had one of those telepathic moments all best friends share; she was not okay and we both knew it.

Renata had a concussion, a mild traumatic brain injury (mTBI) which had resulted from repetitive hits to the head over the last week. Her prescription was to rest until her symptoms went away.

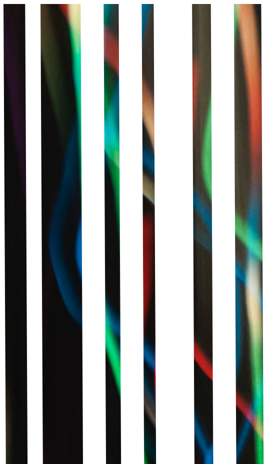
For months I struggled with her through the dark rooms, the delayed exams, wearing sunglasses indoors, and avoiding loud places. As days turned into months, and months into years, we progressed slowly. For Renata, the headaches never really went away. Although, she became less sensitive to light and sound, she struggled deeply with visual and vestibular defects. Any sort of head movement – from turning her head or driving a car – would make her nauseous and leave her with horrible headaches. Even reading was nearly impossible. She went through intensive visual therapy to re-train her eyes, but to this day many of her worst concussion symptoms continue to linger.



Despite these struggles, Renata fought through life one step at a time. She was determined to finish her bachelor's degree in kinesiology and pursue her passion in biomechanics. “I was so fortunate to have maintained my ability to think like myself,” Renata said. “Cognitively I was still able to function and that was a key part of my return to classes.” However, it wasn't always smooth sailing. I distinctly remember a frantic phone call from Renata after her first exam post-concussion. She had passed out in the stairwell and couldn't move because of the pain. There were plenty of scary moments like this where we both never thought she would recover. The only way forward was to reach out to counselling and disability services at the university to receive accommodations for her exams. This included writing her exams in a quiet room and being allotted extra time. All she knew was that giving up was never an option.

In addition to academic challenges, Renata faced many personal battles and struggled to re-define herself after her concussion. Born and raised in Brazil, Renata was a natural athlete and she held that very close to her identity. Upon moving to New Zealand at the age of six, she competed in a vast variety of sports from a young age. Renata followed in her brother's footsteps and added inline hockey to her many pastimes, eventually becoming a member of the New Zealand Women's Inline Hockey Team at only 13 years old. But her heart always came back to soccer. Competing at the national level with several international offers, she planned on pursuing a soccer career until an ankle injury took her off the pitch for a season. At this point, it was suggested that she take a shot at ice hockey. At 17 years old, Renata laced up her ice hockey skates for the first time. Within a year she was playing semi-professionally in Linköping, Sweden and

> Before I knew what was happening, I was on my feet and running down to the ice.



> “
> I was so fortunate to have maintained my ability to think like myself.

was quickly recruited to York University after a coach watched her play on the New Zealand National Women’s Ice Hockey Team at the International Ice Hockey Federation World Championships.

With less than two years of ice hockey experience under her belt, Renata moved across the world to Toronto, Canada to play on the York University Lions Women’s Ice Hockey Team. Renata was a rising star for the Lions both on and off the ice. During her three years with the team, Renata was a leader and influential player while continually being named an Academic All-Canadian and a member of the Dean’s Honour Roll.

But after her concussion, Renata was no longer able to exercise. For the first time in her life, she was forced to leave the world of sports behind. Redefining your identity is not easy. As athletes, Renata and I had dedicated our lives to becoming the best at what we did. All of that was gone for Renata before she was ready to give it up. She began to fully dedicate herself to her studies, remembering that it was her love for biomechanics that drew her to the kinesiology program at York University in the first place. Her interests in biomechanics and mathematics blossomed as she began to further develop skills in this field through completion of her honours thesis focused on spine biomechanics. Once again, I watched as the life began to come back in her eyes as she told me about the work she was doing. Academics was a positive outlet, and an opportunity for her to give back in a constructive way.

Upon graduation, Renata decided to head back to live with her family in Auckland, New Zealand. It was here that she began to re-evaluate her current situation. She knew that there were skills she still wanted to learn, and she felt drawn to academia. However, while she was able to push through her undergraduate degree, committing to a PhD seemed discretionary and something she didn’t have to subject herself to. Committing to future academic endeavours was not something to take lightly after everything she had been through. Taking some time off from academics, Renata returned to her athletics roots as a fitness trainer and enjoyed much needed time with her friends and family to help her heal, both emotionally and physically. While working within her limits, she

> Academics was a positive outlet, and an opportunity for her to give back in a constructive way.

was able to do moderate activity again which allowed her to reconnect with some of her favourite pastimes such as surfing, skateboarding, and snowboarding. Getting back to her roots gave Renata the energy she needed to take a second look at her future.

“Coming out of my degree, I knew that I wanted to develop a skill set in data science and mathematics,” Renata recalled. “Instead of doing an additional undergraduate degree in computer science, I thought I would be crazy and do a PhD in it.” She reached out to her idol, Patria Hume, a professor in human performance in the School of Sport and Recreation at the Auckland University of Technology.

“I went into the meeting, not really having much of a plan at all, I just told her what skills I wanted to learn and what my background was,” Renata said. It was Hume who brought up the idea of applying this to concussion research, suggesting a few different avenues they could pursue together. Renata felt it in her bones; this is what she was going to do! She knew it wasn’t going to be easy, but she found the motivation to dedicate herself to research once again.

Every day is a battle. Plagued with headaches, Renata continues to fight for her education and for the field of concussion research. Reflecting on her own experiences and how she could help herself, she realized a lack of concussion management on a global scale. She became coaxed by the idea of implementing change for concussion patients.

Combining mild traumatic brain injury (mTBI) with data science, Renata is extracting knowledge from national and clinical mTBI data that can aid in the prediction of patient recovery and optimize management pathways. Catering to the complexity of mTBI’s, Renata’s research allows for more personal management of individual patients, eliminating the typical “one-size fits all” approach. This knowledge will be implemented into a prototype clinical decision support tools that she hopes to eventually be used by front-line health care providers in order to support high-quality and consistent management of concussions.

“At times I feel like it’s a great thing that I study concussions, because the outcome is going to directly help people like me,” Renata said. Becoming an expert in the field, Renata has felt empowered in her own injury, knowing that she is the most qualified person to be handling her condition. She regained control over her situation through her studies after so many years of uncertainty.

But on the flip side, there are still times where this becomes a source of anxiety for Renata because there is still so much that we do not know. She explains that this can be deterring when trying to stay motivated because it affects both her research and her personal life.

“I was struggling to read a sentence that stated how concussions can cause concentration issues and lack of memory retention,” Renata recalled. “I’m sitting there with a massive headache thinking that’s what I am feeling right now. It can give you a bit of a complex.”

Having such an emotional connection to your research is rare, but it provides Renata with the passion she needs to persevere. Although she insists that she is not too involved in her degree, there are certainly times where the lines become blurry. “Bias and passion can be easily mistaken for each other,” Renata said. “I don’t think I have bias, but I definitely have passion. So I am scared that people would see that as

the same thing.” In academic situations, Renata says that she finds it difficult to remain impartial due to her personal experiences, and often catches herself using them as examples.

Renata’s passion certainly bleeds through her personality. Personally, I don’t know where I would be without her. Struggling with my own concussion throughout my undergraduate studies, we leaned on each other to get through every tough day and set back. Renata’s resilience and determination is infectious and she inspires everyone – especially those struggling with invisible illnesses – to fight through adversity. Leveraging her personal experiences, she became an expert in the mTBI landscape in New Zealand. Her work will redefine patient care and allow others to receive more personalized and advance treatment after sustaining a concussion.

Renata is not defined by her concussion. She chooses every day to fight against her limitations. It’s not easy, and not every day is pretty, but, from thousands of miles away, she inspires me every day.

> “
>
> At times I feel like it’s a great thing that I study concussions, because the outcome is going to directly help people like me.

text ROULA FARAG
photos EDEN HENNESSEY

#DistractinglySexist

Confronting Sexism in STEM with Eden Hennessey

The hashtag, #womeninscience, has been used on Twitter over 100,000 times.

Across the social media landscape, we hear about consistent underrepresentation of women in Science, Technology, Engineering, and Mathematics (STEM), but how many of us understand the how and why?

One of the difficulties women face when it comes to discrimination in science is how they respond to it. Eden Hennessey, a social psychologist, has devoted her career to studying the cost of confronting sexism in science.

Even in the 21st century, research has shown that science is still perceived as something masculine, whereas the arts is considered more feminine [1]. As a result, having women in science is often viewed as counter stereotypical.

To understand the cost of confronting sexism, Hennessey treats the issue as a research problem. She believes that discussions around the topic shouldn't only come from opinions but also from empirical research. But the work doesn't always come easy.

"A barrier to studying perceptions of sexism is the willingness to talk about it," Hennessey said. "In the scientific community, I get two responses. One is very guarded, 'I really don't want to talk about this.' Then there are other folks who are like, 'boy do I have a story for you.'"

Hennessey explained that one barrier to confronting sexism is the social cost – being viewed as a "complainer" or someone difficult to work with.

"Being perceived as 'bitchy' and 'bossy' were actually items that I measured during my work," Hennesey said. "And these are really loaded terms that are highly gendered."

Hennessey also believes sexism and racism must both be considered.

"White women may think, 'because the gender equity piece is making some headway I can confront.' Whereas a Black woman may not, because it's not safe to do so in the context of both racism and sexism. We have to consider that those barriers are going to substantially differ between people."

In addition to barriers, Hennessey's research also delves into how people perceive women confronting sexism and their responses. Generally, when asked to read a story about a woman confronting sexism in science, men had a negative perception, whereas women's perceptions were more positive. However, Hennessey notes that there are many contributing factors such as the approach and the context of the situation. The bottom line is, it's much more complicated than it seems.

To place a spotlight on the issue, Hennessey channeled her work into a series of photo exhibitions in a collaboration with photographer, Hilary Gauld. This personal and unique approach meant her research would reach an audience outside of science and academia.

"I have this artistic and creative side and being able to bring that into my research has been a really sustaining process."

In 2015, Nobel Prize-winning scientist, Tim Hunt, made a series of sexist comments during a conference about women being problematic in research labs because they fall in love and cry when criticized. This elicited significant backlash from women, especially in the science community, leading to the hashtag trend #distractinglysexy as a humorous

> "
> A barrier to studying perceptions of sexism is the willingness to talk about it.

In 2015, female graduates only made up

20%	18%	37%
Engineering	Computer + information science	Physical + chemical science

Numbers from Statistics Canada.

52% of Canadians can't name a woman scientist or engineer

in a 2019 online survey of 1,511 Canadians comissioned by non-profit, Girls who Code.

> “It started to become something that people wanted to talk to me about all the time.

response to Hunt’s sexist remarks.

Hennessey seized the opportunity to integrate the idea into her own research and decided to name her exhibit #DistractinglySexist. “Humor is also one of those responses to discrimination that is effective,” Hennessey said. “It diffuses the situation and makes it less emotionally charged.”

The photo exhibit took place in Wilfrid Laurier University during late September of 2015 to huge success. “When it first came out it was a bit of an explosion, it started to become something that people wanted to talk to me about all the time. And people wanted to have [the conversation] in their schools and in their discussion groups,” Hennessey said.

The exhibit paired the stories of nine women in STEM fields who faced sexism during their careers with research findings about gender inequalities in science. The work highlighted some of the common sentiments women in science receive including remarks like, “so you’re going for the whole sexy scientist thing,” and “my advisor told me not to worry my pretty little head about it.”

The work captured only a small sample of the many women interviewed by Hennessey as most of the interviewees preferred to stay anonymous. Ironically, these women feared the consequences of speaking out about their experience – which echoed Hennessey’s own research findings.

Even though majority of the responses to the #DistractinglySexist photo exhibit were positive, Hennessey said there were inevitably “haters.”

However, she was just as interested in these negative comments because it revealed a different response while confronting sexism. This led her to extend the #DistractinglySexist series with another photo exhibit in 2016 titled #DistractinglyHonest. The latter focused on what women are unable to say honestly about their experience with discrimination and sexism.

In early 2018, Hennessey presented her two photo exhibits #DistractinglySexist and #DistractinglyHonest in Trafalgar Square in London, England to celebrate the International day of Women and Girls in Science.

In 2020, Hennessey showcased her latest photo exhibit #TurningTablesinSTEM at the Ontario Science Centre. The work featured the voices of over a dozen more girls and women from across scientific disciplines. One story involves a young schoolgirl who couldn’t even find a children’s dinosaur sweater in the “girls” section due to restrictive gender marketing – highlighting the pervasiveness of cultural stereotypes.

For Hennessey, sharing and amplifying the stories of women is a big part of challenging the status quo.

Amanda Desnoyers
(PhD, Psychology)
and her son

#HonestlyChallenging

Shohini Ghose (PhD, Physics and Computer Science)

#HonestlyIngenious

"If you can make it personable, make it interesting, make it accessible to people, then you're going to get a much wider audience who's listening," Hennessey said.

Apart from raising awareness about sexism in science, Hennessey is also pushing for systemic and institutional change through her work with the Dimensions charter – an initiative that provides public recognition to post-secondary institutions with increased equity, diversity, and inclusion.

"It's a voluntary program where you and your institution can sign up and say you commit to these principles," Hennessey explained. "Things like, recognizing the important contributions of Indigenous people to the knowledge of science and research."

Hennessey also works on issues surrounding sexism in STEM as a member of the Laurier Centre for Women in Science. There, she works alongside centre founder and physicist, Shohini Ghose, to support interdisciplinary research and create opportunities for women in science.

Hennessey explains the three main pillars are, "to do the research, to communicate the research, and to take action based on what the research says."

"Everyone, often, within science is incredibly skilled and talented so how do you distinguish yourself from other people?" Hennessey said. "We need more people to be able to communicate their science."

"We need to work on the stereotype of what a scientist looks like at the same time as representing their work."

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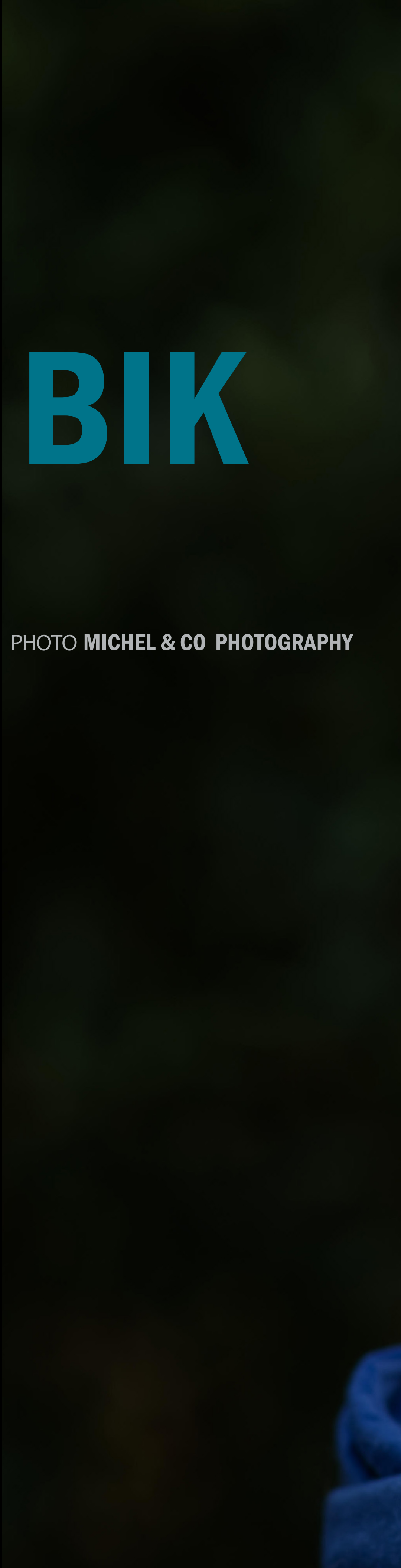
MEET ELISABETH BIK

SCIENTIFIC FRAUDSTER BUSTER

TEXT **ZARWA SAQIB** PHOTO **MICHEL & CO PHOTOGRAPHY**



Elisabeth Bik has caught a lot of public attention through her Twitter account, @MicrobiomDigest, where she reports evidence of image forgery in academic research papers - including from respected journals like *Science* and *Nature Communications*. Bik's unique image sleuthing skills and perseverance have earned her a worldwide following of around 70,000 followers on Twitter. She challenges her growing audience by posting suspected de-identified images under the hashtag, #ImageForensics, and requesting for comments on apparent problems before revealing her answers. "Once you point it out, others start seeing it more," Bik said. "Interestingly, some people have picked up the data cop skills and have started to contact me privately about problematic images they see while peer-reviewing manuscripts or reading papers." Bik estimates that she has spent more than 5,000 hours inspecting papers over the past few years in an effort to corroborate reliable science for not only researchers but also for the public.

A microbiologist by training, Bik decided to quit her full-time job at a biomedical start-up firm in California to better serve the research community as an image integrity data cop – pro bono. “It started as a hobby, but soon I realized my passion for image sleuthing was growing more than my paid job,” she said.

> “IT STARTED AS A HOBBY, BUT SOON I REALIZED MY PASSION FOR IMAGE SLEUTHING WAS GROWING MORE THAN MY PAID JOB.

A 2019 cross-sectional study found that for every 10,000 publications on PubMed 2.5 are retracted, with 65.3 per cent of cases being due to misconduct [1]. Scientific misconduct is not limited to plagiarizing text without giving credits, but it also extends to instances where images are reused and reported as “new data,” or where parts of images are rotated, shifted, or cloned to represent experiments that were never performed. Bik’s Twitter account cited many such papers with apparent problems, such as unconfessed reuse of images, or the minutely botched duplication of parts of images.

Bik first stumbled upon the reports of suspected misconduct in the literature when she found an online book chapter with text plagiarized from her published review on the microbiome. “The plagiarized paper was a patchwork of stolen sentences from various resources, including mine, without any authorship,” Bik said. Then, while browsing through a doctoral thesis, she noticed multiple copies of a western blot (a test used to detect proteins in biological samples) shifted in different orientations to represent different experiments. However, a more concerning fact for her was that these thesis chapters were published as research articles, with the same errors. “Image forgery and doctoring are much worse than plagiarizing text,” Bik said. “It’s significantly misleading science, and if you want to publish data then it should all be done properly and honestly.” In fact, studies have suggested that up to one in five papers in the life sciences include manipulated photographs or images [2]. However, rarely do reported cases lead to retractions or corrections.

In 2019, a study followed 12 retracted articles and reported that only one out of 68 papers that cited the retracted work was re-evaluated and amended to account for the retraction [3]. Frustrated by discovering plagiarized text and doctored images in publications, Bik started using her twitter account as a place to highlight potential problems in the published scientific literature.

Unlike other image sleuths who work behind closed doors and prefer not to be identified, Bik has a reputation of posting detailed comments and criticism seen in papers on PubPeer – a post-publication feedback platform for researchers. Bik estimates that since 2014 she has unfearfully published approximately more than 2,000 comments under her name on PubPeer. Her willingness to attach her name to the criticisms encourages authors and other researchers to take her allegations seriously. The avalanche of reactions and public awareness generated by her work has pressurized journals to investigate papers and have prompted dozens of retractions, including 22 papers from *PLoS ONE*. Bik estimates that her reports have contributed to more than 170 retractions and approximately 300 errata and corrections.

Bik’s courage to call-out data fraud has inspired other scientists to report instances of misconduct more publicly. In 2018, a group of scientists reported and launched retractiondatabase.org, one of the largest databases consisting of 18,000 retracted journal articles, dated since the 1970s [4]. Scientists recognized that the number of retracted papers containing flawed images rose to 24 per cent in 2002, but the number has since been oscillating. “The scourge of fraudulent image doctoring in biomedical research articles is very common,” Bik said. “If your results can’t be trusted then other people can waste their careers, time, and money on trying to replicate data that does not exist.”

Who to blame? Technical glitch or human error?

In 2016, Bik and colleagues published a detailed study where they screened and analyzed more than 20,000 biomedical papers from 40 different journals in an effort to investigate and prove the increasing prevalence of “problematic images” in scientific papers [5]. They reported about 782 papers (or four per cent) which contained deliberately manipulated scientific images.

“Our publication was one of the first to investigate the frequency of problems in biomedical work,” Bik said. “It has led to much greater awareness and scrutiny among journal editors and peer reviewers.” The authors highlighted “problematic images” to be of great concern as it was evident that some aspects of the scientific literature could not be relied upon. The United States Office of Research Integrity (ORI) has reported that the surge in the use of manipulated and fraudulent images increased after the birth of Photoshop in 1990. “Numerous postdocs and students waste months or years chasing things which turn out to not be valid, so it’s not only damaging science but also careers and lives,” Bik said.

Bik admitted that suspicious data doesn’t always indicate corrupt intent as 90 per cent of scientists are sincere and many errors are honest mistakes that don’t necessarily require a paper retraction. “Sometimes authors swiftly reply to me on PubPeer under their critiqued papers to point out honest errors ranging from reasons like: images not being clearly labelled, improving image background contrast for clarity, to mistakenly uploading a file twice when preparing images,” Bik said. Additionally, other honest errors can result due to defective equipment. For instance, a faulty microscope might cause the appearance of similar dark spots on every image.

Or technical artefacts from sample slices sticking together and then flipping in an orientation that can lead to an apparent mirrored duplication. “Not every issue means a paper is fraudulent or wrong,” Bik said. “But some do, which causes deep concern for many researchers.”

A study conducted at Arizona State University reported that the increasing pressure to secure external funds, the publish or perish mentality, and the slim odds of being exposed for fraud were the top motivators in prevailing cases of scientific misconduct [6]. These motivators in-conjunction with new and conveniently available image modifying tools has only increased misconduct. “In the days before imaging software became widely available, tasks like manipulating results or academic figures required considerable effort and professionals who had no prior knowledge about the collected data,” Bik said. However, the technological advancements of the 21st century have not only increased the speed of data collection but also made it more tempting to adjust or modify digital image files before reporting them [7]. A study by Bik and colleagues found that “academic culture, peer control, cash-based publication incentives, and national misconduct policies” all affect scientific data integrity [8].

In late 2019, Bik was cast in the spotlight when she placed a prominent Chinese immunologist, Cao Xuetao, under scrutiny for having several flow-cytometry images doctored in a 2009 paper published in the *Journal of Immunology*. The wide media coverage led to an investigation of a multitude of articles by China’s ministry of education and a re-examination of the manuscripts by Cao himself. Bik found that Cao’s lab published 250 research papers and about 50 of them contained problems ranging from duplicated to doctored images. But even in cases where misconduct may have been deliberate, Bik explained that the primary investigator may not always be the one behind the wheel. “These situations prove that there is not enough oversight,” Bik said. “Primary investigators from huge labs mostly don’t have time – due to other responsibilities and busy schedules – to review papers before publishing. Although, they are not entirely responsible for conducting misconduct themselves, they are still responsible as it’s a joint effort to not only support and promote true science but to also train honest scientists.”

> “IF YOUR RESULTS CAN’T BE TRUSTED THEN OTHER PEOPLE CAN WASTE THEIR CAREERS, TIME, AND MONEY ON TRYING TO REPLICATE DATA THAT DOES NOT EXIST.

More recently, Bik alongside other pseudonymous data cops, including mortenoxe, TigerBB8, Cheschire, schneiderleonid, and SmutClyde assembled and uncovered over 400 research papers in China that all originated from the same paper mill. The company was suspected of generating articles with fake research and fabricated images for medical students. Many students in research programs across the world are required to publish as part of their degree requirements which may encourage misconduct. “The unrealistic goal by the Chinese government requiring medical students to publish research papers during training is really jeopardizing science,” Bik said. “Students don’t have the time to complete research projects but are forced to publish to earn their degrees.”

Open science communication to the rescue

Bik uses an old Mac with an attached monitor and her own eyes to find suspicious figures before notifying the journal in question and politely pointing out suspicious images. Although Bik is proficiently skilled at finding duplicated images, a single person can only do so much. “We need more paid staff at universities and institutes where people can use their talents to deal with these data integrity cases,” Bik said.

Bik explained that combating image manipulation and duplication necessitates pre-screening of accepted manuscripts and other system-wide changes in science publishing. Many journals like *EMBO* are executing steps and standards to check submitted figures for evidence of tampering. *EMBO* has reported that inserting pre-publication check points has helped them catch manipulation in 20 per cent of accepted papers – a stubbornly high percentage considering the journal’s transparency about its screening policy. Unfortunately, many journals still do not pre-screen their images or in some cases, like *Nature*, only randomly spot-check papers before publication [9]. Publishing company, Wiley, publishes some journals that pre-screen images, and is in the process of starting a screening service with the well-known *Journal of Cellular Biochemistry* and the *Journal of Cellular Physiology* [9]. *Science* has arranged for editorial coordinators to examine accepted manuscripts for suspected image manipulation. However, only looking at submissions individually may mean that images flipped, rotated, and then duplicated in a second paper will be missed [9]. Following Bik’s analysis of 960 papers published in *Molecular and Cellular Biology*, which found 6.1 per cent of papers containing duplicated and images, the journal launched a pilot image screening program which has identified problems in 14.5 per cent of subsequent submissions. After Bik highlighted issues of research misconduct in *PLoS ONE*, the journal formed a three-person team dedicated to managing and investigating image integrity and other publication ethics cases in 2018. “I get a sense of job well done when I receive regular notifications of *PLoS ONE* retractions and corrections that have stemmed from my leads,” Bik said. In line with open science efforts, some journals like *eLife* have allowed post-publication feedback on their papers. Other online venues like JournalReview.org and PubPeer have also been created to permit readers to discuss and critique papers from multiple journals. For institutions and journals without internal image detection capacity, companies and organizations including Image Data Integrity (IDI) and the International Life Sciences Institute (ILSI) can provide consultation.

In 2019, the Scientific Integrity Consortium published a detailed recommendation list to encourage ethical scientific conduct [10]. Recommendations encourage scientists to consider the implications of their conducted research on the public, and suggest institutions ingrain the significance of fundamental research ethics in their scientists. This involves fostering the importance of following standardized publication expectations (from appropriate study design to proper data analysis), remaining transparent when reporting study findings, and encouraging a sense of accountability for their research. The consortium also urged journals to value research that may not always represent exciting or positive results due to the nature of the phenomena under investigation. Instead, journals should communicate all types of results by using terms such as “anticipated” and “unanticipated” instead of “positive” or “negative” results [10].

> “
> IT’S A JOINT EFFORT TO NOT ONLY SUPPORT AND PROMOTE TRUE SCIENCE BUT TO ALSO TRAIN HONEST SCIENTISTS

These efforts of ensuring open communication and implementing clear and stringent guidelines for authors to follow highlight the responsibility on authors for ethical and accurate representation of their scientific data. “It’s always good to go over your papers and make sure there is nothing wrong with the images and the text because your name is on it,” Bik said. However, peer-reviewers must also be vigilant in spending time to thoroughly review and investigate articles before acceptance. Furthermore, journal editors must be the final gatekeeper in ensuring publication ethics are well regulated, and quickly following through with consequences for clear cases of image manipulation.

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Can automation replace the human eye?

Many image forensic softwares are being developed to fight image doctoring in academic research. Most publishing houses use iThenticate or Turnitin.com softwares to look for textual similarities in papers, but regular softwares to pinpoint

● ● ● ● ●

THINK YOU’VE GOT WHAT IT TAKES?

These are all figures from retracted papers. Can you spot where sections of the images were flipped, rotated, and duplicated?

CHALLENGE #1

Fluorescence microscopy

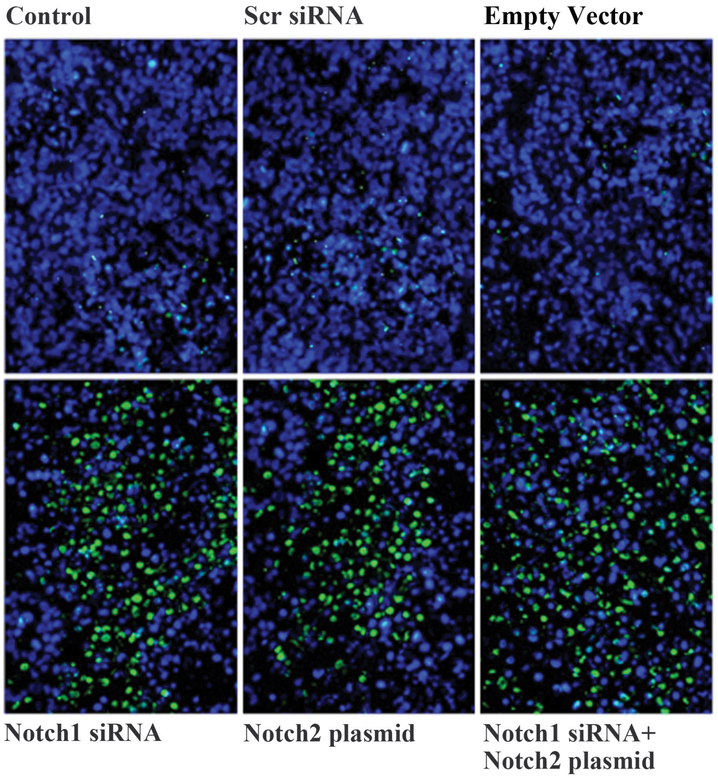


image similarities are yet to be developed. “They are being tested by publishing houses and journals,” Bik said. “But they are not yet on the market.”

Recently, *Nature* reported the development of an image integrity check software by a New York team led by machine learning researcher Daniel Acuna [11]. The software is intended to examine problematic images through hundreds of thousands of biomedical papers for anomalies like rotated parts, changed colors, and inappropriate reuse. The software is potentially capable of comparing every image with every other to report if a certain manipulation was intentional and hence more likely to be fraudulent. Although the software is computationally intensive, the team only accounted for cases of image reuse within and across papers by the same authors. Additionally, when the team manually examined all the flagged papers, only a handful of them actually contained fraudulent images. However, almost half of the true cases identified by the team were cases of the same image being used to represent different results in different papers [9].

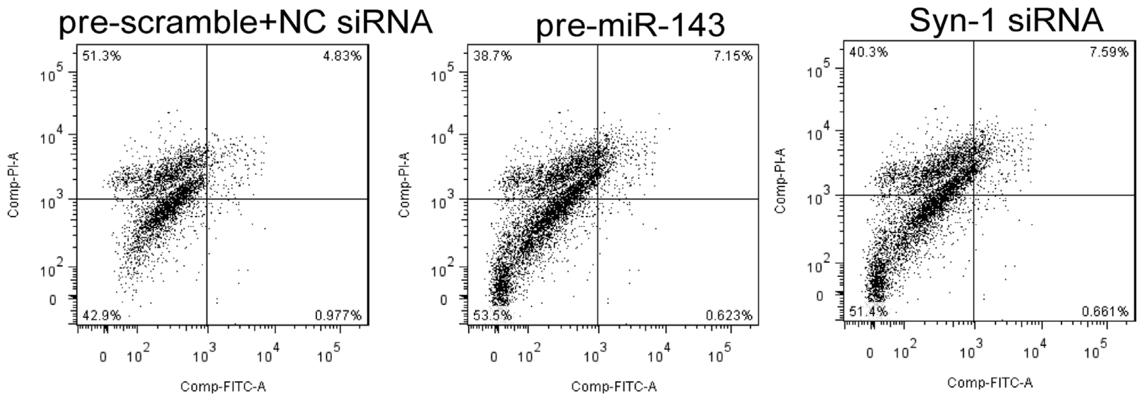
While current technology is capable of detecting obvious duplications involving flipping or rotations, the problem arises when duplications are minute, such as two images that share only a small overlapping area but are otherwise completely different. Further advances in machine learning are required to detect these subtle patterns automatically.

“[Technology] can replace the human eye for screening large numbers of papers and comparing one image against a million other published images faster,” Bik said. “But human verification would still be required to help reduce false positives.” Another problem with developing an advanced software is the need for more data as machine-learning algorithms require training with plenty of images known to contain duplications. To combat the problem, Bik has generously shared with Acuna’s team images from hundreds of “dirty” and “clean” papers from her 2016 study.

Until technology catches up, calling out misconduct will remain a job for image integrity data-cops like Bik. “Many times, other image sleuths and I have attempted informing journals privately via email [of possible misconduct], but the cases are often neglected or go down a long road before the cases are resolved,” Bik said. Although, she acknowledges and respects that misconduct investigations take time, she argues that expressions of concern should be implemented early on in the investigation to notify other researchers and readers of potential serious concerns with the paper while long investigations are pending. “I can tell you that 60 to 70 per cent of the cases [documented] in the mBio dataset have not been addressed even after five years,” Bik said. “So, yes, I’m going to take this and other cases more publicly in hopes of making science more authentic and stopping scientific fraudsters from carrying out misconduct.”

CHALLENGE #2

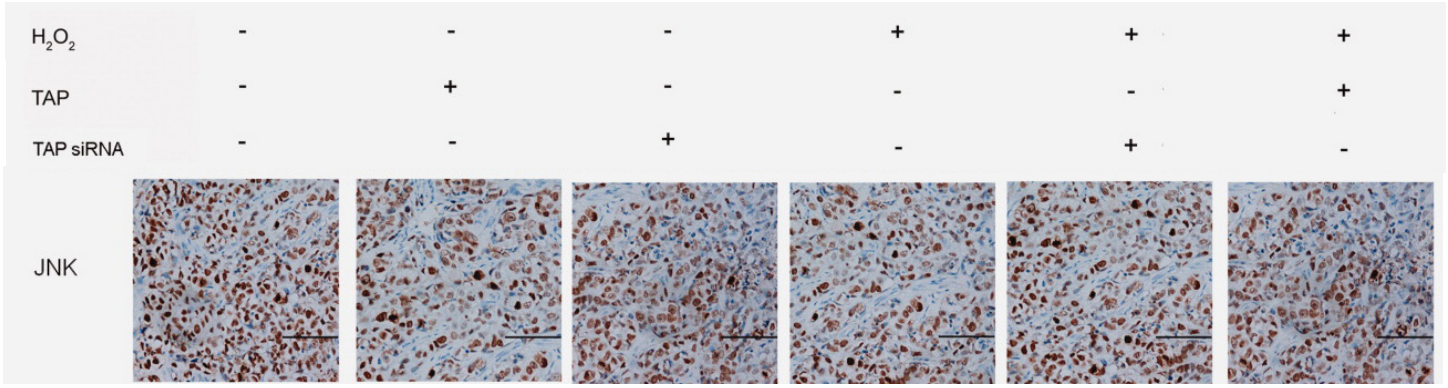
Flow cytometry



Find the answers on page 48

CHALLENGE #3

Immunohistochemistry



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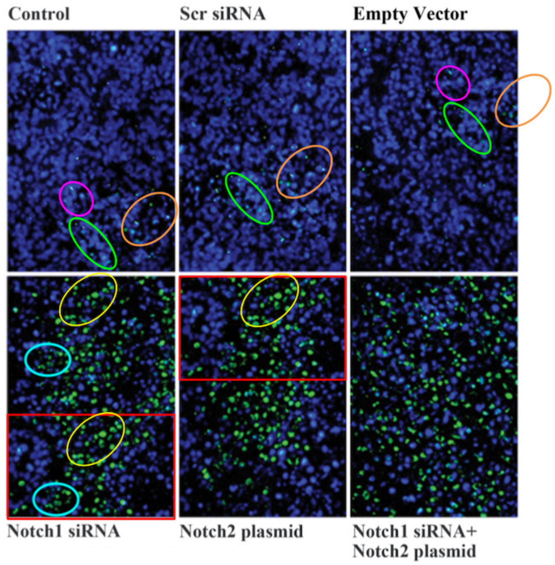
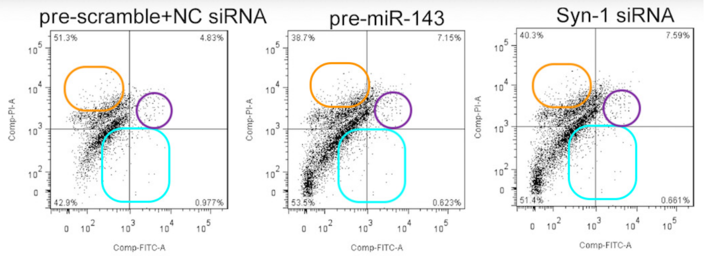
ANSWERS

Learn more about the different types of image duplications and how to report misconduct to a journal on Bik's website: scienceintegritydigest.com

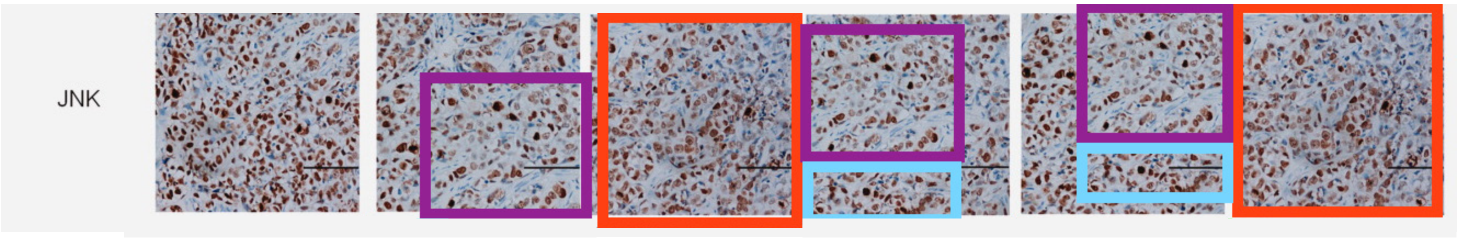
CHALLENGE #1
Fluorescence microscopy



CHALLENGE #2
Flow cytometry



CHALLENGE #3
Immunohistochemistry



Health Science Inquiry IN REVIEW

A decade of graduate student-run health science publishing

TEXT **KEVIN DICK** | PHOTO **PAWEL CZERWINSKI**

Scientific communication is a core facet of the academic process. Universities and research institutions expend considerable resources on student didactics and training to engage them in the pursuit of elusive research questions. However, dedicated training on scientific writing and exposure to the peer-review process are comparatively rarer; knowledge is typically acquired experientially and through mentorship. With a growing pressure on the scientific community to disseminate articles, the "publish or perish" aphorism succinctly embodies this frenetic rate of publication that has evolved the scientific journal article into a unit of research productivity [1]. It is increasingly crucial that, as part of the academic apprenticeship process, graduate students receive dedicated scientific communication training and ample opportunities exposing them to the peer-review process.

Publishing experience is an invaluable part of research training. Students develop an appreciation for the submission, peer-review, and acceptance/rejection phases of the peer-review process. Additionally, they learn to formulate and defend hypotheses while being held to account for reported research findings. Most importantly, the ability to critically appraise emerging research findings and to appreciate their implications in the context of contemporary literature is a fundamental cornerstone of post-graduate education. Experience of the various roles in the scientific communication pipeline, whether as an author, reviewer, proofreader, or editor, can be tremendously rewarding and promotes the development of the requisite soft skills for both academia and the industry workplace [2].

For those interested in pursuing scientific communication more seriously, formal training for a career in scientific publishing is not only rare, it is a growing concern given the need to staff the growing number of biomedical

TABLE 1 | Annual Publication Themes and Subthemes for the past 11 volumes

Vol. No.	Publication Cycle	Volume Theme	Subthemes
1	2009-2010	The H1N1 Pandemic	• Development & Deployment of Vaccinations • Surveillance & Response to H1N1 • H1N1 as a Global Pandemic
2	2010-2011	Cancer	• Treating & Pursuing a Cure for Cancer • Prevention of Cancer • Life after Cancer
3	2011-2012	Obesity & Diabetes	• Advances in Molecular, Genetic, & Clinical Research • A Sociological View of Obesity & Diabetes • Impact of Nutrition on Obesity & Diabetes
4	2012-2013	Mental Health & Neurological Diseases	• Social, Economic, and Environmental Determinants of Mental Health • Age-Related Neurodegenerative Disorders • Advances, Challenges, and Controversies in Diagnosis, Treatment, & Management
5	2013-2014	Primary Health Care & Health Care Reform	• Exploration of Challenges & Opportunities for Primary Care Delivery • Role of Primary Health Care in Prevention & Control of Acute & Chronic Disease • Public Engagement in Reform Initiatives
6	2014-2015	Advancing Human Genetics into Health Action	• Personalized Medicine & Gene Therapy • Ethical & Social Challenges Surrounding Human Genomics • Impact of the Environment on the Human Genome
7	2015-2016	Allergies, Autoimmunity, and Microbiome	• Current Research Advances in Allergies & Autoimmunity • Role of our Microbiome in Shaping & Regulating the Immune System • Environmental Influence on Allergies & Autoimmune Disorders
8	2016-2017	Gene Editing & Personalized Medicine	• Clinical Applications of “-omics” Technologies in Personalized Medicine • The Role of Genome Editing in Health Care • The Social & Ethical Implications of Genome Editing
9	2017-2018	Obesity & Diabetes	• Nature • Nurture • Consequence
10	2018-2019	Chronic Disease	• The Future of Medicine & Treatment • The Future of Technologies in Health & Research • The Future of Health & Society
11	2019-2020	Determinants of Health	• Natural Environment • Technology • Socioeconomic Environment

journals. Not only are opportunities lacking, but the requisite competencies for training an individual in journalology are not fully understood [3]. Promisingly, there exist a [possibly growing] number of graduate-student run biomedical journals in Canada and abroad which provide opportunities to young scholars and early-career scientists to engage in the scientific publication process. In Canada alone, there exist eight active medical student-run journals which collectively publish over 200 articles each year [4]. Here, a meta-analysis of a pan-Canadian, graduate student-run, health science journal is presented in the hopes of exploring both the successes and impact on graduate students and the broader scientific community.

THE HEALTH SCIENCE INQUIRY JOURNAL

The Health Science Inquiry (HSI) is an entirely graduate student-run journal which relies on contributed articles and volunteered time from master's, doctoral, post-doctoral, and medical students across Canada. In the inaugural issue of HSI in 2010, then managing editor, Inderjeet Sahota eloquently captured the essence of what HSI was to embody as a medium for scientific discourse [5]:

> "Writing is an integral part of academia. The free flow of information is what allows science to continue developing, and without the ability to write these ideas down in a coherent and comprehensive manner, this transmission would not be possible. As students of science, the ability to write and allow for this exchange is an important component of our training. Scientific advancement, and arguably human advancement on many levels, relies strongly on this element of discussion. Through dialogue we are able to communicate our perspectives and hear the perspectives of others. In this we have the opportunity to gain new insight, develop new ideas and expand our knowledge of the world."

> " Writing is an integral part of academia.

A retrospective review of the past volumes revealed that the ensuing decade saw the publication of 284 peer-reviewed articles by student-scholars from over 27 Canadian institutions. Every year, a timely theme was selected with three sub-themes serving as a guide to orient contributed articles (Table 1). Notably, the topics covered a broad array of health systems, including the epidemiological facets of the H1N1 pandemic, oncologic research, genomic engineering, and anticipated future developments within medicine. To visualize the relative frequency of the most common terms appearing in each year's issue, the text was extracted for all articles in each issue and a wordcloud was generated (Figure 1); the terms for all years were also combined to generate a wordcloud representative of the decade. While the first nine volumes focused on specific health systems, as seen with word frequencies generally matching the volume theme, the tenth and current themes were more open-ended and amenable to research across the health sciences or to any medical system. Interestingly, the subthemes of the latter half of the decade generally included some element of social impact, environmental influence, technological development, or contemporary medical research (Table 1). With the increasingly interdisciplinary nature of heath science research, the selection of open-ended

FIGURE 1 | Wordcloud representation of each HSI issue & of all published text.

A combined wordcloud representative of all published HSI text (top) as well as individual wordclouds for each issue.

(sub)themes will enable student-scholars with more diverse educational backgrounds, such as engineering and computer science, to contribute their work.

The year-to-year analysis of the number of contributed articles reveals several notable trends (Figure 2). HSI publishes peer-reviewed articles under two branches: *Main Submissions* are externally-contributed technical articles from student-scholars while *Developed Content* comprise internally-contributed news articles, "ask an expert" articles, and "spotlight on career" articles. While externally-contributed artwork and short fiction are also accepted and published, these pieces were excluded from the following analyses. Figure 2 compares the number of annually published pieces by type in addition to the volume total. The main submissions comprised the bulk of published content for the first five years, then fell to all-time lows in 2015 and 2016 before recovering again in the latter three years. As externally-contributed work, volatility can be expected; innumerable factors influence the reception of submitted articles while staff have limited ability to control or stimulate contribution. Conversely, staff have direct control over the generation of internally-contributed content-type articles. We observe a progressively increasing trend in the number of published content-type articles over the course of the decade, roughly converging towards parity.

PAN-CANADIAN VOLUNTEERING

The publication of such a large number of articles could not have been possible without the dedicated time and effort of the small army of volunteers supporting HSI year-over-year. A retrospective analysis of the home institutions of HSI volunteers reveals a strong representation of staff among four institutions with the University of Toronto (UoT), McGill University, McMaster University, and the University of Western Ontario (UoWO) comprising the top-four institutions when sorted by total volunteer-years over the last decade. The measure of "volunteer-years" (Vys) considered in this work is analogous to that of "person-hours ": we count the amount of time dedicated to volunteering regardless of the individual(s) who volunteered that time. Tenure for all positions, regardless of the actual number of worked hours, is held for a single Vy which, though naïve, simplifies the aggregation of contributed effort. For example, the three Vys contributed by Carleton University (Figure 3) may all have been attributed to a single Carleton-based volunteer holding different roles over three years, or to three unique individuals, each only volunteering for a single year. Fortunately, HSI enjoys a consistent retention of volunteering staff where we see many of the same individuals returning, resulting in a strong representation among the most involved institutions.

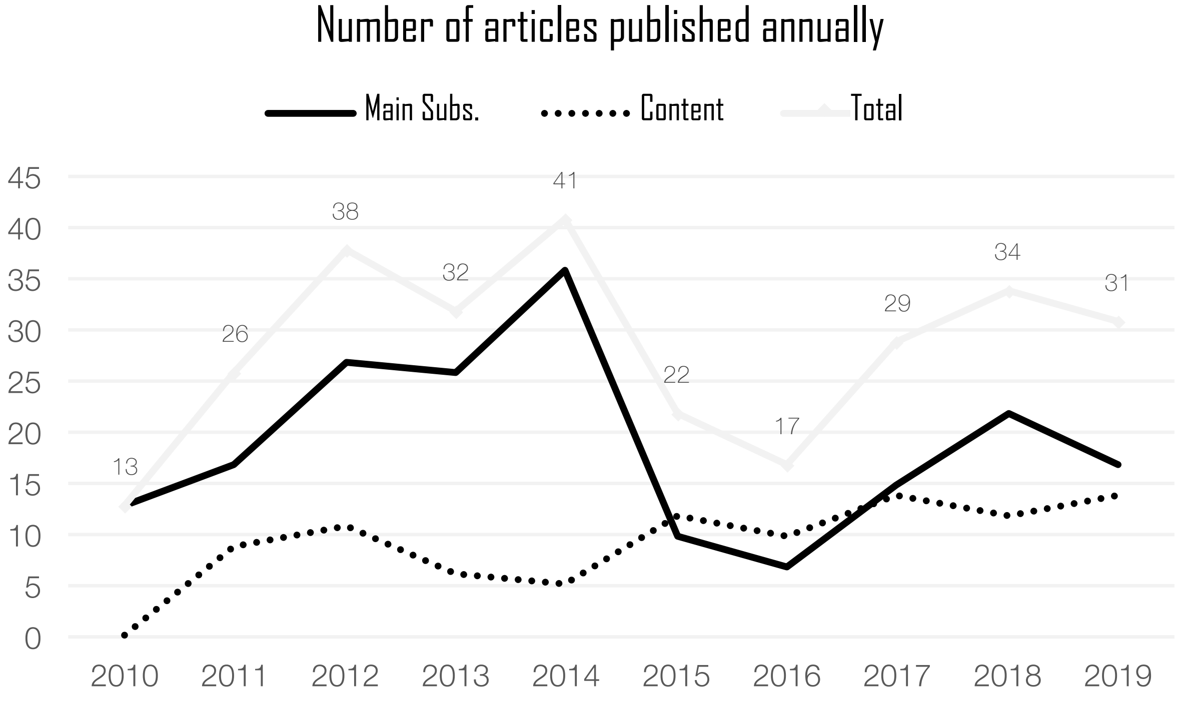


FIGURE 2 | Number of articles published annually by HSI over the past decade.

The main submissions generally comprise the bulk of the published materials except in 2015 and 2016 where the number of main submissions fell to an all-time low and were surpassed by the content-type articles. Since main submissions are externally-contributed we can expect volatility; conversely, content-type articles are internally-contributed and therefore controllably stable. Notably, the latter type are generally annually increasing.

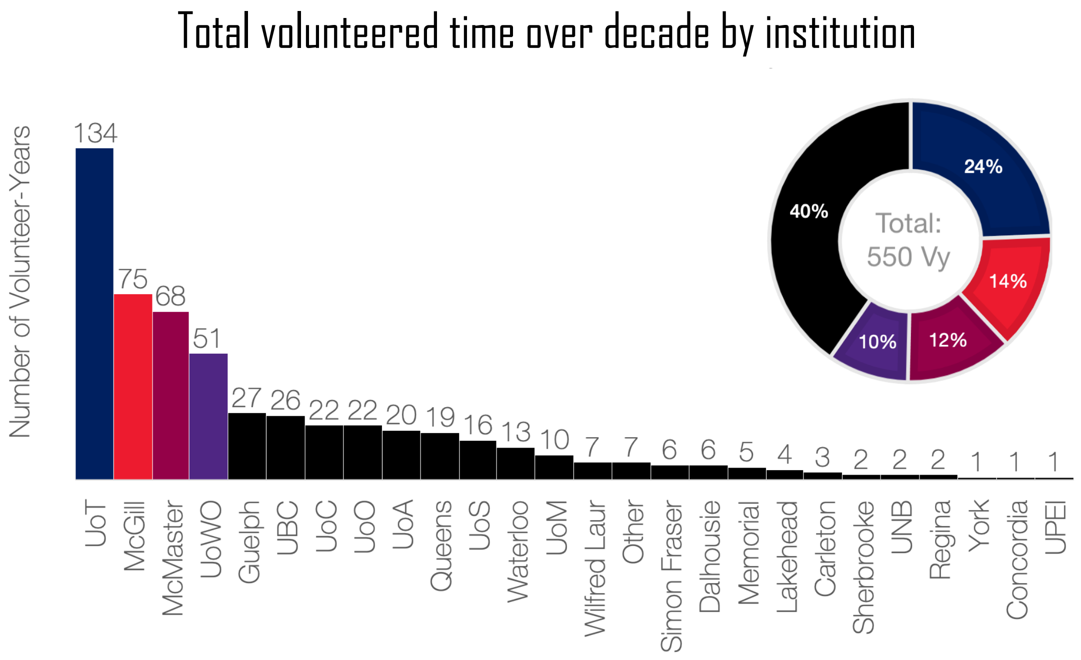


FIGURE 3 | Total volunteered time by institution through the previous decade.

The top-four institutions are highlighted as having contributed the majority of volunteer-years to HSI (~60 per cent). The long-tailed distribution demonstrates the relative contributions of other institutions around Canada. A total of 550 volunteer-years have been dedicated to HSI over the last decade (including 2020 staff). Impressively, UoT comprise approximately a quarter of all dedicated volunteer-years, which might be expected of the founding institution.

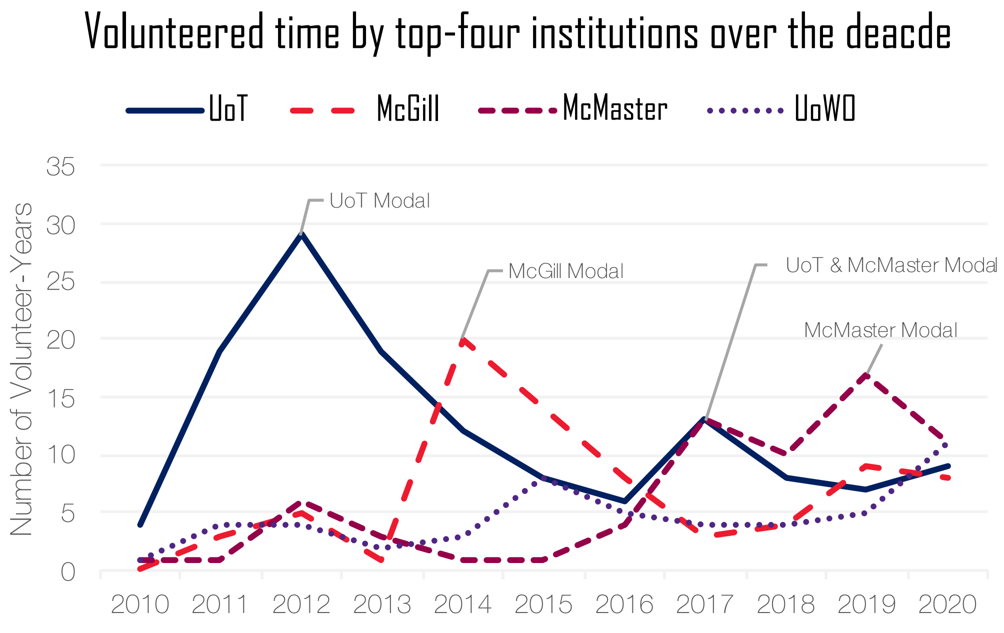


FIGURE 4 | Volunteer-years of the top-four institutions throughout the decade.

Illustration of the waxing and waning trend of volunteer contribution among the top-four4 institutions over ten years. Notably, UoT was the modal contributor within the first four years, which might be expected as the founding institution. McGill then became the modal institution for three years, peaking in 2014. Both UoT and McMaster shared a modality peak in 2017 with the latter taking modality last year. Promisingly, these four institutions share approximately equal contribution in this year's staff. A desirable trend within this next 2020 decade might see an approximately uniform contribution of volunteer-years among these four institutions as well as among the other Canadian institutions.

An impressive 550 Vys supported HSI over the last decade (including the current staff) averaging to approximately 50 staff members annually (Figure 3). The contribution of Vys by institution depicts a long-tailed distribution, where the top-four institutions, highlighted in Figure 2, represent approximately 60 per cent of all volunteered time. The University of Toronto alone comprise approximately 25 per cent of all Vys.

A more in-depth analysis of the contributed volunteer time among the top-four institutions throughout the decade revealed interesting trends in *modality*: the institution from which the greatest number of Vys are contributed (Figure 4). The four years following its founding, UoT was the modal contributor, then overtaken by McGill for the next three years. Both UoT and McMaster shared modality in 2017 and McMaster has been modal since (Figure 4). Promis-

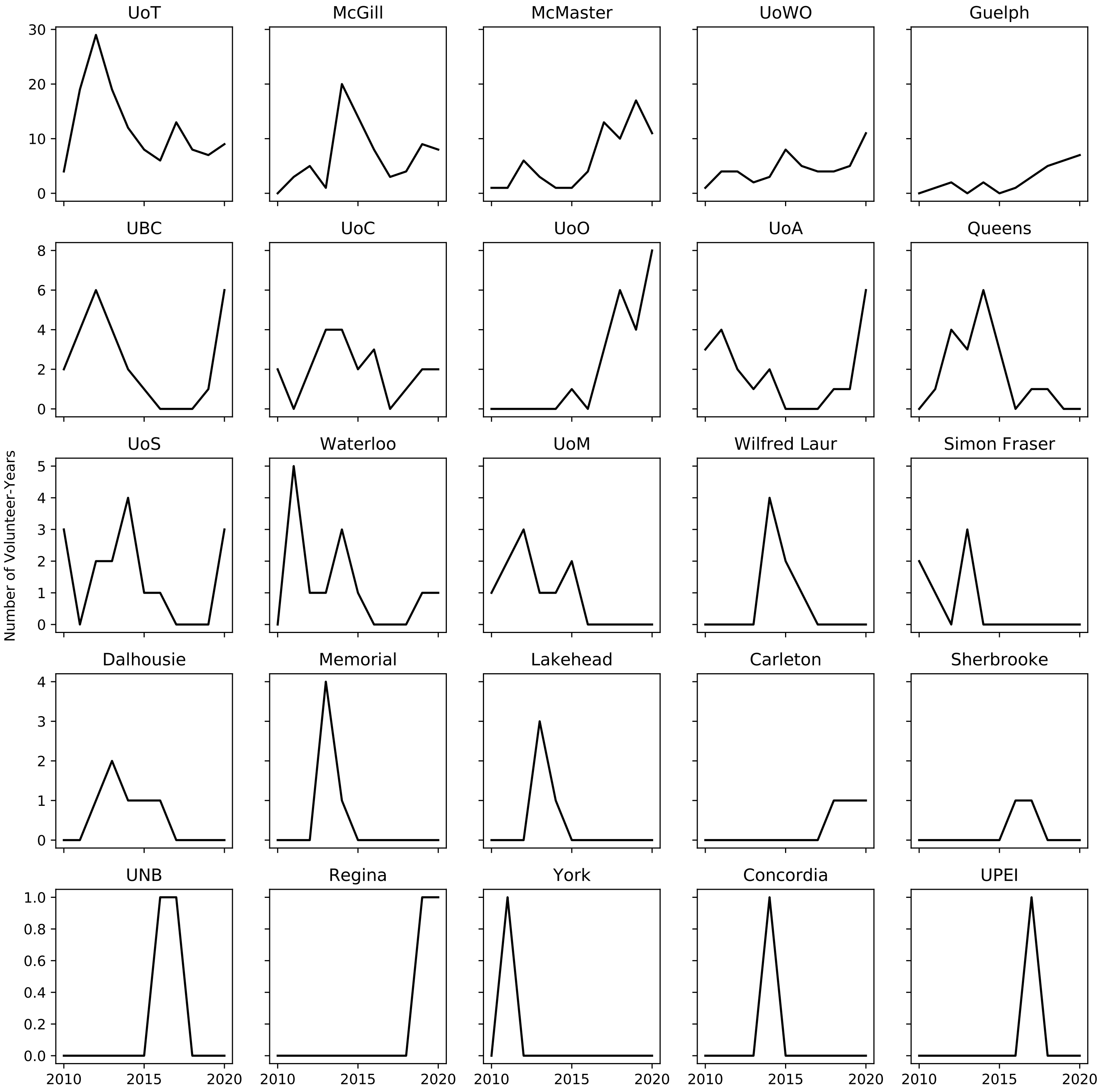


FIGURE 5 | HSI volunteer-year distributions by canadian institutions.

Note that the shared y-axis scale varies by row; the top row ranges from (0,30) while the bottom row depicts binary spikes in the range (0,1).

ingly, the top-four institution each have approximately equal representation among this year's staff, perhaps establishing a desirable level of representation for the HSI staff of the coming decade. The same analysis of institution-specific contribution over the decade was extended to all participating Canadian institutions and is depicted in Figure 5.

INSIGHTS FOR THE FOLLOWING DECADE(S)

Reflecting on the selected themes, the trends in published articles, and the in-depth view of volunteering effort from institutions across Canada, a number of insights might be drawn to orient the HSI as we move into the next decade(s).

Viral & Timely Themes

Ironically, HSI's founding issue theme was selected due to the timeliness of the H1N1 influenza pandemic. With the health concerns of the Zika virus circa 2016 and the present Coronavirus pandemic, it can be expected that viral outbreaks will be thematic in the next decade(s). Furthermore, the recent focus of subthemes on societal, technological, and environmental factors (Table 1) also highlights certain timely issues that may be expected of future themes en route to 2030 and beyond: climate change, globalization, nationalism, digital health, telemedicine, natural disasters, indigenous affairs, urban water crises, data privacy, overpopulation, immigration, the $100 genome, and healthcare in the age of artificial intelligence and quantum computing.

> HSI HAS CONTRIBUTED A TOTAL OF **550** VYS OF EXPERIENCE IN SCIENTIFIC PUBLISHING TO GRADUATE STUDENTS FROM OVER **25** CANADIAN UNIVERSITIES.

Towards Article-Type Parity?

The past decade has seen a varied number of published articles, year-over-year. Figure 2 highlights the volatility in externally-contributed articles, although the majority of lower-tier journals suffer from the same challenge resulting in the over-solicitation of articles from potential authors [6]. The inability to control submissions raises a number of questions related to balancing the ratio of main submissions to internally-developed content: what is an appropriate ratio? What is the *ideal* ratio? Should a minimum be established? Should parity be enforced? With the waxing and waning of contributing staff and individual interests, perhaps it is simply best to allow content to develop organically. Perhaps the coming decade will see convergence or express new trends; you, who is writing the future HSI meta-analysis, what insights have you found?

Towards Equal Representation across Canadian Institutions

Past and present, HSI volunteers hail from over 25 Canadian universities (Figure 3), yet Figure 5 demonstrates that in the majority of cases volunteer participation flashes in and out, with little sustained continuity. While it is promising that the majority of Canadian universities have shared *some* participation as part of HSI, ideally the next decade(s) would see a growing, if not eventually equal, representation from each institution. HSI benefits from its diversity of perspectives and current staff should engage in a concerted outreach effort to solicit future staff from under-represented institutions.

CONCLUSION

The Health Science Inquiry has enjoyed a successful decade of soliciting, peer-reviewing, and publishing the contributed articles of student-scholars throughout Canada. As an organization, HSI has contributed a total of 550 Vys of experience in scientific publishing to graduate students from over 25 Canadian universities. An in-depth examination of the number of contributed articles and the number of volunteers reveals that HSI continues to grow as an organization, promising increased opportunity to present and future graduate students. It is the hope of this article that the reflections of the trends through the past decade will orient future HSI staff members, as well as members of other graduate student-run journals, on aspects of theme selection, the rate of publishing, and contributed volunteer time. With great eagerness, I anticipate HSI's evolution through the next decade(s).

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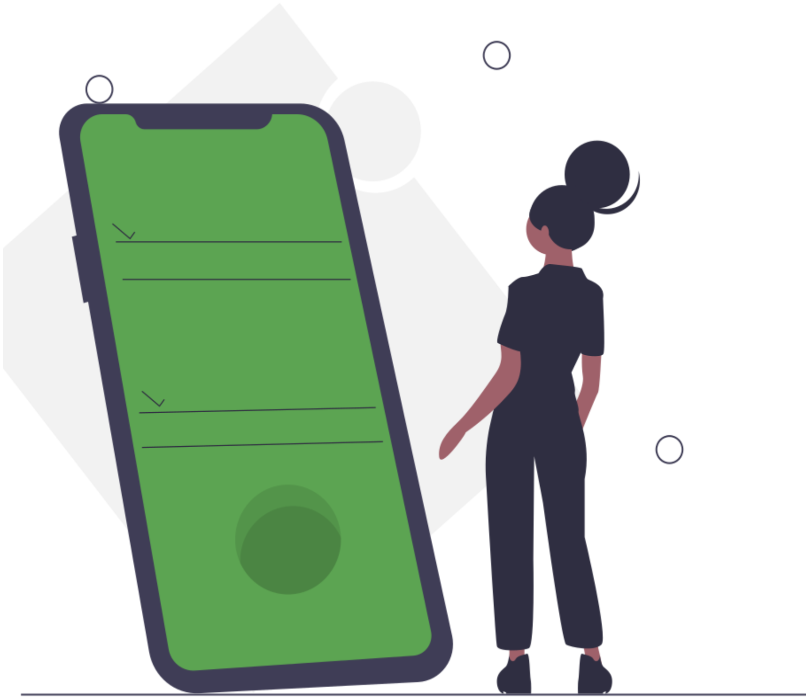
FEATURE

When Social Media Met Nutrition

How influencers spread misinformation, and why we believe them

TEXT **ZOE LOFFT**
VISUALS **KATERINA LIMPITSOUNI**



Over the past decade, the proliferation of social media platforms and the emergence of the role of "influencers" on social media has led to a potentially dangerous online landscape, characterized by mass amounts of misinformation that disseminates faster than ever before.

Misinformation has polluted nearly every topical area, spreading from politics to science. One interesting site pertains to nutritional advice. A pressing issue has arisen as an increasing number of unqualified social media influencers spread unsubstantiated claims about nutrition to vulnerable consumers. Influencers profit from selling meal plans or dietary guides and gaining mass followings. Meanwhile, high-quality, observation-based scientific research in nutrition is over-simplified and extrapolated as collateral damage. Misinformation is potent, spreads quickly, and can be resistant to correction. This multi-faceted problem may never be fully languished but increasing critical thinking and healthy skepticism around information seen online and recognizing instances where influencers may have exploited their power in the past, may help increase awareness of the problem.

Almost six in 10 Canadians under 35 use the internet to keep up to date on health research and news.

Canadians are increasingly turning to the internet and social media as a source for health information. A 2019 survey conducted by Statistics Canada revealed that almost six in 10 Canadians under 35 use the internet to keep up to date on health research and news [1]. Moreover, this demographic was more likely to stay informed on health information though social media [1]. However, the information on these sites may be sourced from influencers –third-party endorsers who shape audience attitudes through blogs, tweets, and other media [2]. Despite this self-directed path of discovery, only five per cent of Canadians reported being very knowledgeable about health research [1].

An important question may then be: why do people fall victim to believing misinformation about health, and particularly nutrition? One aspect of the answer may be explained by how people process information, especially if it pertains to topics they are not well informed on. The heuristic-systematic model (HSM) of information processing suggests that people digest information differently and may be more vulnerable to persuasion depending on how much they know about a topic [3]. A U.S. study looking at factors that influence the perceived credibility of diet and nutrition information websites found that when people are confident in their knowledge of a topic, they process information systematically – analyzing the quality of the message, and scrutinizing it based on what they already know [4,5]. However, if not, they become vulnerable to relying on external variables independent of message quality, such as how long or complex the message seems, or how favourably they view the communicator of the message [4]. The study also reported that when participants believed a message to be more accurate, they were more likely to think the site was trustworthy, irrespective of the credentials of the site's author [5]. The ability of an individual to correctly discern if a message is accurate or not may moderate their opinion on credibility, which could result in them unwarrantedly trusting the source of information.

Naturally, it can be seen how this phenomenon translates into the online world when people are unknowledgeable on a particular topic and vulnerable to being misinformed. Many social media influences in the fitness and wellness space are attractive and have sought-after body types. This commonly leads followers to question how the influencer achieved their physique, and they become eager to emulate the fitness and diet regime of the influencer, trusting them as an expert authority because of their aesthetics alone. This demand creates a position of power for the influencer, making them feel entitled to inform others about diet, nutrition, and exercise. Simultaneously, it sets up the perfect cascade to launch the sale of meal plans, diet e-books, or virtual dietary counseling, even without proper qualifications to do so. Of course, many qualified scientists, registered dietitians, and other professions have social media followings, but they may not be perceived as relatable to the consumer, or their content may not be as visually pleasing, or easy to digest. To increase the value of the nutrition-related content they sell or produce, influencers may seek out more information. The growth of the online world has enabled anyone with an internet connection to reach the growing amount of open access, high-quality scientific information online. However, increased access to information does not always translate to an increased understanding of it.

To appropriately interpret results of a scientific study, it is imperative for the methods to be critically appraised, as aspects of a study design have a dramatic influence on the applicability of the research. For starters, the experimental model – which cell line, types of animals, or human participants – upon which the hypothesis is tested is a fundamental aspect and may affect how results from the studies can be interpreted. For example, if a study population focuses on overweight, Hispanic men with type-two diabetes, the results may not be applicable to Chinese, Caucasian, and African American women with other body compositions or health conditions. Secondly, results depend entirely on the quality of the experimental methods used and how things were

> **In a five-year period, 40 per cent of the most frequently shared links contained fake news, which were shared nearly 500,000 times.**

measured . For instance, there are many different ways to classify someone as overweight, one method uses body mass index, which relies on weight and height measurements alone. Conversely, imaging methods like dual x-ray absorptiometry, measure weight in addition to body composition: the amount of fat, bone, muscle, and water that your body is comprised of. Although both methods offer cut-offs to describe someone as overweight, the quality of information gathered is not the same. The latter is far more informative, due to the ability to discern between lean and fat mass. Finally, even once results are obtained, how results are analyzed can influence research conclusions. This is especially true in rapidly emerging fields where no gold-standard of analysis exist. Even with the best intentions, results can be misinterpreted or used out of context, and due to the large following of social media influencers, the consequences can be especially pronounced.

In a European study reviewing the uses, benefits, and limitations of using social media for communicating health-related information, the researchers noted several limitations, largely pertaining to concerns over the quality of information, and ability to discern what is reliable [6]. A particularly worrisome limitation was that social media may act as a deterrent for patients from visiting health professionals [6], which in the case of nutrition may refer to registered dietitians. Another aspect that makes misinformation so volatile relates to its spread. A study conducted at the Massachusetts Institute of Technology found that false news stories on Twitter spread significantly faster and more broadly than true stories (7). The false news was more novel than the factual, which suggested people may be more inclined to share novel information [7]. The rapid spread of misinformation is further illustrated by a Polish pilot study which found that in a five-year period, 40 per cent of the most frequently shared links contained false news, which were shared nearly 500,000 times [8].

In addition to the rapid spread of false news, the consequences of its dissemination can be particularly potent. In a Slovenian study, researchers found that selective exposure was the primary driver of content diffusion, meaning how we use social media can often create information echo chambers [9]. Social media users can curate their feeds, selecting and sharing content related to the specific narratives they subscribe to and ignore the rest [9]. This is pronounced with influencers who build their personal brand around a dietary pattern, such as following the keto diet or vegan diet. The influencer aggregates a community of followers who subscribe to the same beliefs about food and the ideas get reinforced, whether they are factual or not.

Another common space for the formation of echo chambers is on podcasts. Influencers often select guests based on parallel alignment with their beliefs. Instead of conversing with someone that may cause them to think critically and question their ideas about nutrition, they get validation, and whatever message they ascribe to substantiate their theory is perpetuated. This further reinforces their messages to followers, even erring on the side of advertising if the influencer sells diet guides based on these beliefs. Although it may be subtle, this is a toxic pattern because the strategic reinforcement of an idea from different sources may dissuade people from feeling inclined to independently confirm the facts.

Frighteningly, it is thought that increased exposure alone to an unsubstantiated claim might increase the aptitude of believing it – something known as the "mere exposure effect" [10]. In the realm of social media and nutrition, misinformation often comes in the form of influencers proposing reasons to adhere to a specific diet. In the case of the keto diet, it is often propagated that eliminating carbohydrates will allow our bodies to burn fat instead of storing it. Conversely, many supporters of the raw vegan diet allege that the fat you eat is the fat you wear, insinuating that by eliminating fat and only eating raw plant-based foods, it will be virtually impossible to store excess fat.

Formation of these echo chambers, and repeated exposures to the information can strengthen its perceived validity, making the damage severe and difficult to reverse. A U.S. study aimed at understanding factors underlying effective messages to counter attitudes and beliefs on misinformation found that persistence was stronger, and the debunking effect was weaker when audiences generated reasons in support of the misinformation [11]. People struggled to later question and change their initial attitudes and beliefs when they were able to generate arguments supporting the misinformation [11]. The proposed mechanisms behind the success of a dietary pattern can be a powerful tool to persuade people, even if it is untrue. When trying to debunk the misinformation, the researchers found that labelling something as misinformation was not enough, and corrective information needed to be introduced [11].

Whether the reasoning behind following a dietary pattern is substantiated or not, no single diet or amount of food will be suitable for everyone. The release of Canada's new Food Guide in January 2019 was less quantitative than ever

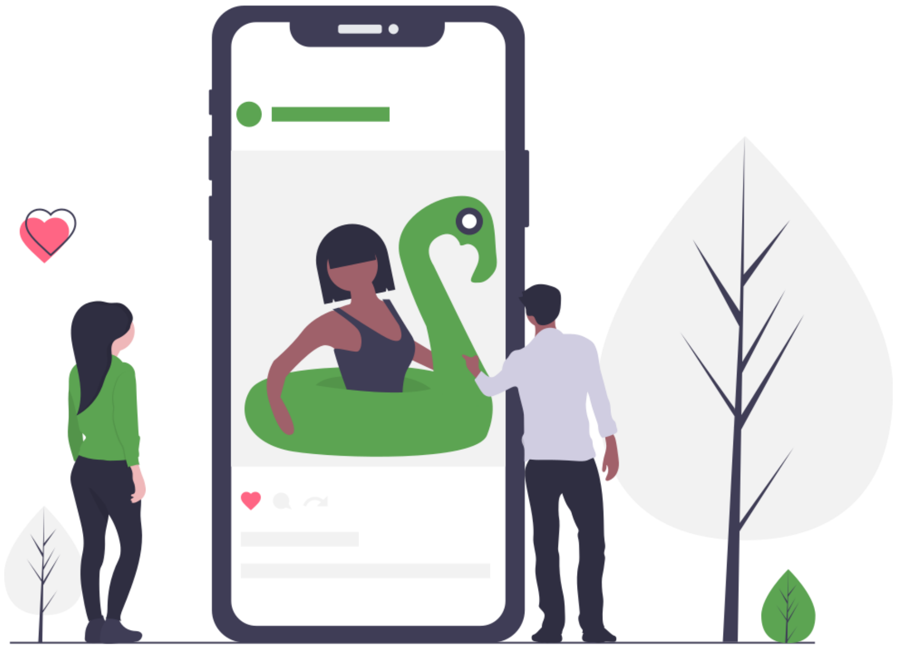
Diet plans may encourage you to believe that the answer is simple and the science is streamlined, when in reality it's not.

> “ I must look at each person’s medical history, diet history, social life, everything. It’s personalized.

before. Recommended serving sizes and number of servings per day were removed, since the optimal intakes for two people could vary widely based on variables like how active they are or their basal metabolic rate – even if they are the same age and gender. Instead, the guide highlighted the general consensus to move toward a more plant-based diet that emphasizes whole foods, and encouraged consumers to use food labels and be aware of food marketing [12]. Many influencers who promote one-size-fits-all diet plans for weight loss may strategically mention select studies to support the proposed reasons behind their efficacy. However, when considering the totality of evidence, recent work from Columbia university highlighted that there really is no consensus when it comes to topics like the age-old debate of low-fat or low-carbohydrate diets for weight loss [13]. Diet plans may encourage you to believe that the answer is simple, and the science is streamlined, when in reality it’s not. Above all, continuously evolving studies coupled with advancements in technology have revealed that it is pertinent to consider highly individualized characteristics when prescribing a diet to someone, such as their genetics and their gut microbiota – the population of microbes in the gut that can influence health status and nutrient absorption.

“I don’t think diet plans should be ‘sellable,’” said Ohood Alharbi, a nutrition and genomics specialist. Alharbi received her PhD from the University of Toronto, and recently founded her own business – Personalize My Diet. Her work centres around personalized dietary counselling and recommendations for clients based on genetic profiling data and high-quality research. “I’ve had non-experts suggest to me selling diet plans, but my integrity doesn’t allow it,” Alharbi said. “It defeats the purpose and the message that I share with my clients. I must look at each person’s medical history, diet history, social life, everything. It’s personalized.”

Moving forward, it is important to recognize that the spread of misinformation about nutrition may never relent. Although protected titles such as registered dietitian exist, this does not seem to stop people from trusting advice from influencers that lack credentials but have large followings. Increased surveillance of nutrition information online may be one step in addressing this problem, but a proactive approach may be more prosperous. Namely, content consumers should continue to be educated on how to think more critically about what they are seeing online, especially when the sale of a product is involved. The requirement of certain disclosures like including the hashtag “ad” when posting pictures that are part of a paid brand partnership are important steps in increasing transparency in general. However, the line is less clear when influencers are not paid by a brand but are rather selling their own products that are not even physical items, such as a diet e-book or virtual personalized dietary coun-

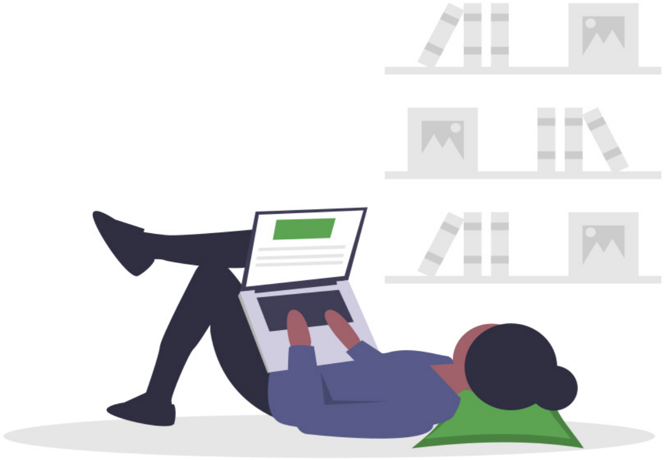


selling. It is especially important to explain these nuances to vulnerable audiences like teenagers.

To increase education around nutrition in general, different tactics have been proposed to make scientific information more digestible. One idea involves the use of narratives to communicate science to nonexpert audiences, due to the increased comprehension, interest and engagement that storytelling may offer [14]. Lastly, audiences can also learn through the cautionary tales of others, like that of Dallas-based fitness influencer, Brittany Dawn.

Although lacking any appropriate nutrition credentials, Dawn built a business with her Instagram and YouTube following of over 500,000 by selling personalized diet and workout plans. Her plans cost hundreds of dollars and came with the promise of updates and direct contact with Dawn herself. But it turned out that clients found it nearly impossible to get in touch with Dawn and if they tried to express concerns through comments on her social media platforms, they would promptly be deleted. In the end, unsatisfied clients banded together and realized their "personalized" plans were in fact identical. Presently, an active petition on change.org has nearly 14,000 signatures for, "Stop Brittany Dawn Fitness Scams." This is not to say that all influencers should be labeled as scammers, nor that misinformation is apt to result in a scandal of this degree. However, it is important to recognize how easily influencers can exploit their power in an environment that is not highly regulated.

It may be a tough pill for those who inappropriately profit from misinformation to swallow, but proper science is no place for clickbait. Rather, the scientific process relies on the accumulation of well executed studies and the evaluation of their impact together, over time. Often, the over simplified or extrapolated message is more attractive. Who wouldn't want to hear that all you must do is eliminate carbohydrates and eat mostly fats to become a lean, fat burning machine? Everyone is searching for a panacea, but unfortunately, there is no miracle diet plan nor secret superfood elixir that will launch you into good shape or longevity. With the mass volumes of user-generated content being uploaded every hour to various social media platforms, it may be unfeasible to monitor all of the nutrition information shared, and likewise, it would be unrealistic to expect the lay public to be an expert on it. Moving forward, it will be important to instill a healthy level of skepticism and critical thinking surrounding nutrition information, and to emphasize the role for increased knowledge translation around nutrition research.



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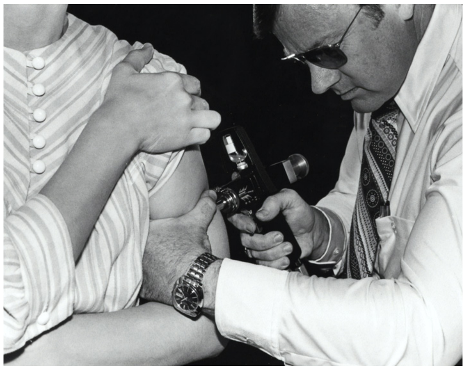
ANTI-VAXXERS

WHY PEOPLE REFUSE VACCINES

TEXT BY SARAH ASBURY



“IF vaccines really are perfectly safe and do not cause any injuries or deaths, then the numbers of antivaxxers would be shrinking. It’s not. We are growing in numbers. That should tell you everything.”[1]

This is the perspective of a vaccine hesitant Twitter user @KassandraKitson, and they’re not alone in their sentiments.

It may be difficult to understand why a growing number of parents are choosing against vaccination as a method of protecting their children from lethal or debilitating childhood diseases [2]. However, the social media of vaccine hesitant parents reveal a clear story. They’re motivated by what most parents want – to protect the health of their children. In fact, vaccine hesitant parents are typically well-educated upper middle class individuals [1,3] who actively seek out information about vaccines [4].

Skeptical by public education campaigns that emphasize the benefits of vaccines, vaccine-questioning parents resort to researching vaccine risks online [4–6]. Many unverified or fictitious vaccine risks are discussed on social media by anti-vaxxers [7], who typically lack the biomedical, statistical, or epidemiological training to critically assess scientific studies and scientific media. As a result, vaccine-questioning parents may unwittingly be drawn into a social media misinformation trap that exaggerates vaccine dangers and instils doubts difficult to dispel without comprehensive science education.

For example, VaccineTruths or @Rectitude20, a Twitter user who had over 12,000 followers, shared a post urging parents to ask their doctors about a scientifically unfounded vaccine risk – that vaccines increase the risk of neurodevelopmental disorders (NDD) [8]. The Tweet was first posted in December 2019 before the account was suspended in June 2020.

The Tweet referred to a graph from a study published in a seemingly legitimate scientific journal, the Journal of Translational Science, by lead author and professor of epidemiology, Anthony Mawson, from Jackson State University [9]. However, the study was retracted by the original publisher, Frontiers of Public Health, due to major flaws in research design [10]. The work also conflicts with the majority of studies conducted in the area.

The body of scientific evidence clearly demonstrates no relationship between vaccination and neurodevelopmental disorders including autism, attention deficit hyperactivity disorder, and learning disabilities [11–14]. This includes a massive report using data collected from 1.2 million individuals – a statistically high-powered study ideal for identifying rare adverse events – which found no relationship between vaccines and autism [11]. However, these reproducible and credible large-scale epidemiological studies have failed to impact anti-vax opinion, and Mawson's publication continues to circulate in the anti-vax community.

Irrespective of well-founded contradicting evidence, there are fundamental flaws in Mawson's methodology that casts doubt on the veracity of their work. Most importantly, data was collected via an online survey: Mawson's team solicited self-reported medical information on vaccination, neurodevelopmental disorders, and preterm birth from mothers with homeschooled children. This method of data collection exposes the work to multiple sources of inaccuracies including a selection bias, a small sample size, and an inability of the researchers to verify their participants' medical history.

"There are all sorts of biases surrounding the recruitment strategy, the statistics are problematic, and the peer review wasn't done appropriately," said Dawn Bowdish, a professor of immunology at McMaster University and the Canada research chair for Aging and Immunity.

"The first issue is that there are no confirmed diagnoses," Bowdish added, referring to the lack physician diagnoses for neurodevelopment disorders (NDD) reported in the study.

Without a physician diagnosis, it is impossible to verify if the children with neurodevelopmental disorders in the study actually fit the diagnostic criteria. This alone makes the relationship between children reported to have NDD and vaccination status dubious.

Furthermore, "there's a selection biases for homeschooled parents," Bowdish said. When designing a study, the sample population should represent the population that the findings will be extrapolated to – in this case the general population. Over-selecting a particular subpopulation facilitates discovery of idiosyncrasies unique to that subpopulation rather than answering the research question for the entire population.

"There's data suggesting that children who have neurodevelopmental issues are more likely to be homeschooled than the general public, because they struggle in the conventional school system," Bowdish said.

> "There are all sorts of **biases** surrounding the recruitment strategy, the **statistics** are problematic, and the **peer review** wasn't done appropriately."

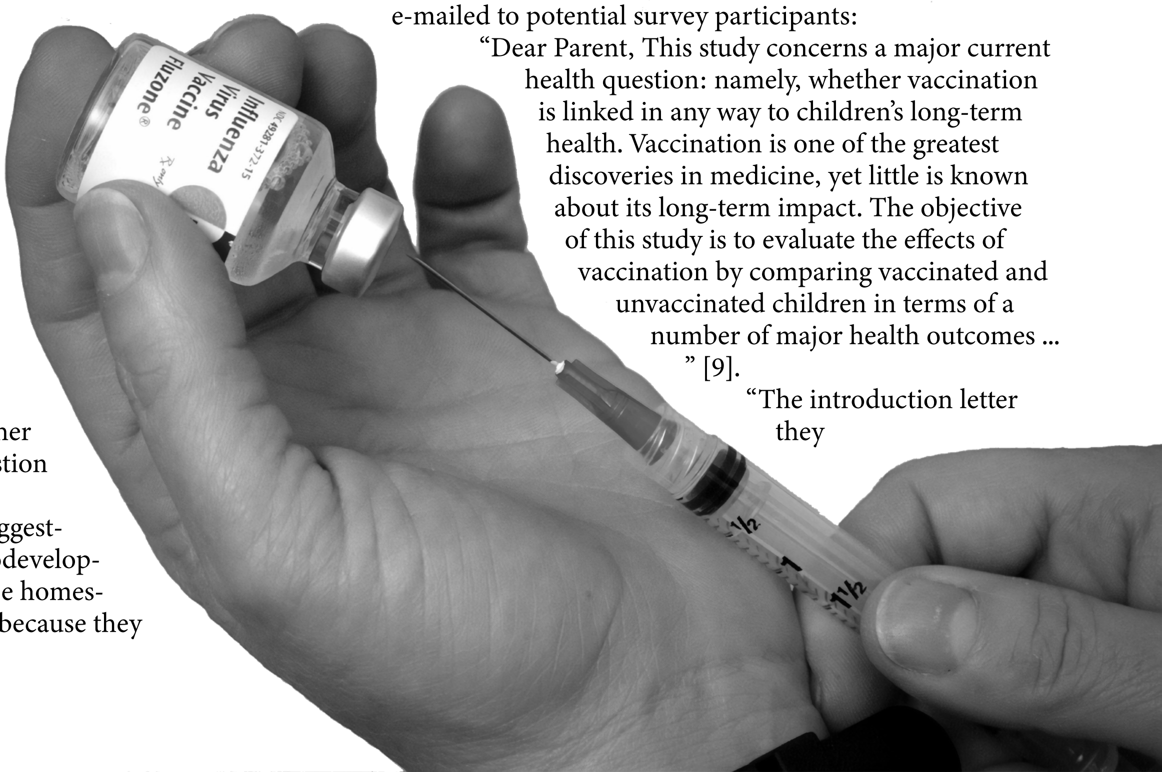
Homeschooling populations also have higher frequencies of parents who are anti-vax [15–17], because school vaccination mandates provoke vaccine-refusing parents to seek alternative schooling [18].

Using a homeschooled population makes it difficult to disentangle whether a lower frequency of NDD in unvaccinated children is a genuine finding, or an unexplained correlation between NDD and vaccinations in the homeschooled population. Simply put, it is statistically inappropriate to use a homeschooled population to broadly conclude that there is a biological relationship between vaccines and NDD risk.

However, there are also subtler flaws stemming from their methodology. Part of that is in the introductory letter e-mailed to potential survey participants:

"Dear Parent, This study concerns a major current health question: namely, whether vaccination is linked in any way to children's long-term health. Vaccination is one of the greatest discoveries in medicine, yet little is known about its long-term impact. The objective of this study is to evaluate the effects of vaccination by comparing vaccinated and unvaccinated children in terms of a number of major health outcomes ... " [9].

"The introduction letter they



gave to the participants gave away the major hypothesis of the study," Bowdish said. "And that biases people."

Bowdish explained that biasing survey participants prior to administering the survey increases the risk that the dataset is inaccurate because surveyee responses can be subjective.

For example, pre-term birth is a well-documented risk factor for NDD [19–22], yet Mawson's study found no relation between them. This may indicate that having surveyees self-report medical information curated low quality data. For instance, asking mothers to self-report pre-term birth may provoke subjective responses. "37 weeks is considered term. But if you had a baby at 37 weeks a mother might still say she had her baby pre-maturely if she had it early [in the week] but that is actually within the normal range," Bowdish said.

Mawson's study did not provide the survey questions for vaccination, NDD, or pre-term medical information in their publication, and therefore the extent of survey bias is challenging to assess. It is also possible they did not include enough children with NDD to statistically discern a significant relationship between pre-term birth and NDD, as only 49 of the 666 children had reported NDD. Regardless, Bowdish said that the lack of relationship between NDD and pre-term birth may be a litmus test that their dataset is precarious.

Despite the flaws in data quality, population sampling, and survey methodology, Mawson's study was nonetheless published – a possible oversight in the scientific peer review process.

Effective peer review is crucial to credibility, because other experts in the field assesses whether or not the paper conducted meticulous unbiased science. Typically "peer reviewers are people who have expertise in the field. Often, you have more than one, because you want to cover different areas of expertise," Bowdish said. "For example, one reviewer might have knowledge of the statistical tests, but not actually understand the content of the biology ... another might have expertise in the biology but not in the statistics."

> [Tampered peer review is a **serious infringement** on the reliability of a study.]

Tampered peer review is a serious infringement on the reliability of a study. Bowdish believes that the reviewers selected for Mawson's work did not adequately encompass the expertise needed to review such a paper. For example, the reviewers included a chiropractor, who lacked expertise in neurodevelopmental disorders, epidemiology, and vaccinations. Another was an epidemiologist, who lacked expertise in vaccine safety and neurodevelopmental disorders.

Despite the oversight in peer review, the study's extensive flaws provoked a retraction by the original publisher, Frontiers of Public Health. According to Bowdish, papers can be retracted for many reasons, including misinterpretation of conclusions and biases in the peer review process. If a study has been retracted "it should be struck from the record," Bowdish said. "Because if it's retracted, there are issues so large that it's not trustworthy."

Mawson's team later re-published their study in the Journal of Translational Science, which also reportedly retracted the study [10]. However, there is no retraction warning when accessing the text through their publisher website [9], which leaves readers – like vaccine-questioning individuals who read VaccineTruther's tweet – unaware of the paper's scientific negligence.

While Mawson's study is an example of misinformation caused by rifts in the scientific and peer review process, vaccine misinformation can also originate from misinterpretations of study findings.

Twitter user @susan_welch7 tweeted a link [23] to a science news article titled "Mayo Clinic Doctor: Measles is a Natural Cancer Killer – why are we trying to eradicate it," written by alternative medicine journalist Bryan Hubbard on his website and magazine *What Doctor's Don't Tell You* [24]. Hubbard's article refers to clinical researcher Stephen Russell's research on oncolytic viral therapy – an emerging form of cancer therapy using laboratory-modified viruses that infect and kill tumour cells [25].

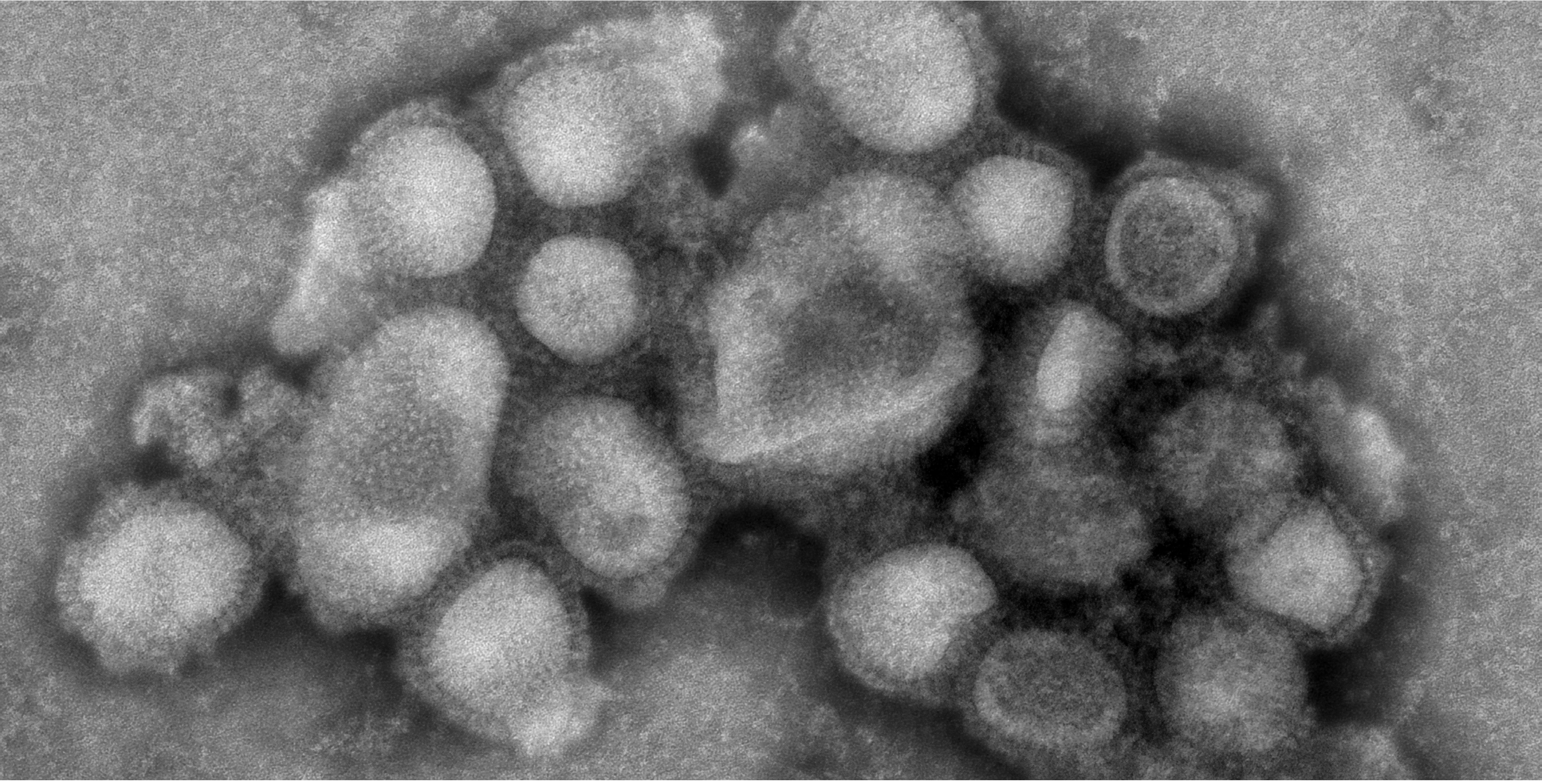
"Health authorities may want to think twice about eradicating measles," Hubbard writes. "Researchers are discovering that the virus can fight cancer."

Oncolytic viruses engineered from measles can be useful for treating blood cancers, which originate from immune cells [26]. However, the behaviour of the measles-derived oncolytic viruses differ significantly from its naturally circulating counterparts. Therapeutic viruses are typically genetically engineered or modified in the laboratory to enhance its ability to kill tumour cells and prevent the virus from infecting healthy tissues, as it would in a natural measles infection [27].

In Russell's study, the measles virus was used to target myeloma, a form of blood cancer [25]. Viruses were modified to allow them to selectively enter myeloma cells through a cancer-specific protein. This modification does not exist in naturally occurring measles [28].

Having a measles infection will do nothing to prevent cancer. Although there are rare isolated cases where a natural measles infection has contributed to tumour regression, which seems to have misled some people into thinking natural measles can be a "cancer cure." But this tumour regression is a rare phenomena restricted to patients with blood cancers only [29,30] and is likely an inadvertent effect of a severe measles infection non-specifically wiping out all immune cells – including cancerous ones.

The ability of measles to eradicate immune cell populations is part of why the infection can be so devastating [31].



Even when a patient recovers from measles, their immune system is weakened and loses its ability to recognize bacteria and viruses its seen before, leading to more infections in the future [32].

“[Measles patients] essentially go back to being a baby immunologically,” Bowdish explained. “People who get measles are much more likely to need antibiotics in the next few years because they get serious infections. There is a very real link to dying from other infections.”

Laboratory-modified oncolytic viruses like the ones developed through Russell’s research are exciting new cancer therapies, but they are not credible evidence for keeping the naturally circulating measles strain like Hubbert suggests. There are real dangerous health consequences of the measles infection. Articles like Hubbert’s may appear credible because they cite a scientific study, but they represent a major threat to science communication, incurring doubt to confuse and disorient readers from factual medical information.

Both Mawson’s study and Hubbard’s news report demonstrate how misleading academic studies and scientific news can be distorted to convince parents they should be skeptical of vaccines. Certainly, the purported scientific findings on vaccine dangers expressed in both of these articles would be deeply disconcerting to a parent concerned about vaccine risks, and are challenging to debunk without comprehensive experience in health science research.

The heart of the issue, as described by Bowdish, is that “if you need a PhD to be able to interpret the literature, then how are we going to make this more manageable for the lay public?” What can be done then, to curb the science misinformation crisis – especially in the context of vaccines?

Canadian guidelines now recommend healthcare professionals provide parents a balanced perspective on the benefits and risks of vaccines, which is a shift from previous strategies that focused largely on benefits of vaccines or debunking anti-vax claims [5]. There are indeed rare side effects to vaccines that should be recognized – although these risks are lower than risks associated with severe complications from vaccine-preventable diseases [2,33]. When parents are provided with a reputable unembellished understanding of vaccine risks, they will ideally be less likely to seek out potentially unreputable vaccine risk information online, such as Mawson’s study or Hubbert’s article.

As the open-access science movement grows, journals and scientists should also openly adopt writing lay abstracts for the general public to decrease the opportunity for misinterpretations like the Hubbert article. A 2019 3M survey on Canadian perceptions of science found that science scepticism was increasing: about one in three individuals were skeptical of science, with trust in individual scientists remaining around 60 per cent [34]. Researchers writing lay abstracts

> [“Because if it’s **retracted**, there are issues so large that it’s **not trustworthy**.”]

directly to the general public, instead of relying on science journalism, may not only be helpful for reducing science misinformation but also bolster public trust in the science [35].

Finally, as more complex medical research becomes available through the internet, scientific literacy education should be leveraged to improve the public's ability to make evidence-based personal medical decisions. By educating people scientific studies exist on the characteristics that constitute quality scientific evidence, they may be less likely to be mislead by poorly designed studies.

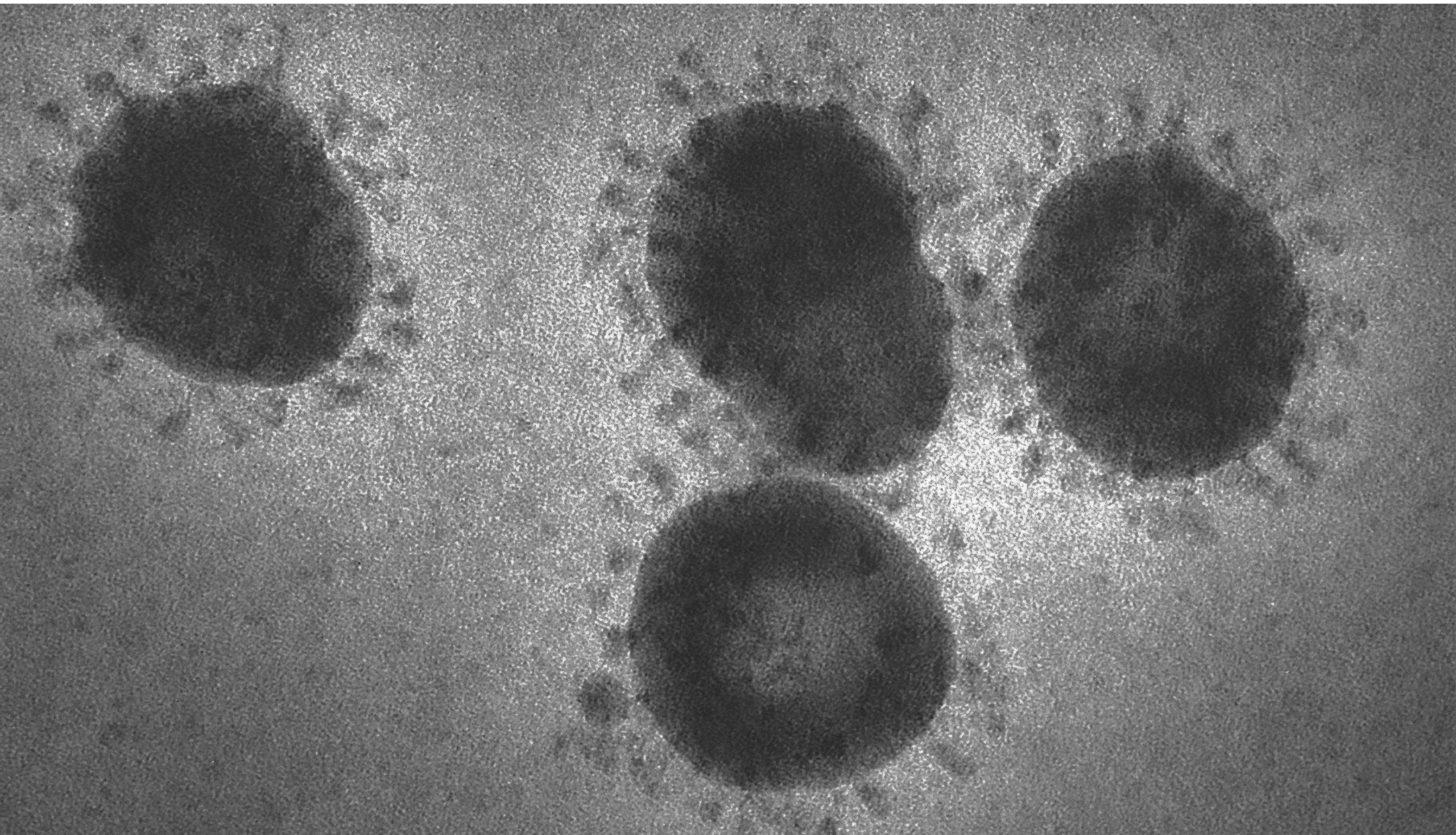
Research from Stanford University found that high school students with strong scientific reasoning skills were more resistant to vaccination misinformation [36]. When presented with a biased science article, the students were able to identify misleading words, biased language, and flaws in logic. High schoolers that were the most susceptible to misinformation were the ones who lacked strong reasoning skills and were inclined to believe faulty logic and weak arguments based on the author's credentials alone.

By including a brief component on scientific reasoning and media literacy in public high school education, it could give future generations the tools to assess the vast medical information now accessible in the digital age.

> **["If you need a PhD to be able to interpret the literature, then how are we going to make this more manageable for the lay public?"]**

Vaccine refusing parents who are convinced by unreputable information accessed on social media ultimately represent a fissure in science communication between the general public and the scientific community. There are unique science communication challenges brought on by the information flood that accompanied the digital age. Our methods of scientific communication and science education must evolve to face these challenges, to decrease the momentum of fear-based movements – such as anti-vax – which are rooted in science misinformation.

By promoting more public health campaigns with balanced perspectives, encouraging scientists to communicate their research to general audiences, and strengthening scientific reasoning education, we may be able to reduce health misinformation in the digital age.



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FEATURE

The ART of Science Storytelling

TEXT
ERIKA SCOTT

PHOTOS
CYLITA GUY
ALEXANDRA GELLÉ

The PASSION began at a young age.

“My parents fostered a sense of curiosity about the natural world,” Cylita Guy said. “We went to the [Ontario] Science Centre a lot.” The experience inspired her to join a school program where she spent a semester in grade 12 at the Ontario Science Centre. When she discovered they were short-staffed during her undergraduate degree, it was only natural that she would be hired to teach students much like herself just a few years earlier. She had unknowingly ignited a passion for science communication.


Cylita Guy


Alexandra Gellé

Following her Ontario Science Centre days, Guy completed a PhD in ecology and evolutionary biology at the University of Toronto, and set out on her quest to transform the world of science communication. Together with her passion for science, Guy also wanted to showcase that women, and those from diverse backgrounds, could be leaders in their respective fields. Right now she's a data scientist at Assurance IQ and working on her first children's book for Annick Press.

Alexandra Gellé also fell into science communication unwittingly. "I didn't realize I was doing science communication when I was," Gellé said. "I had always been telling people that without chemistry, we couldn't do anything. I just didn't realize that this was a form of science communication." Gellé is currently working on her PhD in chemistry at McGill University where she is designing sustainable ways to speed up chemical reactions. She had felt that her own research didn't sound very life-changing to people outside of her field, so she wanted to reshape the way people viewed chemistry.

What is Science Communication?

"[Science communication] is anything but speaking to your own peers," Gellé explained. "You want to share your research with people who are not experts in your field and speak about science in general to lay audiences." It's about telling a story – engaging people who may not otherwise be interested in, or knowledgeable about, a particular field of research. Moreover, science communication is about "sharing

> "SCIENCE COMMUNICATION is anything but speaking to your own peers.

a message with people and using that message to persuade them to take action," Guy said. Now, arguably more than ever, during the COVID-19 pandemic, it is critically important for scientists to effectively engage with non-scientists. Scientists need to be able to communicate the severity of viral transmission and infections such that provincial and federal leaders can make decisions about which sectors of society should remain open or whether a state of emergency should be declared. Provincial and federal leaders then need to be able to knowledgeably address members of the general public on the importance of, and reasons for, good hygiene practices and proper social distancing. All of these steps require science communication skills to effectively reach the target audience.

Breaking into the SciComm World

"Communication – like any skill – is something that we learn and develop through practice," Guy said. "It's helpful if you can find a communication course to take if you aren't comfortable talking to people outside your discipline." Attending a science communication workshop or conference may also be worthwhile. Guy and Gellé are two of the founders of ComSciConCAN [1], an offshoot of ComSciCon [2]. The brand encompasses a series of conferences from Harvard University that brings together graduate students already engaged in science communication to network and broaden their skills. Both Guy and Gellé were among the first Canadian attendees. Following the first ComSciConCAN conference in 2019, the organization is now planning smaller local meetings across Canada to train graduate students who are new to science communication. The first French-only meeting took place in June 2020 and the first Toronto meeting will be in fall 2020.

In addition, Gellé is the director of Pint of Science Canada [3], an informal science speaker series that takes place in bars across the country. Speakers give short, interactive talks to an audience with a wide range of knowledge on the subject and then answer audience questions for the rest of the session. Attending these talks given by more advanced science communicators can instill you with ideas for how to make your own presentations more engaging. Once you've acquired some skills in science communication, signing up as a speaker for this event can then help further hone your abilities.

Guy notes that one of the fundamental skills of science communicators is understanding your audience – whether it's young children, adults who may not know anything about science, or scientists in a different field [4]. Depending on who you are speaking to, you will need to change what message you are conveying and how you share it. You may use more science jargon when talking to other scientists, but not when talking to children or adults outside your field. Nevertheless, "it's important to be empathetic," Gellé said. "People often talk about having to 'dumb something down,' but instead they should be talking about how to rephrase using common terms. Your audience may be very knowledgeable, just not about your field of research." Being able to relate to your audience will help you present your message in a more meaningful way [4].

Science communication can also manifest in different forms. Traditionally, journal publications as well as conference posters and talks have been the primary platforms for science communication. However, they are limited in scope such that only those who

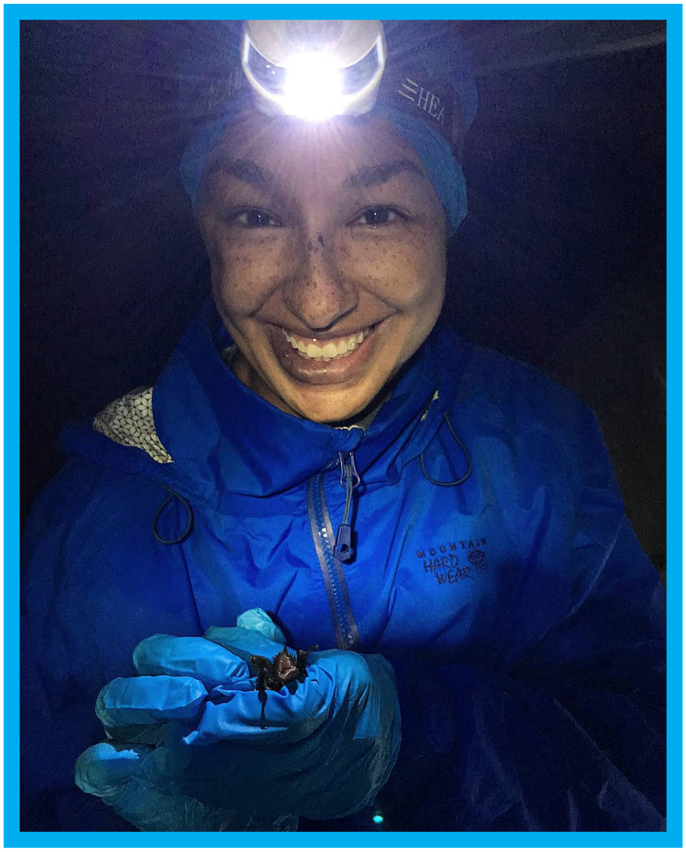
have access to the journals or conferences, and understand the jargon, are able to receive a scientific message. Science communication can also be conducted in ways that are more accessible to the general public, such as through working in a museum or science centre (like Guy), assisting government policy makers, or writing for a magazine or journal that the general public would read. In recent years, social media has become another platform for science communication, with Twitter being one of the major sites used by scientists to network and share the latest developments in their research [5]. Live-tweeting from conferences also allows researchers not in attendance to stay on top of cutting-edge research in their field and participate in conference discussions remotely [6]. For both Guy and Gellé, social media has fostered a strong sense of community as well. "It has helped me meet a lot of other people with shared interests as well as other ecologists with diverse backgrounds," Guy said. Gellé adds that social media has helped her stay in contact with other science communicators that she has met at conferences. Both agree that the networks they have developed through social media have led to collaborations with other scientists as well as invitations to give talks and workshops that otherwise may not have transpired.

> "YOUR AUDIENCE may be very knowledgeable, just not about your field of research.

Joining the Social Media Crusade

In this digital age, social media can be used to share many different pieces of information through the click of a button: statistics showing the number of active COVID-19 cases in a particular region, videos on what songs to sing while washing your hands, articles touting miracle cures for COVID-19, and blogs about the latest baking trends during quarantine. Information – and misinformation – can be shared and absorbed instantaneously. Therefore, it is important for readers to remain vigilant. "Many people claim to be an authority on a particular subject, so how can we help people determine which articles are truthful and which aren't?" Guy said. This is a question that science communicators have wrestled with for decades, and the anti-vaccine and climate change denier movements are evidence of the continuing struggle. For Gellé, addressing misinformation is important. "If I see a post on social media that I know is untrue, I will reach out to that person and engage with them about the topic." Again, knowing how to relate to the person you are addressing, and understanding where they are coming from, will help you better interact with them.

Taking it all into consideration, creating a social media account for science communication may seem daunting and time-consuming. On Twitter alone, there are many different things to consider – a personal bio, character limits, tweets, retweets, hashtags, followers, tags, etc. Guy has developed workshops that focus on using social media to communicate science and has some tips. "First, you need to decide on your personal brand," Guy said. "What do you want people to know about you? Then you need to make sure the content you post aligns with that brand." In other words, knowing what you want to accomplish through your social media presence will help you shape your online interactions [6]. In terms of which social media platform is best for science communication, Guy says it depends on the message you want to share. With Twitter, you have a character limit, but with Instagram, you can make longer, more visually appealing posts. Regardless of the platform, Guy emphasizes that "using elements of storytelling in your social media posts is important. Thinking about what you want to convey, who the main character of the story is, and how you can pull the reader in will make your posts more engaging." In these times of physical distancing, social media will likely become even more popular among scientists to develop and maintain networks and share their research. Virtual conferences taking place on Twitter or other platforms may become the new normal for the time being; learning how to effectively communicate scientific research through social media is timelier than ever.



Creating Space for Every Voice

While science communication has certainly advanced in recent years, the field, like many, could benefit from improvements that come with increased appreciation. Guy and Gellé agree that minorities, such as certain science disciplines and audience backgrounds, are often not involved in science communication. Gellé said that research in certain areas of chemistry or physics, for example, may be more difficult to communicate to the general public because it isn't as fun or trendy or easy to visualize. As a result, the general public is less aware of the importance, or even existence, of these fields of research. More researchers in these fields with a passion for creativity and science communication may help to change this. "French communities, for example, often lack voices," Gellé said. "We need science communicators who are able to spread information to these communities as well." Likewise, while Guy knows many other amazing diverse science communicators, the field is still dominated by White voices. "Highlighting the work of diverse communicators is critical if we want to engage and encourage the participation of all communities in science," Guy said.

> “Highlighting the work of DIVERSE COMMUNICATORS is critical if we want to engage and encourage the participation of all communities in science.

Making a Difference

Ultimately, developing skills in science communication will help you become a better scientist. Not only does it strengthen your understanding of your own research, but Guy said it also provides an avenue for people in the audience, who might not have otherwise heard of your work, to collaborate with you or use your methodology. In addition, by promoting your latest paper on social media, you could conceivably expand your paper’s readership and, consequently, the number of citations your paper receives [7]. Being able to effectively communicate your science can have a positive impact on your career and the quality of your research. It can also satisfy the underlying motivation for many scientists – the desire to make a difference. Both Gellé and Guy cite this as the reason they are so passionate about science communication. “People often forget about chemistry and how important it is to their daily lives,” Gellé said. She found that the most rewarding feeling was when children come up and tell her they want to study chemistry after attending one of her workshops. It’s a feeling of accomplishment she can’t get working in the lab by herself. Guy feels a similar way. “I want people to feel like they have the right to do what I do,” Guy said. “Helping people get excited about something they didn’t know or didn’t understand or didn’t feel like belonged to them before – that’s why I love doing this.”

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RESOURCES for Beginners

Want even more tips and tricks? Check out these guides from:

American Association for the Advancement of Science

Lifeology

Blue Elephant

Story KEVIN MERCURIO

Illustrations MICHELLE KU

BEEP.
BEEP.
BEEP.

Nothing.

BEEP. BEEP. BEEP.

Jamie reached out his hand, searching the nightstand for the alarm.

BEEP. BEEP. BEEP.

He couldn't find it. He groaned.

BEEP. BEEP. BEEP.

"Jamie!" His mother shouted from the kitchen.

"Turn off your alarm already, it's time for breakfast."

He stuck his head out from under his pillow. With all the effort he could muster, he found his phone on the floor. He shut off the alarm and quickly dozed off again.

BEEP. BEEP. BEEP.

"DAMN SNOOZE BUTTONS!"

Jamie sat straight up, grabbed his phone, typed the 6-digit security code and turned off the alarm.

“Jamie!” His mother called out again. “Your pancakes are getting cold.”

“Just a sec mom!”

His eyes caught glimpses of red circles with numbers around them. They were all over his phone menu. What did I do the night before again? Jamie thought.

“Jamie!”

“WAIT ONE SECOND MOM.”

Jamie opened his Nostalgiabook app first. He had six notifications and two Delivery responses. A shot of dopamine flooded his brain. Most notifications were pretty meaningless, consisting of old friends asking him to like their new businesses and friends of friends' birthday reminders. There were 24 likes on the photo he posted – apparently from last night. The picture was of him and Daron in front of a house filled with fellow graduate students. She had joined him to attend the semester's residence party. That explains the massive headache I have.

He flipped through his newsfeed looking for photos from last night's party, scrolling past news articles on the earthquake that happened in Puerto Rico, life hacks, and Donald Trump's impeachment trials. If he recalled correctly – which by no means he was completely sure of – there were hundreds of students that attended, including many of the girls in his classes. Did I score last night? Jamie wondered.

“Jamie! I'm not going to call you again.”

“ALRIGHT I'M COMING. GOD.”

Jamie rolled out of bed, slipped on a pair of university sweatpants and a Superbeam brick-coloured shirt and waddled downstairs to the dining room. His plate of pancakes had already been laid out for him, along with a banana and a glass of orange juice. Jamie's mother was feeding his baby sister on one end of the table, while his father was reading the newspaper on the opposite end. Jamie poured maple syrup and began chowing down.

“How was your night, Jamie?” His father asked, looking up from the Sports Section.

“Fine,” Jamie replied. As he said this, he felt a vibration in his pants pocket and pulled out his phone. It was a Delivery message from Daron: Need to talk. Let's meet after morning class.

Jamie started feeling a bit anxious and tried to recall any memory of last night. Had I done anything wrong?

“What time is your class?” His mother asked.

“I'm 26 mom, I know I'm running late.”

“That's not what I meant. I genuinely wanted to ask you about your class and what it's about.”

“Jah moo gie,” Jamie's sister added. His sister was just two years old. She was holding her favourite toy, a blue stuffed elephant, trying not to get it in her bowl of cereal. There was a huge gap in their age and so Jamie didn't really do anything with her unless his parents asked him to babysit. His parents would often go out to the movies, have dinner at exotic restaurants, and go dancing at the Latin Discotheque.

“It's just about molecular biology. You probably wouldn't understand.”

Jamie gulped down the remaining pancakes and banana, chugged the glass of orange juice, and flew upstairs without another word. He showered, got dressed and was out the door in efficient time. He put on his headphones and opened the JukeboxInfinify app to listen to the latest music from his favourite artists. He felt relieved scanning through his suggested playlists and seeing the top listened songs of his preferred genres. He saw the bus was already at the stop as he rounded the corner of his street and ran as fast as he could to catch it.

“Just in time,” the bus driver said, “you must be going somewhere important.”

Jamie didn't hear nor look up at the bus driver as he scanned his pass and sat down. He was preoccupied with hypothetical things that could have happened last night. Had he been mean to Daron? Had he hooked up with one of the other girls in his class and left her there alone? Jamie was so preoccupied inside his head that he didn't even notice that he sat down on someone's lap.

“Boy, get off me!” The lady exclaimed.

“I'm sorry,” Jamie said, as he took the seat next to her.

The lady was an elderly Jamaican woman who had just gotten off work, doing overnight custodial duties at the new hospital next to his house. She was a single mother of five children, two of which had moved away to California to pursue their acting aspirations. Her eldest daughter was a computer scientist at Frugal and stayed home during the night to watch over the other two children, young twin boys who really liked playing tackle football in the house.

“W'ur you learn how to si'down?” The lady grumbled.

Jamie wasn't paying attention to her. He really wanted to find out what had happened last night. He opened the Filteram app and started scrolling through the front page. Among them were photos of famous celebrities having fun at the beach, graduate school peers hiking through some rainforest in South America, and pets happily obeying their owner's commands. Kevin's cat playing fetch with a rolled-up paper ball made him grin with delight. Finally, he got to the pictures of the party. Lots of people having a good time dancing and playing games. There's one with him in the background talking to his crush, Ariana! Dopamine shot. There's another one with him, Daron and a group of other students! Another shot.

He arrived on campus full of energy and ready for morning class. When he got to the room, he scanned for Daron but couldn't find her. He decided to sit near the back of the class where the professor wouldn't be able to see his laptop screen, nor would other students in the room. There were 15 other students there, all with laptops out. Some were listening and jotting down notes as the professor changed the intonation of her voice. Others were not paying attention, but instead were checking emails, using the Frugal app to search for nearby food places to eat at lunch, or catching up on the latest fashion news. That last one was Ariana. He noticed she was perusing fashion trends, which made him open her Filteram profile. What an insane number of followers, Jamie thought.

Class ended but Jamie had barely noticed until Daron walked up from near the front of the class and sat beside him. She looked terrible. Her eyes were really puffy, as if she had been crying the night before. Her blonde hair was not brushed and there was no attempt at putting on any makeup. Jamie was concerned.

"How's it going?" Jamie asked.

"Can we talk outside?" Daron replied.

"Have you been crying all night?"

"C'mon. Let's talk outside."

Jamie and Daron walked out of the building and sat in a semi-secluded area surrounded by small hedges. There were other students there; two were doing various yoga positions, while two others were playing a card game.

"I want to talk about last night," Daron began.

"Is there something that happened?" Jamie's heart began to race.

"I'm upset about what you did."

"What did I do last night?"

"You posted a picture of me on your Chirper profile," Daron said, tearing up again.

Jamie knew about the Nostalgiabook post but not this other picture. He took out his phone and opened the Chirper app. He did post a picture last night. Well actually it was a picture of himself, taking a selfie in what seemed to be the backyard of the residence in front of a beer pong table. His expression was that of a puzzled smile, holding two beers and a ping-pong ball all in one hand. Beside him was his friend Tyler, who had just made the craziest trick shot that Jamie had ever seen. He captioned the photo: Guess I won't be the only one scoring tonight.

"I just see the picture I took with Tyler."

"Look in the top right corner."

Jamie's gaze went to the top right corner. There was Daron, embraced by a tall man in a sports jersey. They were making out. His face looked familiar.

"That's John, my ex-boyfriend."

"Oh no," Jamie whispered.

"Why did you post that! Eric saw that post and was messaging me all throughout the party. On every single app. You know how my phone dies super early every night. Stupid battery keeps running out! I couldn't answer and explain myself."

"How could I know that was you in the corner of the picture? It could have been any couple making out!"

"Well it was me! Thanks a lot."

"What happened when you got home?"

"We had this huge argument and broke up. He said he wouldn't have been so angry if I had just contacted him to explain what was going on. It's all your fault!"

"Hey, don't put all the blame on me! What were you thinking, making out with your ex?"

"I didn't know he was going to be there! I only noticed when he posted on Nostalgiabook that he was having fun at a party tonight. Then he posted a picture of him and some friends in the residence on Filteram. Just a huge coincidence. I remember my heart pounding and I went out to get some air. And there he was."

"Still doesn't explain why you guys made out."

"I don't know, Jamie! Life is complicated, full of feelings and thoughts that you can't always put into a few words. It's not simple. It was a lapse of judgement. I feel terrible about it."

"You want me to take it down?"

"No. It's too late now. I'm just so depressed. I downloaded the Spark and Buzz apps to try and move on. It's making me feel a little better, but I still feel so alone."

"I think you need to just relax and take it easy. I'm subscribed to this guru on ShortVideoAddictions who meditates every single day. He seems really happy. Maybe you could try it."

"I don't know. I'm not much into siting down and being aware of where my mind wanders. I just need to get over this quick. Anyway, I'm late for class, I'll talk to you later."

"Okay. Sorry again, Daron."

Jamie watched as Daron got into her PersonalStranger car and sped off to class across campus. Jamie looked at his phone, it was past noon. He realized he had two Nostalgiabook messages that he had not checked before. One was from a group chat he was mysteriously added to with no actual content. The other was from his mom reminding him that they had Latin dancing lessons at 1:00 pm today and needed him to babysit his little sister. Damn, I forgot, Jamie thought.

Jamie called a PersonalStranger car and went home. It was just in time too, as his parents were about ready to leave.

“You’re late,” Jamie’s dad said.

“Sorry, there was a lot on my mind after class. Micro-stressing over things.”

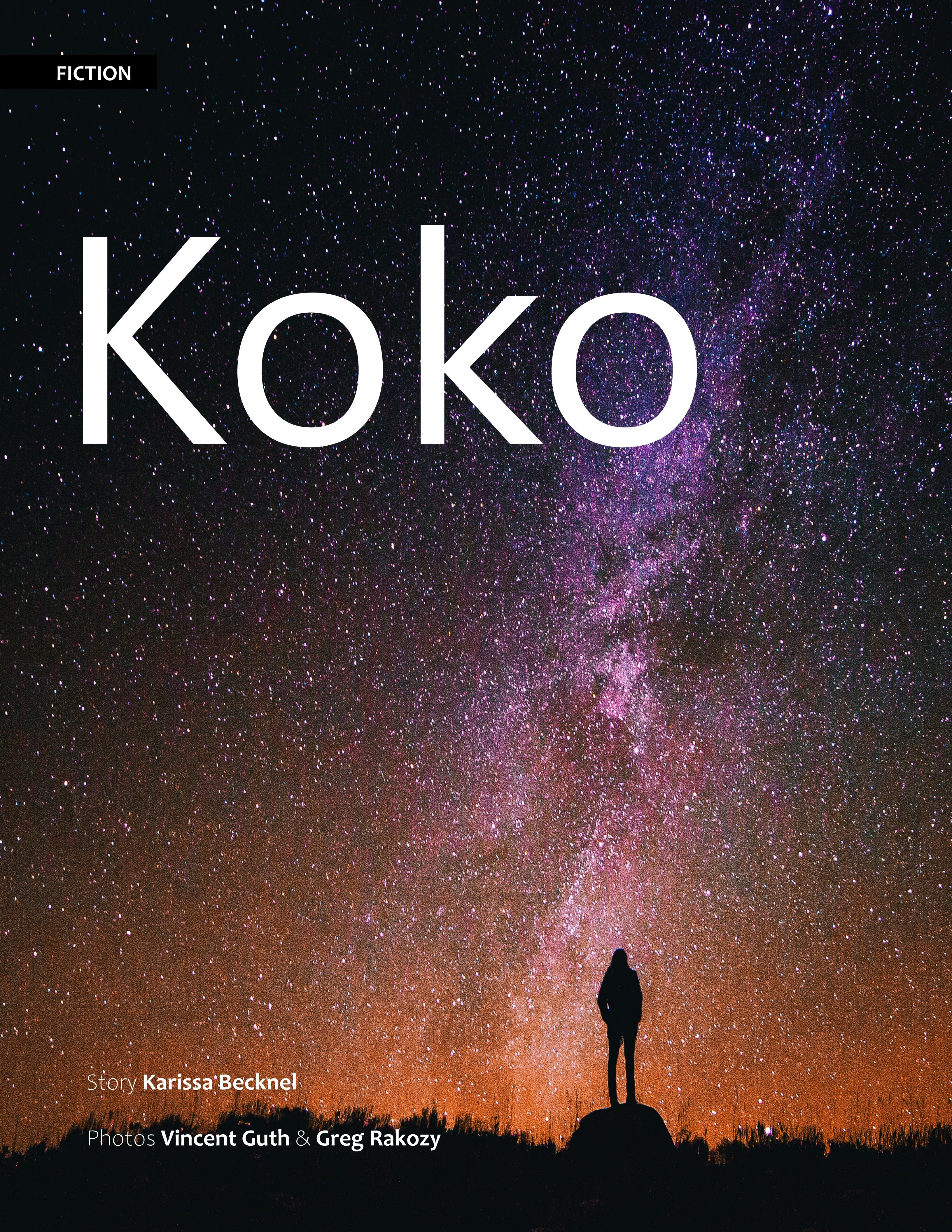
“Talk later?” His mom asked, putting on her coat.

“Um, yeah sure.”

Jamie and his sister watched his parents leave the driveway and then sat down on the couch. Jamie’s sister started crying. Confused, he stared at his phone, then put it down and started looking around the house for her blue stuffed elephant.

FICTION

Koko



Story **Karissa Becknel**

Photos **Vincent Guth** & **Greg Rakozy**

Growing up where I'm from
people didn't dream much about
anything.

As a kid, your imagination allowed you to miss the nuances of everyday life. In the summer, we played outside by the lake in search for buried treasure. Sometimes we played hide-and-seek or tag. It didn't seem odd that my childhood home didn't have running water, or that we shared the single bedroom between my mother, older sister, and me. But the fog began to fade the older we became.

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There's one elementary, middle, and high school in my town. They're all old and small. The brick walls meant to fortify our buildings were worn and breaking. We learned using textbooks held together by duct tape and outdated chalkboards. Many times on my way home from school, I walked by our neighbour lying on his back in the middle of the road. I would kneel and roll him over face down. The elders in our community told us to always roll someone face down. On any given afternoon, it was commonplace to see him like this. I realized later that this was abnormal behaviour for healthy adults. Neighbours, uncles, older cousins, aunts, and even my own mother needed to be rolled over from time to time.

My best friend in the entire world was Joel. He lived across the street from me. His house looked like mine: small, old, four walls, and a green paneled roof to complete it. Every summer we spent hours gazing up at the stars and tried pointing out our favourite ones. Joel's dad died when he was a baby, and his mom was never really at home because of her job. However, when I did see her, she smiled brightly. She baked us cookies and gave us candies. One time I saw her take out a metal box and prick her finger. Then, her smile faded.

One day in class, we took tests to determine what our future careers might be. My top five choices were therapist, dentist, physician, nurse, and professor. We spent the following days dissecting the roles and responsibilities of our top five choices. This is the moment when I realized I wanted to be a doctor. I remember running home and telling my mom the great news. She cupped my face with her hands and said, "I hope that your dream doesn't die Koko."

The night before my first day of middle school, I found my mother face down in the kitchen. She was non-responsive; I checked her pulse – something we learned in class a few months before. We used the landline phone to call for help and waited for what seemed like an hour for the ambulance to arrive. The closest hospital was still quite far from our town. During the wait, we tried keeping her head up. I remember my sister sobbing, and I too scared to cry. Josie, our aunt, came to speak privately with the doctor. We spent the night at the hospital. The doctor told us my mother had alcohol poisoning. Josie stayed with us for the next month or so. She said that everything will be okay, and to continue with school. We never spoke of the incident again. It took me four years to learn that my mother and other close members in my community struggled with alcoholism.

When we entered high school, Joel tried out for the varsity football team. I was taken to live performance art, so I joined the drama club. Joel was always a natural athlete, so it came to no surprise when he became the youngest student in our school's history to join varsity at 14 years old. He made friends with his teammates, and I formed friendships with actors from the drama department. We never really hung out much after that, and I'll always regret not reaching out to him sooner.

To make some extra money, I got a job at the local and only grocery store in town called Dene's. It looked like something out of the 1960s, complete with outdated checkered uniforms. The food was overpriced, and not the best in quality. My coworkers and I complained to the owner about the quality and selection of products. Dene's carried at best a few vegetables, some fruits, and a whole lot of liquor. Some parents came in to buy produce from our small selection, but sadly most customers came for the alcohol. It didn't matter if they were old, young, or middle aged.

One evening I saw Joel and his teammates drive up. They grabbed a bag of chips, some beer, and a bottle of vodka. As I stocked the shelves, Joel came up to me. He stammered out, "Heeeyyy Koko, how is high school treating you? I hope it's been well."

"I'm healthy and living Joel, can you say the same?" I

replied. “I have a leading part in the school’s play, you should check it out.”

His friends – who I surmise carried fake IDs – called for him as they finished paying. Joel stared at me with sunken eyes, “I miss you Koko. We should watch the stars again, and I’ll try to make it out to your play. I’ll talk to you soon.”

He gave me a big hug, lingered for a bit, and smiled at me with sad eyes. He turned and walked away. I yelled after him, “I hope that you guys win Friday night!”

He offered a sly smile and waved goodbye. We never got to look at the stars again, and I never spoke to him again. Sometimes I would see him come to class wearing the same clothes that he wore the day before. Sometimes I would see him in the hallways with dark bags under his eyes. Joel committed suicide on May 12, 2014. He drove his father’s old pick-up truck to the abandoned lot, took out his shotgun, and pulled the trigger. I remember hearing his mother’s cries, and the memorial around his locker. The football team retired his jersey number. The next night I laid outside in our old spot and watched the stars.

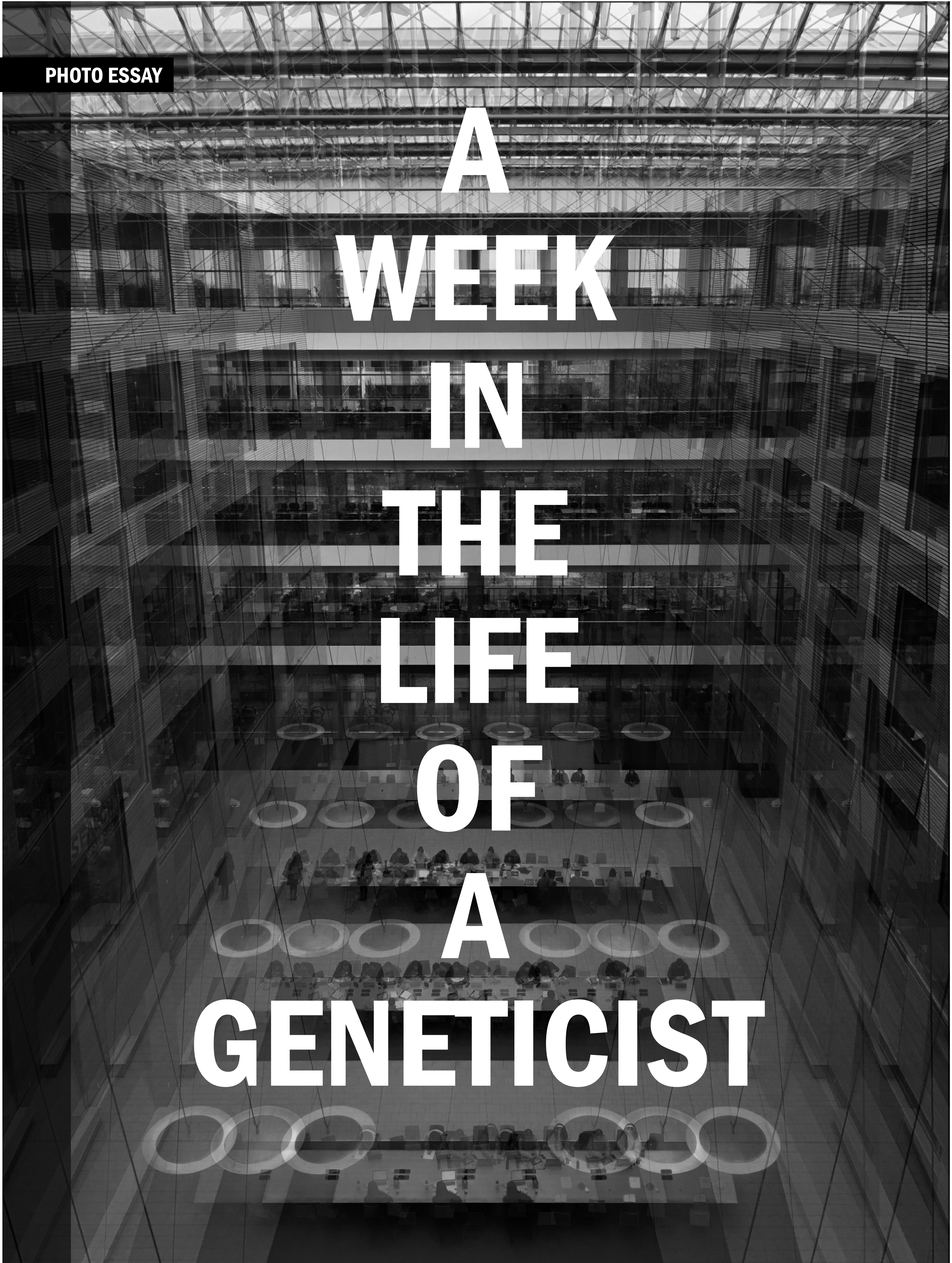
Joel’s mother and I got closer after this experience. She revealed that she was a diabetic, and insulin wasn’t cheap when you’re poor and without insurance. Apparently, every month Joel drove over 70 miles to get reasonably priced insulin for her. After she lost her job, Joel picked up shifts at the repair shop, but it was never enough. It got to the point where they couldn’t afford to drive to the first pharmacy, so they settled for a closer one where her medication cost much more. She blamed herself. I tried to cheer her up and spent much of my free time with her. I assisted her to doctor check-ups. She complained that many of the physicians she’d seen over the years just didn’t care all that much about her. She felt ignored. She never forgave herself for Joel’s untimely passing, and the next year she too passed away due to complications from her illness.

The remaining years of high school quickly passed, but I was determined to do well. My older sister, a year older than me, dropped out of high school. She mostly stayed around our house taking care of our mother. In fact, in my town most people don’t finish secondary school. The class sizes in our high school got smaller and smaller. At the end of my junior year, the principal pulled me aside. She told me that the community would sponsor me a scholarship to a university of my choosing. They would also provide the resources I needed to prepare my application. I was ecstatic because my dream was to be a physician. After graduating high school, I went to a university many miles away. Being a first-generation university student was challenging, but I made very good friends and studied what I enjoyed most: biology.

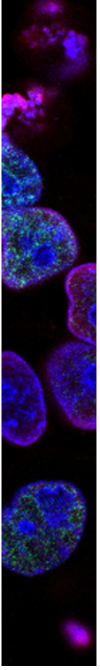
On the day of my commencement ceremony, I looked upon the audience to see the smiling faces of my mother and sister. Today was the day that I accomplished a dream no one in my family has ever done. As I stood in line eyes closed waiting to hear my name, I imagined stars against a dark violet night sky. An image of Joel and his mom pierces through the starry veil; I hope that wherever they are, they’re happy. I take a deep breath, open my eyes, and prepare for my name to be called.

I want to tell my story, of who I am and where I come from. Many people like me don’t get to tell our stories of a life that appears alien to most. I am Koko, a member of the Blackfoot Indians. The first in my family to finish post-secondary school, and the first in my community to enter medical school. I don’t know exactly what the future may hold, but I will never forget the community that made me. I will work towards building a greater understanding between communities like mine and healthcare and medicine.

PHOTO ESSAY

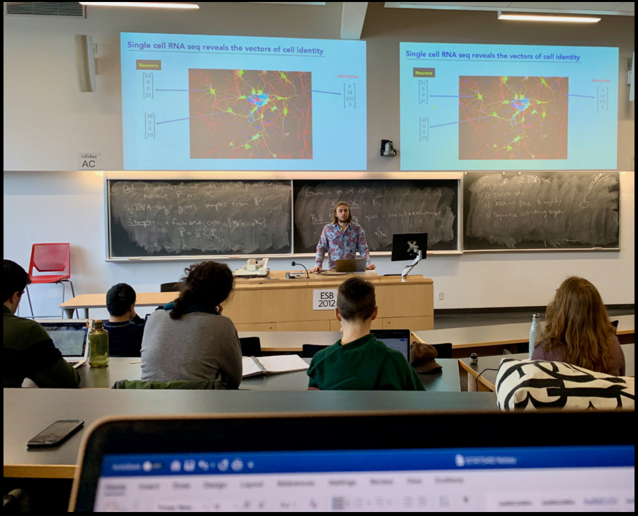


A WEEK IN THE LIFE OF A GENETICIST



MONDAY

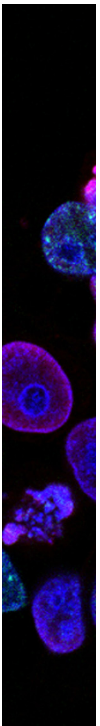
It’s the start of the week, and I’ll be heading to UBC’s main campus to attend my first lecture of the day. It’s a beautiful morning, and I’m looking forward to enjoying my 25 minute bus transit.



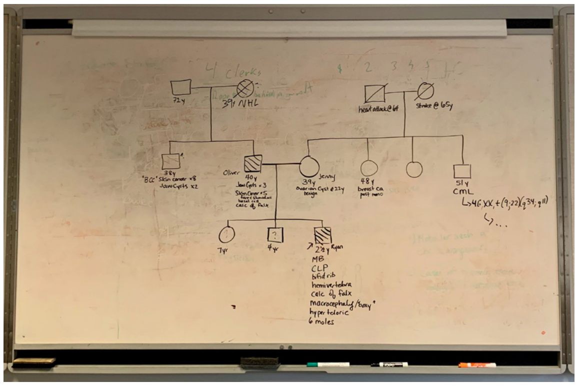
One of the elective classes I decided to take was “Statistical Methods in High Dimensional biology.” My PhD project involves a lot of data analysis, and I thoroughly like every lecture of this course. Today, we have a guest lecturer who previously worked at MIT’s Broad Institute and is explaining how to track the development of the different cell types that can arise from a single cell.

It’s lunch time, and I’m now at the BC Children’s Hospital Research Institute, where one of my two labs are based. I’ll catch up on my emails now, and complete all of my non-time-consuming tasks.

Almost the end of the day, and I’m in need of a caffeine pick-me-up before heading to a class on the physiology of the mother, fetus, and newborn. Second Cup’s flat white coffee keeps me good company through this two hour long, content-heavy lecture.



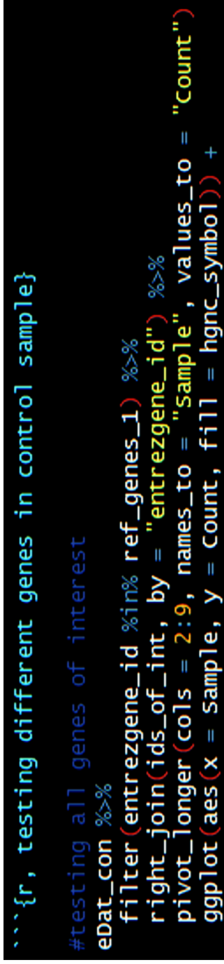
TUESDAY



We’re on the hereditary cancer section of my human genetics course. Each class is a case-study, and we’re given information on a certain individual, and have to determine the genetic cause of their condition. Drawing a pedigree, as shown here, is a common first practice in order to elucidate hereditary disorders.

Class is over, so I've headed to the site of my second lab – the BC Cancer Research Centre. Located on West Broadway, it's in one of the more lively areas of Vancouver.

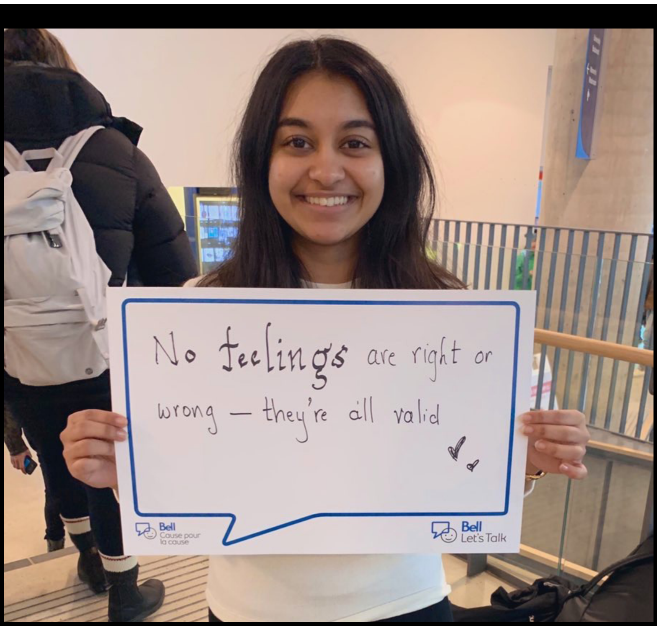
I'm in the process of extracting RNA from placental tissue – a procedure that can take anywhere from an hour and a half to five hours. Since I've just started lab work, I'm borrowing one of the lab benches, but I'll be moving to my own lab bench in a different lab bay soon.



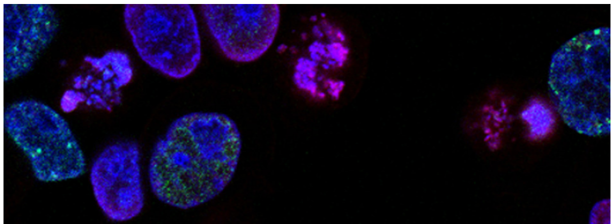
~~~
```{r, testing different genes in control sample}

#testing all genes of interest
eDat_con %>%
  filter(entrezgene_id %in% ref_genes_1) %>%
  right_join(ids_of_int, by = "entrezgene_id") %>%
  pivot_longer(cols = 2:9, names_to = "Sample", values_to = "Count")
  ggplot(aes(x = Sample, y = Count, fill = hgnc_symbol)) +
~~~

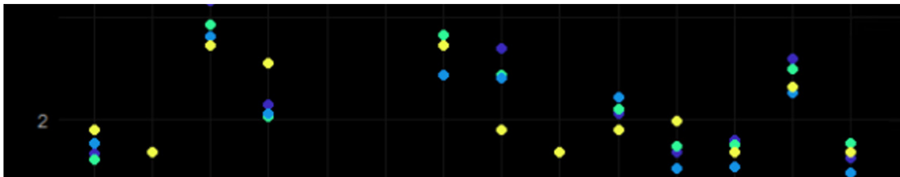
The RNA has been extracted, and I'm heading back home after a long day. I'll take the SkyTrain from Cambie Street, and I purposely walk the longer way to get this breath-taking view of the Downtown skyline and of the mountains.

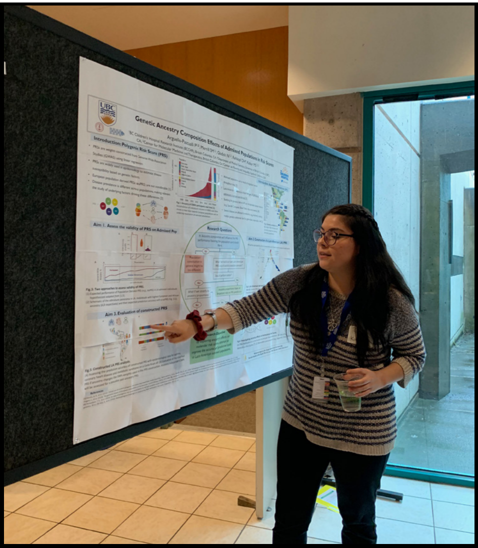
WEDNESDAY



While on my way to the bus loop at UBC, I walk through The Nest – UBC's Student Union building. Bell, the telecommunications company, was hosting their Let's Talk event to promote discussions around mental health. I decided to share a few thoughts on the topic.



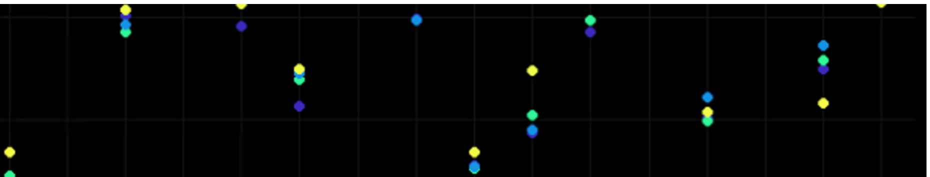


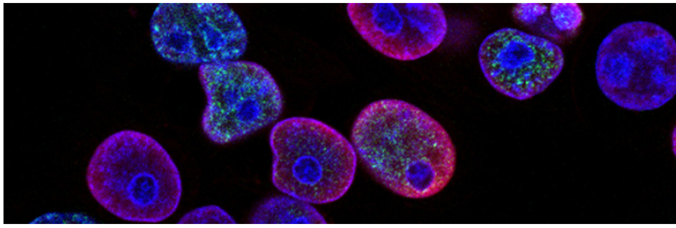


It's Research Day at the research institute! Students display their work through scientific posters, and we have a few presentations and talks. Lunch was provided – which is always a bonus (#studentlife), and a reception with snacks to follow. Here, my friend Paola describes the hypothesis and planning of her research project.

The Vancouver Community College showcases the Fashion Meets Science kids clothing line that was designed with the collaboration of one of the labs in the institute. I absolutely loved the orange dress inspired by the common fruit fly, but the denim skirt depicting an ELISA plate was my favourite.

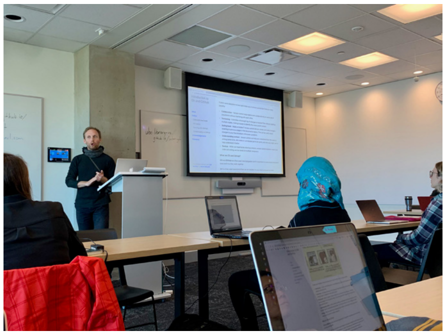
My human genetics class had an in-person objective: visit a pharmacy that offers genetic tests claimed to be for health concerns. I posed as a clueless, concerned daughter of a father having heart problems, asking the 'expert' at the store about information on the test and it's accuracy. I was, unfortunately and predictably, not impressed.



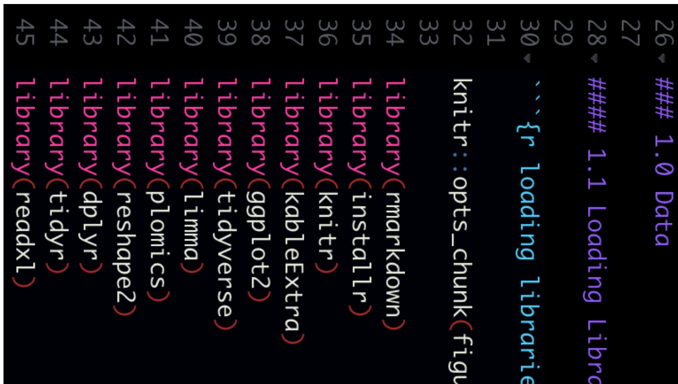


THURSDAY

After class at UBC on Thursday morning, I signed up to attend a workshop offered by the Graduate Student Society. This building shown is one of the two larger libraries on campus – the Koerner's Library. If seen from an aerial view, it looks like an open book. The workshop took place inside.



The workshop is on the Git software and the online GitHub open-access code sharing website. I conduct all of my analyses in the R Software for Statistical Programming – and GitHub is one of the tools that is heavily used for storing and downloading the specific packages (or plugins) that are required for computation.



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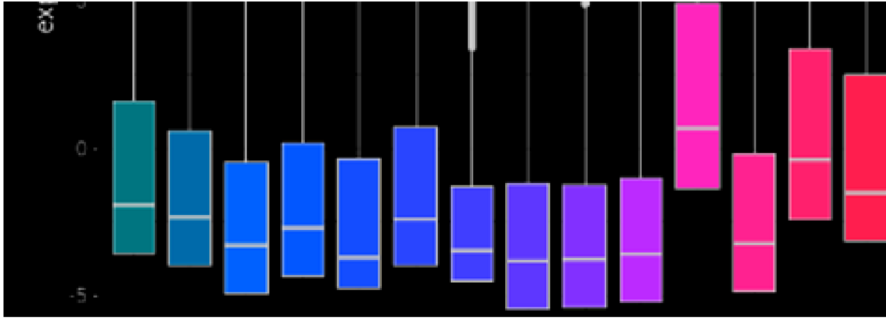
I'm back at the research institute to pick up a few samples before heading to the cancer centre. My lab bench here is fairly clean, and our lab – very unsurprisingly – stocks pink gloves (since we're a placenta lab).

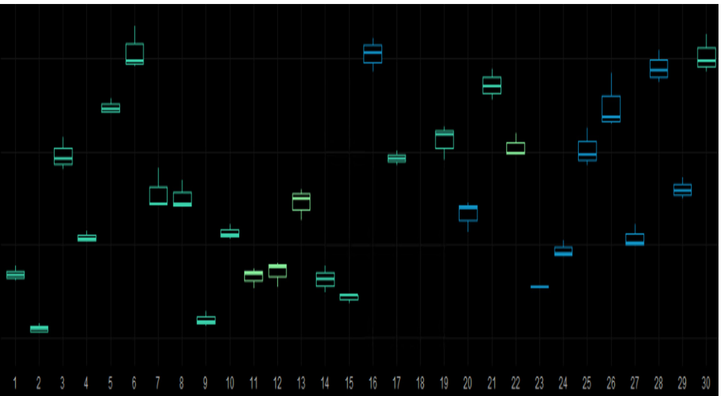


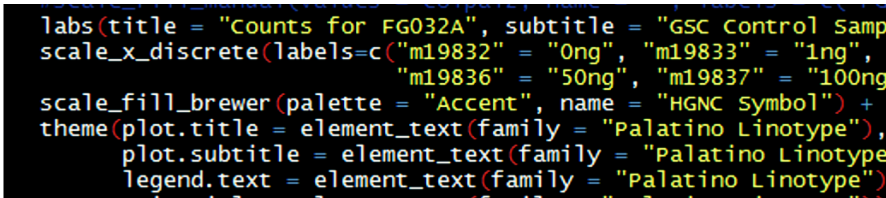
At the cancer centre, this is the view I get to enjoy while I'm waiting for my samples to finish incubating. Words do no justice to the beauty that is Vancouver, or British Columbia.

FRIDAY

No classes on Friday, so I take my time waking up and enjoying some tea in the morning. My little plant always cheers me up – a good start to the day.

The Genome Sciences Centre is celebrating their anniversary today and has opened their doors to the public. This screen shows the number of genetic bases that have been sequenced at the centre, since its founding. The number is in petabytes!





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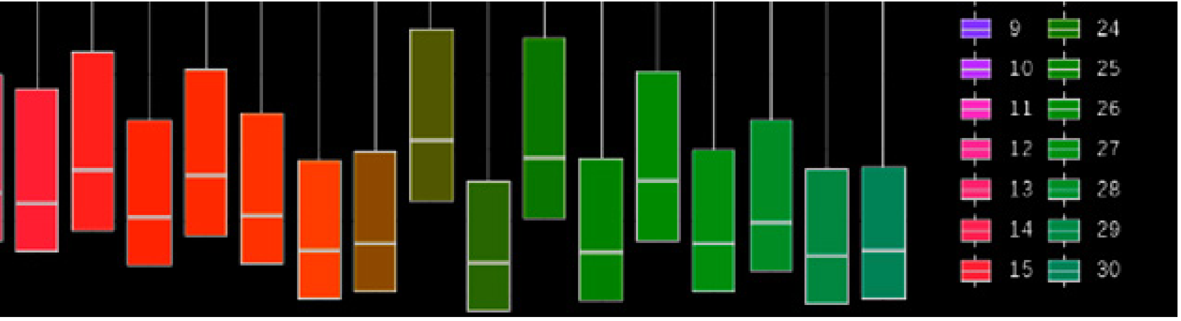
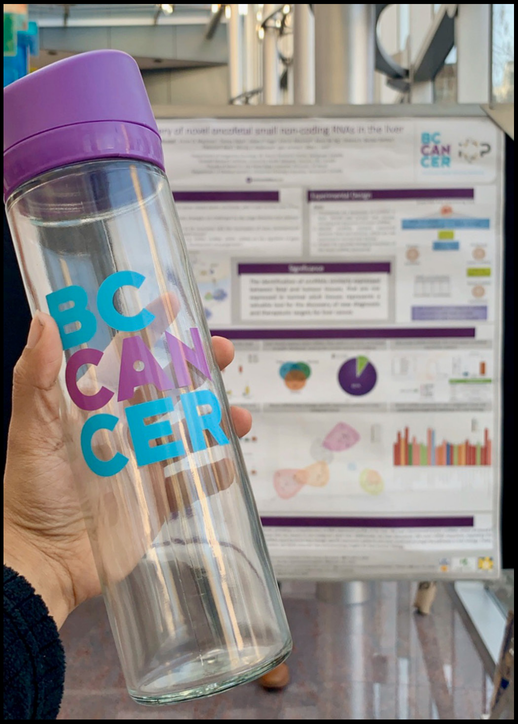


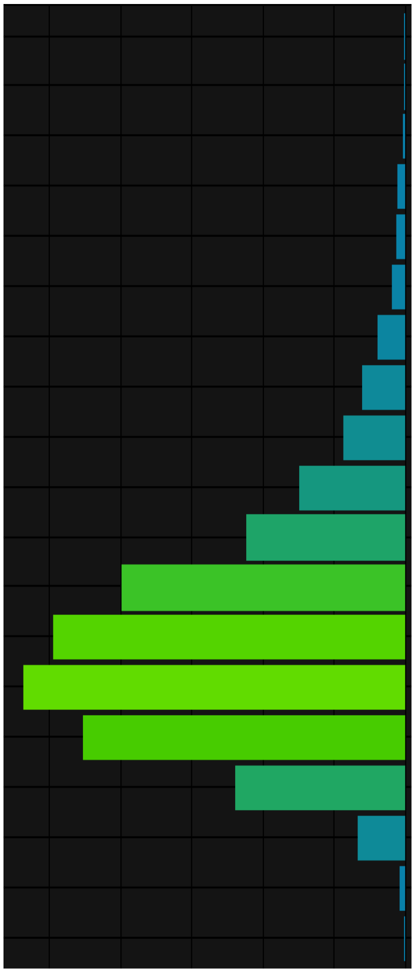


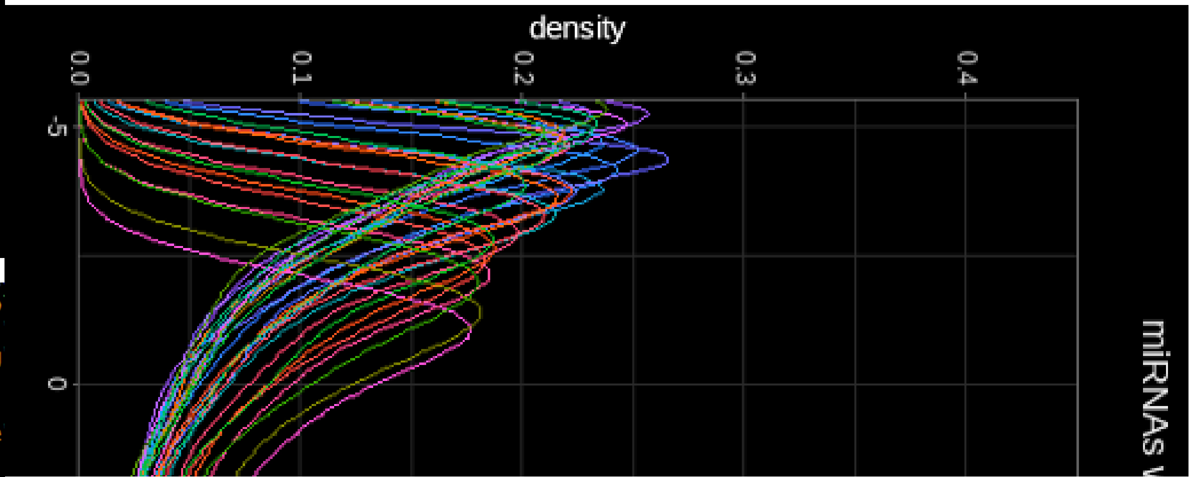
The BC Cancer Summit is also happening today and I have a poster on display. Free goodies are always fun, but the talks at this conference were even better. Networking is crucial in any subject area – and I got the opportunity to meet and listen from some of the top names in the field.

The BC Cancer Summit concluded with a dinner at the Sheraton Wall Centre Hotel. An evening to dress up after the days of talks, my cancer lab and I take small quantities of all of the decadent food served in order to be able to taste the whole spread. The medley of desserts signals the end of my dynamic week – where no week is the same as the last one.

ABOUT THE PHOTOGRAPHER

Nikita is a first-year Medical Genetics PhD student at the University of British Columbia. When not analysing data, she enjoys reading, photography, expanding her repertoire of cooking recipes and music taste, and drinking Italian Roast coffee. If she could have a superpower it would be telekinesis, and would want to time-travel back to Ancient Greece.





Challenges in remaining "UpToDate": A case study identifying errors in evidence-based point-of-care resources

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Abstract:

Our understanding of the prevalence of mental health disorders (MHDs) in society is in the midst of a paradigm shift: where MHDs were once considered rare within a population, studies through the last decade have converged to the conclusion that they are, in fact, near universal. Consequently, the demand for mental health treatment has resulted in the training of Primary-Care Physicians (PCPs) to identify, diagnose, and treat common MHDs. As generalists, PCPs require specialised point-of-care clinical resources to educate their patients and provide them with evidence-based treatment plans; UpToDate is one such resource. As a database of synthesized peer-reviewed medical information, written and approved by physician-experts from their review of contemporary peer-reviewed literature, this resource is considered a gold standard. Here, we examine an MHD-specific investigative case study on Generalized Anxiety Disorder where the synthesized UpToDate medical information was found to be in conflict with the original studies. In this era of unrelenting bombardment of digital data, the responsibility of assessing the truth of the information falls to the consumer. While a reliance on reputable information-sharing platforms facilitates both the access and assessment of truth, we discuss the risks of unintended errors, their propagation, and the potential impact at the point-of-care.

Introduction

Individuals who experience mental health disorders (MHDs) have been assumed to be relatively rare within a population. Conversely, individuals who live MHD-free lives are considered prevalent, commonplace, and consequently, are overlooked. Given that the majority of MHD prevalence evaluations are based on point-based, cross-sectional analyses of a population, where the number of MHD cases currently observed in the population are examined *at a single point in time*, these assumptions hold true [1]. However, a *longitudinal* view of lifetime prevalence reveals these disorders to be much more commonplace than originally assumed, resulting in a paradigm shift in our view of MDH in society [1] . Through the past decade, population-representative estimates have converged to the conclusion that diagnosable disturbances in behavioural or emotional health at some point in an individual's life is near universal [1] and, most worryingly, the rate of mood disorders and suicide-related outcomes have increased significantly in specific sub-populations [2].

To illustrate the impact of historical studies on our understanding of the prevalence of MHD in society, consider the simulated and simplified example in Figure 1. The lifespans of ten individuals are depicted with portions of their relative lifespans highlighted to represent a period in time when they were diagnosed with an MHD. While each individual exhibits a varying number and duration of MHD period within their intra-person lifespans, we highlight that the four cross-sectional studies used to evaluate the point-based prevalence of MHD in this population consistently identifies ~10-20% of the population as having a MHD at each time point (study #1: individuals 2, 7; study #2: individuals 2, 3; study #3: individuals 1, 9; and study #4: individuals 5, 9). Interestingly, this holistic view of MHD periods over individual lifetimes reveals that almost all individuals experience at least one MHD within their lifetimes; only individuals 6 and 10 appear to have lived MHD-free lives. Not explicitly captured in this example is the prevalence of undiagnosed MHD or contextual life-events, factors contributing to additional layers of complexity in appreciating societal impact. Modifying the metric with which we quantify the prevalence of MHD within a population has sweeping consequence across the continuum of care.

With the more holistic understanding of the prevalence of MHD in society comes the realization of the dire

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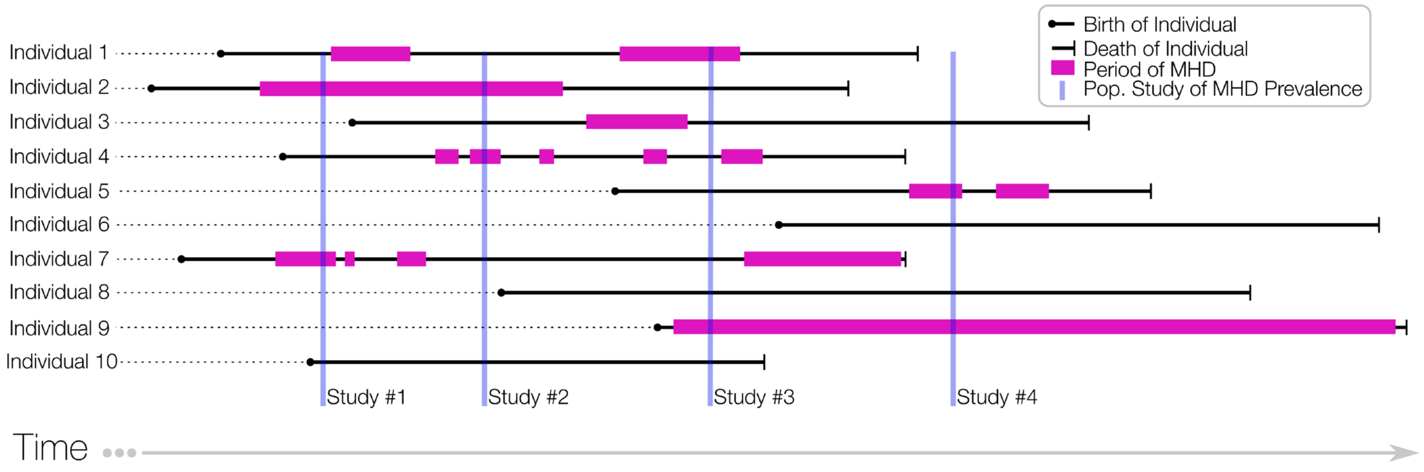

Figure 1 | Simulated example of a series of point-based, cross-sectional studies to determine MHD prevalence. Studies that measure the prevalence of MHDs in a population as the *percentage of the population that are diagnosed with an MHD during the study period* will fail to capture the incidence of MHDs at other periods of an individual's life, that is, the period of time before the study and the period of time following the study. While this figure is a simulated example, by modifying our definition and view of MHD over the course of an individual's lifetime, we can appreciate that MHDs are much more commonplace than originally defined necessitating increased medical support.

need for increased medical support. Unfortunately, the availability of physicians treating MHDs has remained essentially unchanged and has even seen a periodic decline in the number of psychiatrists [3,4], exacerbating the mismatch between MHD treatment supply and demand. With the recognition of this disparity, there has been a concerted effort to train Primary Care Physicians (PCPs) in identifying, diagnosing, and treating common mental health conditions including Depression, Anxiety, and Attention Deficit Hyper-Activity Disorder (ADHD) [5]. Moreover, the vast majority of patients with psychological problems, between 90–95%, are seen only by their PCP [6]. As generalists, PCPs must be trained and provided with clinical resources enabling them to educate patients on their options as part of an evidence-based treatment plan. Evidently, such resources must consolidate the myriad of peer-reviewed research to represent the state-of-the-art in medical treatment. One such resource for evidence-based medicine is the UpToDate electronic resource for clinicians. Unfortunately, despite the best efforts of the curators of such information, these resources are not void of errors. Here, we explore a case study where a PCP leveraging the UpToDate resources may be faced with conflicting information in an effort to educate a patient on their MHD treatment options.

The UpToDate clinical resource for point-of-Care medicine

UpToDate is a subscription-based resource enabling physicians to access current clinical information [7]. Considered to be a gold standard resource for evidence-based medicine, UpToDate's website reports that it is used by over 1.9 million clinicians and over 7,100 physician authors, editors, and reviewers contribute to the synthesis of contemporary medical research to produce evidence-based recommendations [8]. Articles in the UpToDate system are written by physician-experts who perform a review of literature on specific medical topics and synthesize the salient information. Each article is then peer-reviewed and approved by other physician-experts. In essence, originally peer-reviewed research articles are consolidated within a document that itself undergoes another round of peer-review.

In this information era, UpToDate is one of several clinician-focused tools to facilitate access to evidence-based information at the point-of-care. Two other commonly used resources, DynaMed and Essential Evidence Plus (EEP), publish clinically-organized topics that are readily reviewed and updated. Topics in all three systems include comprehensive reviews of diseases, health conditions, and abnormalities, as well as more targeted topics related to patient evaluation, differential diagnosis, and healthcare management [9,10].

Case study on mental health treatment

Let's consider a hypothetical adult patient who has recently been diagnosed with generalized anxiety disorder (GAD) who expresses concerns about going on medication due to its side effects. Their PCP might wish to consider alternatives to medication such as cognitive behavioral therapy (CBT) and uses UpToDate and related resources to investigate the effectiveness of CBT compared to the first line medication treatment for GAD in adults.

At the time of writing, the PCPs search of "generalized anxiety disorder" in UpToDate returns the top-ranked article entitled "Approach to treating generalized anxiety disorder in adults" that compares and discusses the use of CBT versus medication in newly diagnosed patients with GAD. In the subsection “Choosing between CBT and medication”, the article cites a meta-analysis including 65 studies that compared CBT to pharmacotherapy and concluded that the effect sizes between the two groups is roughly equal [11]. However, upon further investigation, the study’s conclusions about the differences in efficacy between therapy approaches is weak justification due to the limitations of the meta-analytic methods used. Given the fixed-effect approach the author used in portions of their analysis, the data could not be generalized to the greater population [11].

The UpToDate article cited another meta-analysis which included 79 randomized clinical trials with a total of 11,002 study participants diagnosed with GAD [12]. UpToDate states that the studies evaluating the efficacy of pharmacotherapy and evidence-based psychotherapy found no significant difference in effect sizes between the two groups ($g = 0.59$ vs. 0.76, respectively). However, further examination of the meta-analysis text itself revealed psychotherapy showed a medium to large effect size ($g = 0.76$), while medication showed a small effect size ($g = 0.38$) on GAD outcomes. UpToDate mis-reported the meta-analysis’ results and erroneously reported the pharmacotherapy effect size for *depression* ($g = 0.59$) rather than GAD ($g = 0.38$). This incorrect citation of the source’s results invalidated UpToDate’s conclusions on the equivalency of CBT and pharmacotherapy. The meta-analysis further describes a secondary analysis that revealed psychotherapies, particularly CBT, had better outcomes among younger patients. In summary, while UpToDate concludes that the treatments are expected to have equivalent effect sizes, the originally cited literature evidences the conclusion that CBT may, in fact, be the superior approach to managing GAD.

Our findings were corroborated by a similar investigation using the EEP and DynaMed resources. Both EEP and DynaMed are evidence-based point-of-care resources designed to assist clinicians. EEP comprises several searchable databases that organize information as topics and sub-topics [10]. Each sub-topic offers a summative “Overall Bottom Line” of the most recent clinical evidence [10]. Similarly, DynaMed organizes information as “Evidence Reports” and assigns a numeric label from 1–3 representing “likely reliable evidence”, “mid-level evidence”, and “lacking direct evidence”, respectively [9]. Additionally, recommendations are assigned a letter from A–C representing “consistent high-quality evidence”, “inconsistent or limited evidence”, and “lacking direct evidence”, respectively [9].

In its “Bottom Line” recommendation, EEP concluded that CBT focusing on overvaluation of worry, worry-proneness, and dealing with uncertainty appeared to be as effective as pharmacotherapy for treating GAD while appearing to have lower attrition and greater durability in adults, children and adolescents [13]. Citing a systematic review of 22 studies with 1,060 participants, 13 studies compared CBT to “treatment as usual” which included pharmacotherapy among other psychotherapeutic methods [13]. The authors concluded that CBT was more effective than “treatment as usual” in achieving clinical response, as well as reducing anxiety, worry and depression symptoms [13]. The EEP article assigned a strength of recommendation value of B defined as “inconsistent or limited-quality patient-oriented information” [10]. DynaMed cited the same systematic review as EEP, assigning a “Level 2/Mid-Level” evidence grade to the study conclusion that CBT reduces anxiety symptoms in adults with GAD. Level 2 grades are given to outcomes supported by “some method of scientific investigation, but not meeting the quality criteria to achieve Level 1 evidence labeling” [9]. DynaMed did not directly compare pharmacotherapy and psychotherapy in its conclusions; rather, it considered them separately.

Discussion

Whether the prevalence of MHD within a population is perceived as common or uncommon, a patient’s access to the requisite treatment is influenced by a myriad of factors. From the individual’s perspective, physical barriers, perceived trust in healthcare institutions, MHD stigma, financial barriers, and personal motivations are a handful of examples of patient-specific factors limiting access (depicted as bottom-up factors in Figure 2). Conversely, a cascade of top-down, health

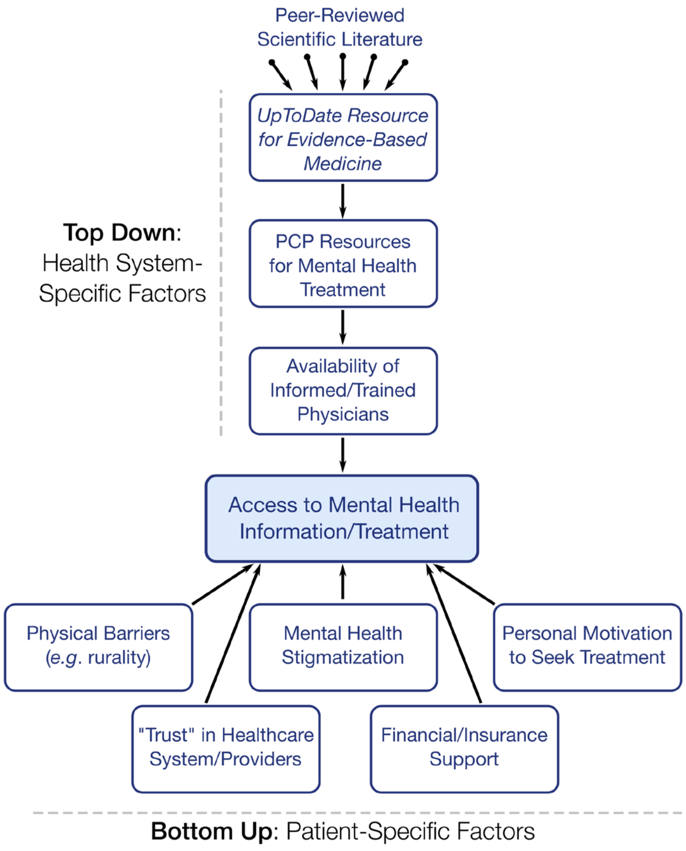

Figure 2 | Flowchart of factors influencing patient access to MHD information and treatment. Top-down factors are a cascade of health system-related factors. Bottom-up factors are independent and patient-specific.

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system-specific factors, each dependent on the previous, also limits the supply of MHD-specific treatment (Figure 2). Notably, the availability of the UpToDate resource occurs early in the cascade as it is foundational for developing PCP-specific resources to grow the pool of MHD-knowledgeable physicians. More importantly, a recent study demonstrated that the use of UpToDate reduces diagnostic errors rates [14]. However, a subset of those erroneous diagnoses or management, despite the use of this clinical knowledge support system, may be attributed to potential errors within that system itself.

This case study, specifically, highlights errors within an MHD-related UpToDate article. All too often, peer-reviewed information is taken at face value with the assumption that the scientific publication process strictly enforces truth within the work [15]. Moreover, peer-reviewed articles that synthesize information from other peer-reviewed work (*e.g.* review articles, meta-reviews, textbooks) benefit from a compounding effect; the assumption of their technical correctness is greater still. In Figure 3, we adapted the work of [16] to situate the UpToDate articles within the hierarchy of previously peer-reviewed and published works. As a ‘Summary’, these articles report information that may have gone through upwards of three previous rounds of peer-review [16]. The introduction of any form of error at this level can have widespread and possibly detrimental impact. While the typographic error identified in this case study may appear innocuous at the outset, it did fundamentally reverse the recommended treatment which is an error that may propagate further within the literature or within a patient population. Furthermore, the risk associated to these (allegedly) unintended errors must also be appraised with the risk of intended error or personal biases of the UpToDate authors and editors. A notable medical ethics study investigated the conflicts of interests between UpToDate authors or editors who had a financial relationship with a company whose drug was mentioned in the article; of the medical conditions considered, all UpToDate articles demonstrated a conflict of interest in contrast to DynaMed for which no author or editor had a documented conflict [17]. Finally, UpToDate is often considered an evidence-based resource, however the information reported in the database is not strictly evidence-based. Unfortunately, UpToDate does not share its literature monitoring and search methods which prevents stakeholders from determining whether or not important studies have been overlooked [17]. The UpToDate authors synthesize selected literature with their own domain-specific knowledge to develop patient care recommendations. Ultimately, the interpretation and assessment of this information falls to the consumer, however this poses evident challenges when this information is consumed as part of training material for a non-domain-expert.

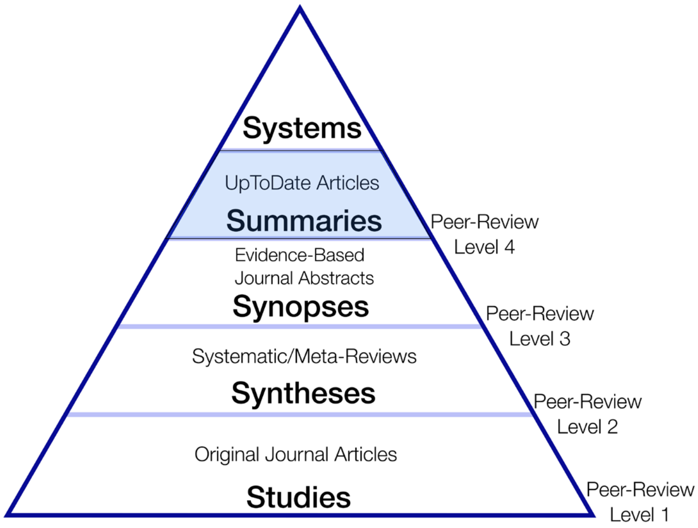

Figure 3 | Adaptation of Haynes' 2006 hierarchy of the "5S" levels of organization of evidence from healthcare research.

With a growing demand for MHD healthcare services, PCPs must be adequately trained and provided the necessary resources to educate and support this patient population. It is an unfortunate reality that scientific research as a whole is in the throes of a “reproducibility crisis” which calls into question the validity of a given research article and erodes the trust in the peer-review process as a whole. In this work, we sought to shed light on the impact of errors within summarized medical recommendations. Finally, this work seeks to open a dialogue on some of the more philosophical foundations at the core of the scientific process: to what extent can we trust *any* peer-reviewed document? How much peer-review is *enough* peer-review? Who is responsible for errors introduced within medical recommendations?

Conclusions

While MHDs were originally understood to be rare within a population, through the last decade, studies have revealed them to be near universal when viewed across an individual’s lifetime, commensurately increasing the need and demand for treating physicians. Levied upon the generalists, PCPs require specialised point-of-care clinical resources to educate both themselves and their patients in order to provide evidence-based treatment plans. While the UpToDate database of synthesized peer-reviewed medical information is considered a gold standard, we investigated an MHD-specific case study on GAD and found the synthesized UpToDate medical information to be in conflict with the originally cited studies. This finding, corroborated by other concerns for the independence of recommended treatments in the face of commercial conflicts of interests, inspire discussion about the oversight of documents used in first-line patient treatment. This work is limited to a single case study of a specific illness and a handful of supporting documents, motivating the need for a systematic and independent review of UpToDate to determine the prevalence of errors on the platform. More generally, it is our hope that this work will promote reflection on the validity of multi-peer-reviewed documents, the need for methodologic transparency when synthesizing existing research, and the systematic review of these summaries.

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The rise of electronic cigarettes: A brief look at their cardiovascular effects and what makes them so popular

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Abstract:

Electronic cigarettes (ECs) have quickly gained popularity among adolescents and adults, and have begun to replace conventional cigarettes as a source of nicotine. Although little is known about the impact of the exposure of chemical constituents of ECs, two major constituents, propylene glycol and vegetable glycerin have been implicated as formaldehyde-releasing agents. The wide variety of EC flavours appeal to users of all ages with reports showing a positive correlation between EC use and sweet flavorings. In addition, although marketing strategies advertise ECs as tools to facilitate smoking cessation, the evidence supporting this role is weak. In terms of its effect on users with pre-existing cardiovascular diseases, the data is conflicting regarding whether ECs have an impact on cardiovascular function. Although it is obvious that their safety and efficacy needs to be better understood, it is nonetheless essential to review what the research conducted so far has shown.

Despite the prevalence of conventional cigarette smoking by adolescents and adults at historically low numbers, public health agencies across North America are grappling with a new and different type of problem – the use of electronic cigarettes (ECs) [1]. The mid to late 2000s saw a rapid increase in the use of these battery-powered electronic devices which heat liquids (mainly propylene glycol, glycerol, and nicotine solution) stored in a disposable cartridge into a vapour form for inhalation [2]. This is in contrast to conventional combustible cigarettes which deliver nicotine primarily through the burning of tobacco and are widely known as a risk factor for several preventable diseases including cardiovascular and pulmonary diseases, and certain types of cancers [3]. ECs have quickly risen in popularity with over 15.4% of the U.S. adult population having tried them at least once in the past [4]. Although heavily marketed as a 'healthy' alternative to conventional cigarettes due to their ability to deliver nicotine without the burning of tobacco and as an inexpensive smoking-cessation tool, recent evidence questions their safety, leading to the introduction of stringent regulations across North America [5]. Under the new proposed rules which took effect in 2014, the U.S. Food and Drug Administration (FDA) banned the sale of ECs to individuals under the age of 18 and regulated the sale of ECs as tobacco products [3]. As of 2017, Canada has prohibited manufacturing and sale of ECs containing nicotine [6]. In spite of such regulations, ECs remain widely available online and in retail outlets which calls for the need to better understand the effects on both short- and long-term health.

Chemical constituents of ECs

In a conventional cigarette, majority of the smoke toxicants are generated due to the burning or combustion of tobacco containing nicotine at temperatures around 700-950 °C [7]. The smoke from this reaction contains over 7,000 chemicals, 69 of which are known carcinogens that have been implicated in major diseases [8]. In contrast, ECs differ in product design such that they do not burn or contain natural tobacco [9]. Instead, they deliver nicotine directly through the heating of the EC-liquid solution containing nicotine, flavourings, and other products which produce an aerosol of ultrafine particles (often called "vapour") which are then inhaled by the user [9,10] . It is still unknown whether these ultrafine particles produce similar toxicity effects to those generated by conventional cigarette smoke [11]. However, the available evidence suggests that ultrafine particles from air pollution and tobacco smoke encourage pulmonary inflammation and consequently increase the risk of cardiovascular and respiratory diseases, even after short-term exposure [11].

Despite the variability in EC-liquid composition due to a wide range of nicotine and flavouring concentrations used, two nicotine-solvent compounds, propylene glycol and vegetable glycerin, represent the majority of the EC-liquid volume [10,12]. Although these two ingredients have been approved by the FDA for commercial use, their role in ECs has not been well characterized [13]. Evidence has shown that repeated exposure to propylene glycol can cause irritation

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of the respiratory airways [13]. To make matters worse, the degradation of propylene glycol and glycerin during the heating of ECs in the presence of oxygen produces formaldehyde and acetaldehyde, which are known human carcinogens, at levels approaching those from conventional cigarettes [14]. In comparison, the emission levels of other smoke toxicants such as volatile organic compounds and tobacco-specific nitrosamines remain either undetectable or as a fraction of what is typically found in conventional cigarette smoke [14,15]. A study looking at EC vapours found that over 2% of the solvent molecules from the aerosol vapours were converted from propylene glycol and glycerol into formaldehyde-releasing agents [14]. Although the disposable cartridges themselves have shown to have zero or only trace amounts of these harmful chemicals, heating of propylene glycol in the EC cartridge may result in the formation of these chemicals [16]. Although it is unknown how formaldehyde-releasing agents affect the respiratory tract, the classification of formaldehyde as a group 1 carcinogen calls for a more detailed understanding of its role in ECs [14]. Results from toxicological studies show the presence of formaldehyde in conventional cigarettes as well, where it is known to be generated during tobacco combustion from saccharides such as sugars and cellulose used as tobacco ingredients [17]. If formaldehyde-releasing products from ECs do carry the same risk per unit of formaldehyde as gaseous formaldehyde from conventional cigarettes, then long-term vaping may lead to a 5 times increase in lifetime cancer risk compared to long-term conventional cigarette smoking [14]. This data was based on earlier studies looking at daily exposure of formaldehyde from ECs and was derived using protocols from Health Canada and the International Organization for Standardization, and the Massachusetts Department of Public Health [14] . In addition, EC smokers experience an increase in serum cotinine levels which are comparable to levels seen in conventional cigarette users [18]. Cotinine is a major alkaloid metabolite of nicotine and has been used as a biomarker for tobacco exposure in humans [18]. These findings demonstrate that the popular claim that EC emissions are "only water vapour" is false [19].

Impact of the wide availability of EC flavours

The availability of over 7,000 EC flavours make them one of the most frequently used flavoured tobacco product around the world [20]. In a 2014 study, 81% of the youth attributed the flavour availability as the primary reason for their initial use and/or continued use of ECs [21]. Multiple studies have found that the addition of flavours increase the palatability of the liquid in the ECs [22]. In one study, higher ratings of perceived sweetness of different EC flavours were positively associated with liking the product [22]. Another study looking at EC flavour preferences of a high-school in the U.S. found that adolescents were significantly more likely to prefer flavours perceived as sweet, such as "fruit," "candy/dessert," and "vanilla" compared to adults [23]. In the past, the disproportionate preference of flavoured tobacco cigarettes by the youth population led to their ban by the FDA [23]. The wide availability of flavours can create the perception that their addition makes the ECs less harmful and therefore contribute to the increased popularity among youth [22].

ECs as a smoking cessation tool

The tobacco industry has marketed ECs as a lower-risk smoking-cessation tool for individuals who would otherwise be reluctant to quit smoking [24]. This includes promoting them as a healthier alternative on social media sites such as YouTube, Facebook and, Twitter which do not require age verification from its users, and through banners on entertainment websites visited frequently by youth [24]. However, data from epidemiological studies have been inconsistent in terms of whether the use of ECs are associated with long-term abstinence from cigarette smoking [10]. Although some population-based surveys have found a positive correlation between EC use and quit attempts, other longitudinal studies report no such association [10]. A randomized control trial conducted in the U.K. found that EC smoking led to significantly higher rates of abstinence (18.0%) compared to those using nicotine-replacement products (9.9%) at a 1-year follow up [25]. Nicotine replacement products include nicotine-patches, gums, and lozenges which are commonly used as smoking cessation tools by individuals looking to quit conventional smoking [25]. However, these findings are contradicted by results from a randomized trial from New Zealand where adult smokers interested in quitting smoking achieved similar levels of smoking abstinence after 6-months using ECs compared to those given nicotine patch vouchers [26]. Meta-analyses of these studies suggest that there is little evidence to support the idea that nicotine-containing ECs help with smoking-cessation [27]. However, the number of attempts at smoking-cessation may be dependent on the type of EC device used, the amount of nicotine in the product, as well as the frequency of use [10]. Cross-sectional data shows that individuals who use the earlier versions of ECs tend to be dissatisfied with their device and show lower cessation rates compared to those who use newer versions which allow them to customize flavours and nicotine strength [28]. Similarly, the amount of nicotine emitted per puff second (nicotine flux) by an EC can influence cessation rates [29]. Certain brands with low "nicotine flux" may not provide enough nicotine replacement for a smoker to quit, and others might provide too much leading to undesired side effects such as nausea [29]. However, the studies on the use of ECs as a smoking cessation aid has only been conducted in adult populations and remains untested in youth [24].

Effects of ECs on the cardiovascular system

There is substantial evidence supporting the adverse effects of conventional cigarettes on cardiovascular health. A key question is whether similar effects are evident with ECs. Although oxidative stress and endothelial dysfunction is more pronounced with conventional smoking, the use of ECs could

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predispose individuals to adverse cardiovascular conditions, and has been linked to short-term pulmonary inflammatory reactions [30]. Increased aortic stiffness was observed following a 30-minute session use of EC, which was similar to the effects observed after 5-minutes of smoking tobacco [31]. However, since arterial stiffness returned to normal within 30 minutes after EC use, this may be only a short-term association [31]. Limited preclinical studies using mouse models have aimed to establish the impact of chronic EC use on cardiovascular health. Mice subjected to 8 months of chronic EC use at low levels exhibited significantly increased arterial stiffness and reduced vascular relaxation to a vasodilator [32]. Similarly, exposure to EC vapour increased systemic inflammation, systolic blood pressure, and showed an upward trend in diastolic blood pressure [33]. However, most of the current data on the cardiovascular effects of ECs comes from preclinical and cross-sectional studies. The results from these preclinical cell-culture and animal studies need to be replicated in human subjects in an ethical manner to assess for safety and efficacy of ECs. Similarly, since cross sectional studies rely on observational data from specific points in time, it is not yet possible to infer causation.

In addition to looking at EC use by the general population, it is also important to evaluate their impact on chronic tobacco users with pre-existing chronic obstructive pulmonary disease [COPD]. One recent retrospective study found evidence of a reduction in respiratory conditions including decreased respiratory infections and absence of deterioration in respiratory physiology [34]. They also reported improved general health and physical activity in COPD patients who reduced their tobacco consumption after switching from conventional cigarettes to ECs [34]. Similar improvements in health outcomes has been reported by an internet-based survey of individuals with COPD, majority of whom were smokers who attempted to avoid the adverse effects of smoking by switching to ECs [35]. These positive findings are in contrast with studies conducted in preclinical cell culture and animal models. For example, a study conducted using A/J mice widely used in cancer research due to their tendency to develop tumours, found increased cytokine expression, airway hyper-reactivity and lung-tissue destruction after prolonged exposure to nicotine-containing glycerol or propylene glycerol [36]. Another mouse study found a significant decrease in bacterial clearance from the lungs of the animals exposed to EC vapour for one week following infection with Streptococcus pneumonia [37]. It is well-known that patients with COPD experience exacerbated viral and bacterial complications which are a major cause of COPD-related morbidity and mortality [37]. Therefore, if EC use can impair immune responses against infections in mouse models, it is possible that they can accelerate disease progression in patients with COPD [37]. The contradictory findings among studies makes it difficult to get a clear understanding of the effects of ECs. Such differences result from a lack of defined models for EC exposure in both in vitro and in vivo studies and due to methodological drawbacks including differences in EC devices or in the concentration of EC vapour used [38,39].

Concluding remarks

With the continuous rise in the use of ECs by the youth population, it is concerning that their potential health effects remain to be fully elucidated. Although multiple studies have looked at the chemical constituents of ECs, the research has been conducted under controlled conditions which may not be the best representation of actual EC use [40]. It is becoming clear that the appeal of wide selection of flavours, including non-tobacco flavours such as candy, fruit, and dessert, likely appeal to consumers of all ages and may play a part in the initiation of EC use especially in youth [21]. An argument often posed by the proponents of ECs is their supposed role in smoking-cessation [41]. However, current evidence supporting their smoking-cessation role is weak and may provide the same benefit as nicotine replacement products available on the market [41]. Finally, while cross-sectional studies suggest there is a slight advantage of ECs over conventional cigarettes in individuals with pre-existing cardiovascular conditions, this evidence does not allow for strong conclusions to be drawn [42]. Any correlation between ECs and cardiovascular health is further complicated by short-term animal studies showing endothelial dysfunction following EC consumption [42].

With hundreds of EC brands dominating the market, it is important to develop a mathematical model which can accurately predict EC nicotine emissions and account for the variability in device design, ingredients in the EC-liquid solution, and user behaviour [40]. This would allow researchers to standardize parameters of the EC devices and generate results to determine causal relationships [40]. Furthermore, although observational studies can gather information on large number of users, randomized control trials can allow for experimental control over variable factors such as a user's nicotine dependence and previous attempts at smoking cessation [40]. Although these studies are conducted under idealized conditions and might not accurately depict real-time use of ECs, they are still needed to confirm the results shown in observational studies. Nonetheless, it is important to recognize the gaps in knowledge and use them as the foundation for future studies to accurately characterize the risks of ECs.

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Vaccination policy strategies in Ontario: Transitioning from parental vaccine hesitancy to vaccine acceptance

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Abstract:

Vaccination is considered to be one of the greatest public health achievements, contributing to a substantial decline in infectious disease mortality in Canada. However, a growing threat of vaccine hesitancy has led to an upsurge in the prevalence and incidence of vaccine-preventable diseases across the globe, including Canada. Vaccine hesitancy is on the rise in the province of Ontario. Parental vaccine hesitancy, vaccine misconceptions, rising non-medical vaccine exemption rates, and low childhood vaccination coverage has led to a resurgence in vaccine-preventable diseases, especially measles. Given the importance of achieving high vaccine coverage to avoid vaccine-preventable diseases and their dire consequences, vaccine hesitancy is an important issue that needs to be addressed. There is no perfect solution to address vaccine hesitancy. Understanding the complex mix of factors that determine individual and collective vaccination behaviour is vital to designing effective vaccination policies, programs, and targeted interventions. This article critiques current vaccine policy strategies and outlines a policy approach to address parental vaccine hesitancy and prevent future vaccine-preventable disease outbreaks, specifically in Ontario, and more broadly within Canada. Providing support to healthcare providers and primary care physicians; and empowering parents, schools, students, families, and communities in Ontario, will slowly but surely mitigate vaccine hesitancy and enable healthy vaccination behaviours. Healthcare system-based interventions seem to be the most comprehensive approach that requires coordinated efforts and partnerships between community-based organizations and vaccination providers to ensure inclusive and integrated service delivery.

Background

Vaccine hesitancy (VH) is the reluctance or refusal to vaccinate despite vaccine availability and is a leading risk factor resulting in low immunization uptake. Parental concerns regarding adverse effects following immunization (AEFI), especially in the developed world, has increased hesitancy to vaccinate [1]. In 2019, the World Health Organization (WHO) ranked VH as one of the top 10 global health threats [2]. The reasons for VH and/or vaccine refusal are complex and multidimensional. Given the importance of achieving herd immunity [mandated vaccination coverage for attaining adequate disease-specific thresholds] to avoid vaccine preventable disease (VPD) outbreaks, VH is a critical public health issue that threatens to reverse the tremendous progress in combatting VPDs in the past. VPDs, particularly those as serious and highly contagious as measles, are increasing in prevalence across the world [3], and Canada is not immune to this negative trend [4,5]. The 2016 Canada Communicable Disease Report [6] noted that approximately 20% people believed vaccines are directly linked to autism – a link that was officially discredited in 2010 [7], resulting from a 1998 research paper [8] that ignited a global confidence crisis in the measles, mumps, and rubella vaccine.

VH is on the rise in Ontario, Canada. Parental VH, vaccine misconceptions, rising non-medical vaccine exemption rates, and low childhood vaccination coverage has led to a resurgence in VPDs, especially measles. This article critiques current vaccine policy strategies and outlines a policy approach to address parental VH and prevent future VPD outbreaks, specifically in Ontario, and generally in Canada.

Adverse effects of vaccine hesitancy

Vaccination is considered to be one of the greatest public health achievements, contributing to a substantial decline in infectious disease mortality in Canada [9,10]. However, a growing threat of VH has compromised the herd immunity for VPDs [11], specifically the nation-wide mandated vaccination coverage of 95% for measles [12]. This negative trend has resulted in an upsurge in the prevalence and incidence of measles [5,13] in Ontario [14,15].

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VH is a complex public health issue that has resulted in the recent measles outbreak across Canada [16–21], including Ontario [14,15,22]. Particular risk factors for this crisis is misinformation on social media [23,24]; anti-vaccination movements [25,26]; vaccine misconceptions [1,27]; growing public mistrust [11,28–30], among others. Currently, there are approximately 20%-30% VH parents in the country [31].

Albeit scientific and medical fraternity is affirmative on vaccination benefits, negative discourse around vaccine safety and efficacy continues to dominate social media [24]. New generations of Canadians are unaware of the risks of many VPDs and their concerns have shifted to vaccination risks [32]. Given the importance of achieving high vaccination coverage to avoid VPDs and their dire consequences, VH is an important issue that needs to be addressed urgently and expeditiously.

Vaccination policy landscape

The recent measles crisis has fueled debate regarding childhood under-vaccination and mandatory vaccination of schoolchildren [33]. Although the Immunization of School Pupils Act [34] mandates childhood vaccination for attending public-school system in Ontario [34,35], the province currently permits non-medical vaccine exemptions on the basis of religious and philosophical reasons [34]. Under the Immunization of School Pupils Act, parents requesting non-medical exemption have to undergo a mandatory vaccine education class before such an exemption is granted [34]. In the event of an outbreak, unvaccinated children may also be subject to a temporary exclusion from school [34]. A failure to vaccinate children can further result in a fine of up to $1,000 [34].

In Ontario, considering the issue of steadily rising non-medical exemption rates [22,36,37] and adiaphorous impact of mandatory VH education classes for parents [38], Toronto’s Board of Health passed a report in September 2019 [39–41], with request in keeping with the recommendations from The Ontario Ministry of Health and Long-term Care – Premier's Council on Improving Healthcare and Ending Hallway Medicine [42]. The Council’s recommendations focused on ensuring robust continuum of care via patient integration, digital innovation, system efficiency, and capacity building measures [42]. Further, The Board of Health made additional policy recommendations to mitigate VH via developing a Vaccine-Injury Compensation (VIC) program, removing non-medical exemptions, empowering the public, regulating search engines and social media, improving electronic immunization record keeping, among other policy options [39–41].

Vaccination policy strategies and avenues: Critical analysis

This section will analyze the merits and demerits of aforementioned vaccine policy approaches and recommend a feasible and viable vaccine policy option [falling under the purview of provincial jurisdiction] with province-wide applicability in order to address parental VH in Ontario.

1. Vaccine-injury compensation program

VIC program is a "no-fault" publicly funded scheme that compensates individuals experiencing potentially rare AEFI ranging from mild to severe, if at all [43]. VIC programs have strong public health ethical justification and currently exist in 19 jurisdictions across the world, including 17 high-income countries [31]. In Canada, VIC currently exists in only one province, Quebec, with a good track record [44]. Thus, implementation in Ontario could help close this provincial vaccination policy gap [45]. Developing a provincial VIC program could strengthen vaccine acceptance [31] and provide a strong foundation to the current vaccine policy framework in Ontario. However, the financial cost estimation of injury is ambiguous since assessing causal relationship between a vaccine and a specific injury is difficult, with a high likelihood of VIC program being abused [46]. Thus, it is unlikely to curb the root cause of VH, that is, skepticism regarding vaccine safety and efficacy. Contrariwise, VIC programs can increase public mistrust in vaccines [46].

Further, with respect to the policy option of VIC, in lieu of developing a provincially administered financial compensation program, it might be more useful to mitigate vaccine safety concerns through improved public transparency on AEFI via streamlining and strengthening the Ontario AEFI system [47,48] as well as enhancing universal functionality of Canada-wide available and searchable online database of AEFI reports, that is, the Canadian Adverse Events Following Immunization Surveillance System [49].

2. Removal of non-medical exemptions

Removing non-medical exemptions based on philosophical and religious grounds, from the Immunization of School Pupils Act could be another way forward. In the United States, jurisdictions such as California, among others, which have removed non-medical exemptions, have shown improved vaccination rates in schools [50] and higher levels of vaccination coverage in comparison to jurisdictions that allow non-medical exemptions [51]. That said, there is a likelihood for abuse [profiteering] by physicians for financial gains and problem of VH parents shopping for vaccine exemptions, as had been reported in California [33]. However, this particular issue might not be of grave concern in Ontario (from the patient’ and physician’ point of view) due to the publicly-funded healthcare system in Canada, covering only those health services with a prerequisite medical reason in order to receive a health service and/or treatment [52].

Further, vaccine scholars and religious communities have noted that religion-based vaccine objections by parents cannot be traced back to any major religious or academic sources [53,54]. Furthermore, similar to the counterproductive aspects of implementing VIC program, ending non-medical exemptions seems counterintuitive [11,29,30] and contradictory [55,56] to lower VH and attain higher vaccine acceptance levels among parents in Ontario.

3. Public empowerment

Public empowerment entails providing support to primary care physicians; empowering parents, families, and communities; engaging collaboratively with healthcare professionals and local public health unit officials to support and enable healthy vaccination behaviours in the province. According to the WHO, VH is a complex and multidimensional issue and the most effective intervention must be multi-component, dialogue-based, and directly targeted towards under-vaccinated and/or unvaccinated population subgroups [57]. Collaborative engagement with healthcare professionals [58], local public health units, and newly formed Ontario Health Teams [59] has the potential to generate holistic insights, develop better healthcare services, and ensure recommended individual and community vaccination behaviours in the province [57,60]. Further, this approach will most likely entail lower financial and/or non-financial investments, relative to other policy options discussed above, with lower negative impact, if any, in implementing this particular vaccine policy and/or program strategy.

Another important facet of public empowerment is home visit interventions [61–63]. Although this strategy might address multiple issues such as parent education, vaccination promotion, among others, it might pose logistical challenges (vaccination scheduling and privacy concerns) and economic challenges (resource intensiveness). On the other hand, school-based interventions [64] could counter some of the above issues and also complement home visit services delivered through healthcare system-based interventions [65]. These interventions could turn out to be relatively less resource-intensive, in terms of both economic costs [lower healthcare costs] and opportunity costs [parental loss of productivity and income associated with child sickness and children's clinic visits]. However, school-based interventions could potentially impede regular channels of communication with primary healthcare provider. Furthermore, healthcare system-based interventions [65] seem to be the most comprehensive approach that requires coordinated efforts and partnerships between community-based organizations and vaccination providers to ensure inclusive and integrated service delivery. That is, public empowerment via formal healthcare system-wide interventions.

4. Regulation of search engines and social media

In relation to regulating search engines and policing social media, the Ad Standards Canada needs to revise the Canadian Code of Advertising Standards [66] and limit the spread of vaccine misinformation and disinformation by adopting the Priorities for Action from the Salzburg Statement on Vaccine Acceptance [67]. This policy avenue is critical to address VH in order to regulate nation-wide social media whilst promoting the spread of evidence-based, science-backed, and fact-checked information.

5. Improvement of electronic immunization records

The policy option of improving electronic immunization record keeping has the potential to strengthen vaccination programs via enhanced parental vaccine reporting. Although promoting vaccinations and providing financial incentives to only local healthcare providers seems financially prudent [42], financial incentives for target population subgroups with lower socioeconomic status [68] and compensation for parents attending mandatory vaccine education sessions could be more beneficial in the long-run. However, this will require a higher budgetary allocation for provincial healthcare expenditures.

Conclusion

VH issue is centred around cultural orientation and predispositions involving certain individual and community beliefs and cognitive biases. Given the current provincial vaccine policy architecture and resource allocation, the most efficient and effective policy strategy to implement in Ontario is public empowerment, in an effort to provide voice and agency to all stakeholders impacted by this issue. Providing support to healthcare providers and primary care physicians; and empowering parents, schools, students, families, and communities in Ontario, will slowly, but surely mitigate VH and enable healthy vaccination behaviours. This public-centered and inclusive health policy and programming strategy will ensure societal consensus on vaccine safety, efficacy, and acceptability. Implementing this policy option could set Ontario on the path to achieving higher childhood vaccination rates as well as the mandated vaccination coverage among adolescents, adults, and the elderly. This approach could prove to be a solution to end VH, not only in Ontario, but across Canada.

In closing, Canada could be a leader in vaccination rates for children, adolescents, adults, and the elderly. There is no perfect solution to address VH. Understanding the complex mix of factors that determine individual and collective vaccination behaviour is vital to designing effective vaccination policies, programs, and targeted interventions whilst also providing insights to refine future policy change processes in order to address VH in the country, comprehensively and harmoniously.

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Mitigating the effects of the climate crisis through health policy

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Abstract:

In Canada, the climate crisis has had profound impacts on health, including increased health problems as well as decreased access to healthcare services. Without mitigation, the climate crisis is expected to exacerbate an abundance of negative health outcomes and health system disruptions in Canada, including: food, water, and shelter insecurity; increased health problems caused by severe weather; and forced displacement from geographically vulnerable areas. Governmental action could be taken to mitigate the effects of the climate crisis and improve healthcare in the country.

This report synthesizes current literature on how the climate crisis is affecting health in Canada. It also recommends 3 actions that can be taken to mitigate the effects of the climate crisis and improve the country's health. Actions include: conducting climate change and health vulnerability assessments (CCHVAs), enhancing support for climate action research, and reducing CO_2 emissions in the healthcare sector.

This report synthesizes current research on how the climate crisis is affecting health in Canada. It references both evidence-based and predictive literature by centering the voices of healthcare providers, environmental academics, social scientists, and media outlets to help establish a well-rounded view of the climate crisis and climate action by way of health policy. Suggestions for government action are given, according to the research.

Background: The climate crisis in Canada

The climate crisis is defined as a severe change in global climate patterns. Currently, the earth's climate system has changed almost beyond repair [1]. If not mitigated, it is predicted that by 2060, all areas of Canada will experience increased mean temperatures, leading to a decrease in public health and access to healthcare services [1].

The climate crisis is affecting public health

Studies across Canada indicate that common concerns around the climate crisis include air and water quality as well as food access [2, 3]. These concerns are well founded as additional research shows that poor air quality has contributed to respiratory diseases [such as asthma] and food-borne diseases [such as Salmonella and Staphylococcus] [1, 2]. Air quality, clean water, and food access are also among the major health risks associated with the climate crisis [4].

With these general concerns in mind, specific social groups in Canada are at higher risk of poor health due to the climate crisis given their economic status, geographic location, and pre-existing health care inequities [1, 5, 6]. For example, poorer populations are susceptible to higher burdens of disease as a result of their social and political environments [6]. Moreover, people of low socioeconomic status often do not have the financial resources for medical interventions or prevention services such as prescription medications and good nutrition [7]. Likewise, populations on the coasts of the country are more vulnerable to flooding as sea level increases [8, 9]. Besides, health inequity is particularly pronounced among Indigenous Canadians [1]. For this population, changing temperatures can impact the distribution and availability of, for example, animal populations – which are important in Indigenous subsistence hunting and are a foundational food resource [1].

The climate crisis is diminishing access to healthcare

The climate crisis makes access to affordable, high-quality care challenging by exacerbating health needs and healthcare provider shortages [10]. This is seen for example in how non-communicable diseases (i.e. cardiovascular disease, chronic respiratory disease, and diabetes) account for 71% of global deaths, and the causes for those diseases are made worse by environmental factors [4, 6, 11]. For example, while

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several factors can trigger a cardiovascular event, exposure to air pollutants – such as byproducts from the burning of fossil fuels – can penetrate past our body's natural defenses and into our respiratory and circulatory system, damaging our lungs, heart and brain [11]. Similarly, prolonged elevated temperatures (i.e., due to global warming) increase the vectoral capacity of disease and the frequency of food-borne illness [5, 6], as evidenced in the Canadian North and Indigenous communities [3, 12].

With increases in the frequency of chronic health problems, more people require ongoing healthcare services. However, research has shown that Canada already has a shortage and an unbalanced distribution of healthcare workers across provinces. In Atlantic Canada, for example, residents wait an average of four years for a family doctor, and wait times for health services are the highest in the country [5, 6, 13]. The climate crisis can be expected to make this worse as more people develop illnesses that are linked with, or exacerbated by, environmental factors.

Possible policy options and their implications

Climate change predictions can aid in developing early warning and response systems for at-risk areas and can provide critical time to put proactive measures in place to reduce the frequency of climate-sensitive health outcomes [14]. Accordingly, recommendations for Canadian governments are suggested in this section to mitigate some of the impacts of the climate crisis.

Recommendation 1: Conduct climate change and health vulnerability assessments (CCHVAs)

A CCHVA is an evidence-based assessment of past, present, and future health impacts of climate change in a given geographic area [15]. CCHVAs are designed to better understand vulnerability – or the degree to which populations are susceptible to the effects of climate change – and they can be conducted in a relatively short time frame (approximately 1 to 3 months) with limited resources. The process in which CCHVAs are conducted includes 5 steps: framing the assessment relative to the geographic area; describing the current condition of health risks, vulnerabilities and adaptive capacity; projecting future climate and health risks; developing programs or policies to manage those health risks; and, establishing a process for monitoring and evaluating climate and health risks [16]. Each step of the process involves a CCHVA team (usually public health authority members) collaborating with local climate organizations and municipal stakeholders to generate context-specific data for the area being assessed. While the CCHVA team aggregates data on historical climate conditions and predicts future climate vulnerability through statistical modeling, interviews and focus groups are often used in order to increase understanding of local climate impacts and associated mitigation and adaption actions [17].

CCHVAs are useful to mitigating the climate crisis because they allow health authorities to better identify which people and places are most vulnerable to the health effects resulting from the climate crisis [18]. Upon identifying these jurisdictions, targeted public health interventions can be implemented. CCHVAs also consider how existing health inequities can be exacerbated by a changing climate and provide guidance on how to direct budgets and personnel to reduce both vulnerabilities and inequities over time [15]. Framing CCHVAs in relation to health equity can lend political credibility to the assessment method given the promotion of health equity is a broadly articulated goal of public health practice in Canada [5].

The success of CCHVA's can be seen in Ontario, where CCHVAs helped pave the way for the development of provincial guidance documents to support the province's Public Health Units in conducting their own assessments [15, 17]. The application of CCHVAs in Ontario prompted policy development through the formation of a framework that enables the identification of community vulnerabilities as well as mitigation and adaptation strategies [17]. As a result, they are able to raise awareness about the health hazards of climate change and reduce public health vulnerability [17, 19]. In the Muskoka region, for example, the Muskoka Watershed Council had completed vulnerability assessments that identified projected environmental risks from climate change [17, 20]. These included increased severe weather events that would lead to infrastructure damage and flooding [20]. The vulnerability assessment allowed the Simcoe-Muskoka District Health Unit to explore and evaluate climate change mitigation and adaptation actions, including the strengthening and broadening of the existing lake level monitoring as well as establishing the position of Director of Climate Adaptation within the District Municipality of Muskoka government [20]. Because of CCHVA application, Ontario Public Health Units, such as that of Muskoka, are now better positioned to meet public health standards mandating the communication of climate change health risks with the public. A similar approach could be taken in other parts of the country.

Despite the benefits of CCHVAs, public health decision-makers may decide not to conduct such assessments due to lack of human resources, lack of technical capacity, limited funds, or the absence of political will to initiate and drive the assessment process. This may be the case when climate change mitigation is not identified as immediate or near-term priority, when there is climate change denial within public health leadership, or when climate change is not understood as a public health issue [15]. Efforts to increase awareness of how the climate crisis is a public health issue will be needed in order to incorporate CCHVAs into governmental practice. Such efforts may include supporting the creation of partnerships between public health officials and provincial governments – partnerships that can ensure climate action continues – as is evidenced in Ontario's application of the assessment [17, 19]. Similarly, raising awareness of the assessments cost-effectiveness could increase their use. The National Roundtable for the Economy and Environment estimates that between

2010 and 2100, the cumulative costs of premature mortality risk attributable to only heat and air quality impacts resulting from climate change will be \$65–\$96 billion CAD for Toronto, \$52–\$77 billion for Montreal, and \$36–\$48 billion for Vancouver [21]. CCHVAs could enable the analysis of cost-effectiveness of identified interventions wherever possible.

Recommendation 2: Enhance support for climate-action research

To provide support for climate-action research, two actions are suggested: for climate action to be prioritized by healthcare funding agencies and for governments to capitalize on environmental data [4, 6]. Firstly, investment in research to understand the health risks of climate change in local populations would allow for a more accurate measurement of the disease-control measures currently in place across Canada [6]. Moreover, opportunities exist to capitalize on the environmental data produced [22]. These opportunities include the development of early warning and response systems that can provide critical time to deploy proactive measures to reduce the number of cases of climate-sensitive health outcomes [1, 22]. Such systems include, for example, warning the population of extreme heat events and ensuring those most vulnerable to the event (i.e. elderly) have access to safety measures (e.g. air conditioning) [22]. In order to develop these response systems, the information generated from climate-action research can be combined with a cost–benefit analysis or other decision support tool to inform priority setting by policy makers as the climate crisis progresses in Canada [23].

Supporting climate action research is useful for mitigating the climate crisis because current policies and measures for the management of climate-sensitive health outcomes were not developed in light of the rate of climate-change. This means that they need modification to be effective over coming decades [1]. By investing in research that measures the accuracy of disease-control interventions, health effects can be better controlled, as population health needs change alongside the climate crisis' progression. In public health, evidence-based models can help achieve the social convergence required for a sustainable global economy whose principal objective is wellbeing for all [24].

While there are costs associated with funding climate-action research, mitigating the climate crisis through climate action research makes economic sense [21, 25]. By 2050, the climate crisis is predicted to cost Canada between \$21 and \$43 billion per year [21]. This total is derived from flooding damages to the coasts (\$1 billion to \$8 billion/year) and poor air quality resulting from higher temperatures. Notably, both events are predicted to cost millions of dollars to the health care systems of Canada's 4 major cities – Toronto, Montreal, Vancouver, and Calgary [21]. The economic benefit of climate action will not only increase public health, but will aid institutions over the longer-term by developing preventative and adaptation strategies, rather than fixing health problems as they occur [2].

The largest barriers to enhancing climate-action support is the lack of knowledge surrounding the economic benefit of climate action [21, 22] and how the climate crisis is a public health problem [1, 2]. Health researchers recommend re-framing climate change as a public health issue, by way of increasing research in the field [2]. Benefits of increasing climate action research are shown in a study of climate crisis perceptions: when climate change was introduced as a health problem with mitigation-related policy options, 83% of respondents saw climate-action centered health policy as a plausible option to mitigate the climate crisis [26]. Increased interest in climate action was also present when an effect of the climate crisis [air pollution] was reframed to government and policy officials through economic cost-benefit analysis for reducing local air pollution and addressing air quality through climate policies [27]. Re-framing the climate crisis as a public health issue could be expanded with more research that relates the climate crisis to public health.

Recommendation 3: Create policies to reduce CO_2 emissions in the healthcare sector

The health sector produces a disproportionate amount of carbon emissions – about 4% of the world's CO_2 emissions come from the health sector [28]. A rapid transition to renewable energy would have direct health benefits now and would minimize health burdens in the future [6].

A step towards low-carbon living has health benefits that will improve quality of life by challenging diseases arising from affluent high-carbon societies – obesity, diabetes, and heart disease especially – and reducing the effects of air pollution [25]. For hospital buildings, this would imply improving building codes with a careful assessment of energy saving potentials (e.g. lighting and operation of energy intensive medical machinery and IT equipment). A switch to carbon efficient heating and cooling technologies as well as carbon efficient vehicles would further contribute to energy savings [29]. Health professionals would play an important role in advocating for policies that will incentivize this transition. Provincial governments would subsequently respond to health providers needs in order to implement policies concerned with CO_2 reduction in workspaces like hospitals and clinics.

If we do everything we can now to reduce global greenhouse gas emissions and ensure we adapt to the future effects of climate change, the average estimated cost is 1% of the world gross domestic product (GDP) every year. However, if we do nothing, the effects of climate change could cost 5–20% of the world GDP every year [25]. With this in mind, the Lancet Countdown to 2030, a working group focusing on climate action, has identified the price of the health impacts of fossil fuels as an important economic incentive to accelerate progress on climate action and health [28]. This incentive can be seen, for example, in the International Monetary Fund (IMF) estimation of nationally appropriate energy prices. Proposed prices incorporate health impacts, could cut ambient air pollution deaths by approximately one third, and reduce gas emissions by more than 20% [30].

Upfront costs for renewable resources are a barrier to reducing CO_2 emissions in the health sector [19, 21]. Knowledge translation and provider advocacy for these products is needed in order to develop policies and actions surrounding CO_2 reduction. Further, efforts to expand knowledge on how the climate crisis is a public health issue will be needed in order to incorporate CO_2 reduction into the health sector's practices.

Conclusion

The climate crisis is negatively affecting public health levels and decreasing access to health services in Canada. Without mitigation, the climate crisis is expected to exacerbate an abundance of negative health outcomes and health system disruptions in the country. With that said, governmental action could be taken to mitigate the effects of the climate crisis and improve healthcare. Three actions to mitigate the effects of the climate crisis and improve the country's health were proposed in this article. The benefits of each action were discussed and included recognition of vulnerable groups, increased economic benefit in the long-term, increased awareness of the climate crisis, and decreased health burdens resulting from the changing climate. Barriers to actions were also discussed – they largely included upfront costs, lack of resources, and a lack of knowledge surrounding how the climate crisis is a public health issue.

Further research on how the climate crisis can be mitigated through health policy may include a comparative analysis of how the crisis is perceived and addressed pre and post CCHVA. This information is missing in the literature as the results of CCHVA's are presented in terms of recognition of health risks and the development of toolkits and systems – which may or may not be useful to mitigating climate crisis effects. Future research may also explore federal-level application of the suggested strategies and how Canada-wide climate crisis mitigation differs from provincial health policy action. Similarly, a comparative study could be completed between Canada's climate action strategies and those of other countries. This may be useful as developing countries are disproportionally affected by the climate crisis and we can learn from their actions should the crisis progress in Canada as predicted.

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Conceptualizing "access" of maternal health services in lower-middle-income countries

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Abstract:

A considerable number of women die each year worldwide due to preventable causes during pregnancy and childbirth. The high mortality of women who die from pregnancy-related issues can be attributed to inadequate access of high-quality maternal health services. However, *access* is a nebulous concept with a compendium of conceptualizations and definitions. In this paper, we discuss the various conceptualizations of access to maternal health services in lower middle-income countries, and compare how issues related to access differ between high- and lower middle-income countries. This discussion informs two priorities that we suggest for researchers conducting health system improvement work in lower middle-income countries: 1) develop a robust understanding of the barriers to access that continue to persist due to cultural, socioeconomic, and political factors, and 2) formulate frameworks and theories specific to lower middle-income countries to guide research.

Introduction

More than 300,000 women die each year worldwide due to preventable causes during pregnancy and childbirth [1]. A significant portion of these deaths can be attributed to inadequate access of high-quality maternal health services, leading to hemmorrhage, hypertensive disorders, sepsis, and deaths through abortion [2]. This is particularly the case for low- and certain middle-income countries, and where the lack of adequate access to maternal health services has slowed cultural and socioeconomic progress.

The concept of health service access serves as a springboard for designing interventions, strategies, and policies to reduce maternal mortality. However, access has a variety of synonyms and definitions, making it difficult to operationalize consistently. In this article, we discuss the various conceptualizations of access in the context of maternal health services. We provide a definition of access applicable for lower middle-income countries – based on the World Bank Atlas method of having a gross national income between $1026 and $3995 [3] – and describe an example where this definition has been useful for research. We then examine how barriers to access differ between lower middle-income and high-income countries, and how this understanding informs intervention design and delivery around the world. We conclude this paper with considerations for future research on maternal health service access in lower middle-income countries.

Access

Conceptualization of access

Gulliford et al. described four dimensions of access: service availability, utilization of services, relevance and effectiveness, and equity. This conceptualization is helpful for developing a common language of access that can support more consistent and coherent research and intervention design [4]. However, there are a number of issues with this conceptualization. First, this framework was published in 2002 and barriers to accessing health services have evolved considerably through the 21st century. Political, educational, and cultural institutions have adapted to changing environmental and social circumstance such as climate change and social unrest. While Gulliford's work may offer important insight into issues with health service access today, it is necessary to develop a framework that accurately reflects contemporary situations. Second, Gulliford's work did not specify application for lower middle-income countries; these countries experience very different political, cultural, and infrastructural issues than low- and high-income countries. A definition of access applicable for low-income countries must be tailored to the circumstances of the country. Third, Gulliford's work was developed through reflections by a handful of experts; however, there is a considerable amount of literature on access that provides a better and more accurate picture of the barriers to accessing mater-

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nal health services. We believe a framework that defines and measures access using a systematic evidence synthesis methodology might offer more important insights [5].

There are also other conceptualizations of access. For example, Taylor et al. defined access to medical care as a social indicator of the "processes and outcomes of individuals' passage through the medical system" [6]. Oliver et al. described equity to access health care by providing equal opportunities for accessing health care to those with equal needs, but unequal opportunities to those with unequal needs [7].

More recently, Jacobs et al. developed a framework for addressing access barriers to health services in low-income countries in Asia [8]. They combined two previously published frameworks to list supply-side (i.e., health system) and demand-side (i.e., patient, family, and community) barriers under four dimensions of access: geographic accessibility, availability, affordability, and acceptability. Most notably, the authors assert that their framework aids in identifying the barriers to accessing maternal health services and developing interventions that can address these barriers [8]. The framework and review of interventions were applied to two case studies in Cambodia to show the utility and applicability of this framework for research and intervention design.

We used this framework in a systematic review and framework analysis of 22 studies discussing the barriers to access maternal health services in South Asian countries (Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, Sri Lanka) [9]. We have used the framework items as categories of different barriers that organized our analysis of the included literature. For example, we counted the frequency of times "community and cultural preferences" (demand-side barrier for the accessibility dimension) appeared in the included literature, as well as the underlying meaning of how community and cultural preferences became a barrier to accessing maternal health services. In some studies, it was the husband instructing their wives to not seek maternal health care [10]. In other studies, mothers were expected to prioritize their family's needs over their own [11].

Overall, with the exception of certain framework items such as "community and cultural preferences", "staff interpersonal skills" (supply-side barrier for the accessibility dimension), "unqualified health workers, staff absenteeism, opening hours" (supply-side barrier for the availability dimension), and "education" (demand-side barrier for the availability dimension), we have found limited utility of this framework for two reasons. First, the framework items do not comprehensively represent the barriers to maternal health service access that we have encountered in our work. For example, we have found multiple instances where community empowerment and engagement were present in included articles. However, the framework is unclear whether and how the lack of community empowerment and engagement can be a demand-side barrier to maternal health service access. There is also a need to expand the framework to be better applicable to current research, as well as the structure and function of health systems in Asia.

Second, we have found the description of framework items to be inadequate to use as a tool for investigating the barriers to accessing maternal health services. For example, does "education" (demand-side barrier to the availability dimension) include elements of "lack of health awareness" (demand-side barrier to the acceptability dimension)? Does "education" incorporate accessibility and availability of interventions that aim to improve knowledge about pregnancy and childbirth? We suggest researchers who are considering using this framework for research to first formulate consistent definitions that are applicable to their topic and research questions. Overall, this section illustrates that although there are definitions and conceptualizations of access, there are important challenges in using them for research and intervention design.

Access in lower middle-income vs. high-income countries

There are notable distinctions between high-income and lower middle-income countries in the structure and function of health systems. These distinctions lead to differences in the challenges and barriers individuals may face when accessing maternal health services. Therefore, using the access framework from Jacobs et al., we have outlined the most pertinent distinctions between high-income and lower middle-income countries that are important for studying health service access in Table 1 [8].

The design and delivery of maternal health interventions in lower middle-income countries

Interventions designed by educational or research institutions play a crucial role in delivering high-quality maternal health services in low-income communities. We recently published a scoping review of the design and delivery of maternal health interventions in Pakistan [12]. We analyzed 23 articles describing maternal health interventions for their intervention characteristics in Pakistan only. This knowledge provided a snapshot of the work that has been conducted in Pakistan, and priorities for future intervention design, delivery, and research. For example, we recommended developing multi-level and multi-component interventions to more efficiently improve maternal health care outcomes. At the same time, studies need to be transparent on if and how they involved stakeholders in the design and delivery of interventions, as well as the potential impacts of their approach to stakeholder engagement. Finally, there were more interventions without a formal evaluation or with evaluation that was planned but not published. This finding may indicate that although there are increasing efforts to design maternal health interventions, these efforts may have been interrupted prematurely due to lack of consistent funding and support.

More importantly, although this work was conducted

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Table 1 | Overview of the major differences between lower middle-income and high-income countries that influence health service access

Characteristic	Lower Middle-Income Countries	High-Income Countries
Evidence-based culture	An emerging, but weak and fragmented evidence-based culture; this limits the quantity and quality of research evidence available on these countries.	Presence of a strong evidence-based culture that promotes the production and use of knowledge.
Transportation Infrastructure	A developing transportation infrastructure, primarily for urban areas. Rural areas continue to be largely inaccessible in the majority of countries.	Strong transportation infrastructure in all urban areas and most rural areas that limit issues of geographic accessibility.
Universal Health Coverage	Although an increasing number of countries have elements of universal health care, there remain important gaps.	The majority of countries have some form of a universal health coverage insurance scheme, either through the government or private employers.
Medical Education	Medical education and training are medium to high-quality. However, these countries are challenged with "brain-drain" where expert healthcare providers immigrate to high-income countries.	Medical education and training are of consistently high-quality. There are also multiple mechanisms to ensure health workers provide high-quality care (e.g., performance monitoring).
Information Access	Access to essential information on health services is increasing, as well as consistent internet access.	Information on health services, government programs, and educational interventions is easily accessible via internet or local healthcare providers.
Health Awareness Campaigns	There are a number of educational health awareness campaigns in these countries, but information does not reach the majority of people, and the culture on prioritizing personal health is still developing	Educational health awareness campaigns reach a greater number of individuals because of a strong culture on personal health and well-being.
Patient Autonomy	Although changing, there is still a considerable amount of paternalism in health care, limiting the extent to which patient can voice their preferences and challenge healthcare providers.	There has been a rapid shift in patient preferences to be more involved in their clinical care. This observation reflects an increase in self-esteem and confidence to speak to and challenge healthcare providers.

on Pakistani studies, it illustrated a mismatch between policy and practice that may be promulgating the barriers to maternal health service access in lower middle-income countries. For this reason, we believe that there is a need to formulate conceptualizations and frameworks of access on how a mismatch between policy and practice influences the barriers to access that persist. Having conducted this scoping review, we are working on a systematic review and content analysis of Pakistani policy documents to better understand the pathway from government and organizational priorities to the implementation of interventions as well as how this pathway can be optimized.

Future directions for research on maternal health services in lower middle-income countries

Based on our discussion, we suggest two steps for future research on maternal health service access in lower middle-income countries, particularly in Asia.

1. Develop a robust understanding of the barriers to access that continue to persist due to cultural, socioeconomic, and political factors

Although there continues to be a need to develop new interventions in lower middle-income countries, it is imperative to better understand the factors that influence their delivery in different communities, belief systems, and circumstances. For this reason, our work steps back from the admirable work by organizations and the government that addresses specific maternal health indicators in South Asian countries. Instead, our work underlies intervention design with the socio-cultural factors that determine whether or not an intervention will have its intended effect when implemented in the real-world and on a larger scale. We are also conducting several targeted reviews for understanding the barriers that exist in different regions in Asia, and how they compare with each other. Our goal from this work is to initiate discussion on the most effective and appropriate strategies that lead to sustainable improvement in maternal health.

2. Formulate frameworks and theories specific to low- and middle-income countries to guide research in South Asia

As we have demonstrated in this paper, the issues to accessing maternal health services differ considerably between low- and high-income countries. Notwithstanding, we have seen frameworks and theories that were developed and tested in high-income contexts be inappropriately applied to health care issues in lower middle-income countries and contexts. We believe that this may be in part why the widespread efforts to improve maternal health services have not observed the predicted successes. It may be more appropriate and effective to enable individuals in these countries, who best understand the socio-cultural and political environments, to formulate theories and frameworks best suited for research in their country. Therefore, we suggest researchers from high-income countries to focus on strengthening the capacity for researchers residing in lower middle-income countries to tailor theories and interventions for their contexts.

Limitations of this commentary

There are a number of limitations in this paper. First, we focus solely on lower middle-income countries; we believe that the literature on low-income countries might offer important insight on issues with accessing maternal health services. Second, the evidence syntheses discussed in this paper are specific to certain South Asian countries. Since South Asian countries face very different cultural and political issues compared to each other, they may also have diverse challenges with accessing health services. While we did not focus on exploring these issues in this paper, we believe that they are a direction for future research.

Conclusion

In this paper, we discussed the various conceptualizations of health service access in lower middle-income countries, and compare how access issues differ between high- and lower middle-income countries. We suggest two priorities for researchers conducting health system improvement work in lower middle-income countries: 1) develop a robust understanding of the barriers to access that continue to persist due to cultural, socioeconomic, and political factors, and 2) formulate frameworks and theories specific to lower middle-income countries to guide research.

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Shedding light on maternal sunlight exposure during pregnancy and considerations for public health policy

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Abstract:

Sunlight exposure during pregnancy could be implicated in the physiological development and growth of the fetus, as well as long-term health after birth. Although several studies suggest the involvement of ultraviolet radiation-mediated vitamin D synthesis, current knowledge regarding the effects of sunlight exposure during pregnancy remains limited. We aimed to (i) summarize the existing body of research studying the influence of sunlight exposure on fetal growth-related birth outcomes and long-term health outcomes and (ii) determine its implications for therapeutics and public health policy. Of the studies identified on birth outcomes, the majority (5/8) demonstrated an association between sunlight exposure and reduced adverse birth outcomes (e.g., low birth weight, preterm births, small for gestational age, etc.), 2/8 studies showed no association, and 1/8 suggested a negative association between sunlight exposure and reduction of these adverse birth outcomes. Of the studies examining long-term health outcomes, sunlight exposure during pregnancy was shown to promote skeletal growth and development (2/6), and reduce the incidence of multiple sclerosis (2/6), asthma (2/6) and pneumonia (1/6). However, several of these studies used different methodologies and populations making it difficult to compare and integrate findings. Based on these results, we examined: the importance of exposure at different stages of pregnancy, proposed mechanisms by which sunlight exposure could lead to optimal outcomes, epidemiological differences influencing the findings, and necessary practical considerations prior to the implementation of public health policy recommendations. While these findings are promising, more rigorous research is warranted to support these recommendations.

Introduction

Sunlight consists of infrared, visible, and ultraviolet (UV) radiation and plays a critical role in regulating normal physiological functions, including vitamin D production and synthesis of hormones such as serotonin in the brain [1,2]; however, little is understood about its effects during pregnancy on offspring. Exposure to environmental stressors during critical periods of growth and development of the offspring could have severe consequences on its short- and long-term health [3], suggesting that differences in level of exposure to sunlight during pregnancy could considerably impact immediate and long-term outcomes. This is highly relevant in both developing regions with abundant sunlight exposure, as well as in regions, such as Canada, where greater seasonal differences result in a lower amount of exposure to sunlight for several months of the year.

Overexposure to UV rays during pregnancy is associated with increased adverse risks in mothers including skin damage and cancers [4]. At the same time, exposure to UV is essential for chemical reactions involved in conversion pathways of cholesterol to vitamin D for several functional roles; these include calcium and phosphate homeostasis, insulin metabolism, bone growth, and remodeling, cell growth mediation and promotion of immune function [2]. Pregnant women are increasingly more susceptible to vitamin D deficiency [5], suggesting there is a greater demand for vitamin D in the body during pregnancy. Maternal vitamin D deficiency during pregnancy is associated with unfavourable outcomes including low gestational birth weight (BW), stillbirths, preterm birth, vitamin D deficiency, hypocalcemia, and childhood obesity [6-8]. Low BW (<2500 g), stillbirth, and preterm births are birth outcomes indicative of fetal growth restrictions, while vitamin D deficiency, hypocalcemia, and chronic health outcomes suggest long-term consequences of this deficiency in later development. These outcomes suggest a threshold amount of UV exposure may be critical for healthy offspring development.

Although no international or national guidelines exist about the amount of UV or sunlight exposure preg-

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nant women should have, the World Health Organization's INTERSUN Programme developed in 1992 remains one of the first international standards to include UV exposure as a health consideration [9]. However, it is limited and only provides general recommendations to the public to prevent adverse health risks of UV exposure. Clinical trials suggest vitamin D supplementation is ineffective in reducing long-term risks in offspring associated with maternal vitamin D deficiency [10]. Moreover, using supplementation could have availability, cost-effectiveness, and ethical (vegetarian or vegan diets) issues. As production of vitamin D depends primarily on exposure to sunlight [11], there might be therapeutic value in considering effects of UV exposure during pregnancy on offspring outcomes.

The objective of this commentary was to review current knowledge to inform policies and considerations for pregnant women living in Canada and regions with lower exposure to UV. This article aimed to (i) examine existing literature on the effects of sunlight exposure during pregnancy on immediate neonatal and long-term health outcomes, and (ii) formulate considerations for therapeutics and public health policy based on current evidence. We searched databases including PubMed/MEDLINE, EMBASE and Google Scholar, and no time, setting, or language restrictions were imposed on the search strategy. Primary research articles such as case studies, systematic reviews and meta-analyses, were included. Studies concerning maternal outcomes and animal studies were excluded. We hypothesize that low sunlight exposure during pregnancy is associated with adverse fetal growth-related birth outcomes and long-term disease outcomes. As a result, we anticipate a public health benefit in implementing regional health policy recommendations.

UV exposure and fetal growth-related birth outcomes

Several studies around the world have considered indicators of fetal development such as BW, preterm births and gestational size, which are common metrics for fetal growth. In a New Zealand study by Tustin et al. looking at seasonal variations over a 5-year period, exposure to bright sunlight during the first trimester was confirmed to increase BW [12]. Another New Zealand study determined prenatal seasonal peak exposures to sunlight was associated with increased BW and heights [13]. Both of these studies used a robust methodology in measuring meteorological data, based on intensity and duration of exposures specific to maternal residence, and adjusting for behavioral factors, such as smoking during pregnancy. A longitudinal study in Norway suggested UV-induced maternal vitamin D during pregnancy is essential for improved BW outcomes by determining increased vitamin D deficiency prevalence in pregnant women living in northern latitudes with lower exposure to sunlight [14]. Although pregnancies during darker seasons were associated with poorer outcomes in this study, this study is limited as there were no other exposure measurements. More recently however, Zhang and colleagues confirmed this trend in the first study of its kind in China, determining prenatal sunlight exposure was associated with healthy BW and reduced incidence of small for gestational age infants [15]. In particular, this study demonstrated prenatal exposure to increasing levels of sunlight exposure in the second trimester of pregnancy was most strongly associated with these positive fetal growth outcomes.

In contrast, a cross-sectional study in America conducted by Thayer determined that average annual UV index positively correlated with low BW [16]. However, the analysis revealed both racial differences and income disparities had a strong association with differences observed with low BW outcomes, suggesting these factors are effect modifiers (i.e., lower income families generally had low BW outcomes independent of UV exposure). The association between preterm birth rates and the average annual UV index were correlated revealing a greater incidence of preterm births with increasing exposures. However, a strong association with poverty factors was also seen. This association was similar to BW trends observed in this study, which utilized the same method of data collection, suggesting it had similar limitations.

Other studies suggested no association between sunlight exposure and BW outcomes in newborn infants [17-19]. Pereira et al. considered the odds ratio of small for gestational age (BW<10th centile for gestational week) and proportion of optimal BW in 140,000 births in Western Australia [15], while Elter et al. compared individual BW to mean BW for 3,333 births in Turkey; both studies observed no significant effects [17]. In both studies, sunlight hours were used as exposure measures and statistical analysis adjusted for meteorological and pregnancy-related variables. A recent study examined vitamin D intake through sunlight and neonatal outcomes including BW in an African population in Ghana [19], using structured questionnaires for exposure assessment. This study reported no difference when recorded sunlight exposure was compared to gestational age and Apgar scores, which are used as a measure of the infants' general health status and responsiveness immediately at birth [19]. As year-round sunlight duration and intensities are consistently high in Ghana [20], homogeneity of exposures in this particular ethnic group or region could explain the lack of difference. While UV exposure appears to be independent of these outcomes, the utilization of self-reports for exposure measurements could increase the risk of subjective reporting bias and is a limitation of this study.

UV exposure and long-term conditions and disease outcomes

When compared to birth outcomes associated with UV exposure, literature considering long-term outcomes of UV exposure during pregnancy is more limited. Despite this, there have been several original studies that examine association between UV radiation and the incidence of multiple sclerosis (MS) in offspring. In the longitudinal study conducted in 1,524 participants identified from an Australian birth registration database, lower exposures to ambient UV during the first trimester of pregnancy was associated with an increased risk of MS in offspring [21]. The authors suggested vitamin D may be implicated in genetic mechanisms, which increase interactions with a locus determining susceptibility to MS. This was also considered by Vio Streym and colleagues, who used the national register database to analyze birth cohorts in Denmark to identify associations between seasonal exposures and long-term conditions including MS, type 1 diabetes, cancer, schizophrenia, ischemic heart disease and pneumonia [22]. The findings of this study demonstrated that incidence of MS and pneumonia in young subjects depended on their season of birth, suggesting low sunlight exposure in the winter months resulted in low maternal vitamin D levels during pregnancy.

Moreover, Wernerfelt et al. performed both a cross-sectional and a retrospective cohort study in the United States, examining the effects of sunlight exposure during pregnancy and the probability of asthma incidence in the offspring [23]. In the first cross-sectional study, data was collected from 264,701 individuals who responded to the 1997-2008 National Health Interview Survey regarding self-reported asthma condition, year of birth, region of residence and was associated with hours of sunlight exposure based on historical meteorological data obtained from weather stations. Although this study used surveys subjecting the data to reporter bias, it enabled the measurement of key behavioral data such as smoking, time spent outside, etc. The second retrospective cohort study created birth month-region-year cohorts and evaluated them using national hospital discharge data to determine asthma status, while sunlight exposure data was obtained from a national database. Both studies accordantly demonstrated that maternal exposure to sunlight, notably in the second trimester of pregnancy, lowers the risk for the development of asthma later in life.

Additionally, one prospective cohort study conducted by Sayers and Tobias suggests UV exposure is implicated in skeletal development during childhood [24]. This study examined 6,995 children in a Finnish cohort after UV exposure in the third trimester of pregnancy, based on meteorological monitoring data, and demonstrated a positive relationship with bone mass and size in later childhood. These findings suggest vitamin D levels during pregnancy have direct effects on fetal periosteal bone formation. In the study performed by Waldie and colleagues, follow-up was performed on infants of the maternal birth cohorts at regular intervals until the age of 26 and it was similarly determined that the prenatal duration of exposure to sunlight differentially influenced participant stature depending on age. However, it is notable that none of these studies made adjustments for environmental, genetic, or social factors in their analysis and this may have an impact on the validity of these results.

Considerations by stages of pregnancy

According to the developmental origins of health and disease hypothesis [3], environmental conditions during fetal development ultimately determine the health and burden of disease in the later stages of life. The majority of the evidence considered thus far suggests UV exposure is critical for different windows of vulnerability throughout fetal development. The first trimester is when the formation of the nervous system occurs [25]. It is possible that UV exposure interventions could be utilized in order to reduce risk of developing diseases or long-term conditions, such as MS, in later childhood or adulthood.

Additionally, reported associations between timing of exposures and positive birth outcomes, suggest these interventions could be useful in the second and third trimester. The second trimester marks the beginning of lung development and production of surfactant [26]. The findings made in the studies conducted by Wernerfelt et al. suggest sunlight exposure during the second trimester could lead to a reduced risk of developing asthma in later life [23]. This is conceivable as surfactant dysfunction is a risk factor for chronic airway inflammation, a signature of asthma. Similarly, interventions in the third trimester maybe essential to lowering the risk of pneumonia [22], as it is the stage when key developmental events for normal lung development occur. Larger BW outcomes could also suggest UV-induced vitamin D is implicated in normal fetal growth. There were also effects described in the third trimester [24], when skeletal development is occurring in the fetus and the presence of UV-induced maternal vitamin D could be required. By determining these time points, it may be possible to target sunlight exposures, particularly in mothers whose gestation overlaps with months where there is a lower exposure to sunlight.

Considerations by mechanism

With exposure to sunlight, UV radiation-induced maternal vitamin D synthesis was not the only possible mechanism for fetal changes. Tustin et al. suggested sunlight exposure early in gestation increased levels of insulin-like growth factor (IGF)-1, a hormone involved in bone and tissue development, to facilitate fetal growth [12]. Furthermore, Waldie et al. speculated maternal melatonin production was inhibited by sunlight, resulting in increased levels of growth hormone (GH), a hormone similar to IGF-1 involved in growth and metabolism, which could also progress fetal growth [13]. These proposals may suggest the involvement of a pathway associated with melatonin production, which is critical in regulating circadian rhythm and sleep-wake cycle signaling, in fetal growth and development. This melatonin-dependent pathway may be independent or interact with vitamin D to increase GH/IGF-1 production.

Zhang et al. proposes the involvement of a UV radiation-dependent vitamin B9 depletion pathway [15]. Vitamin B9 consists of different forms including folate and folic acid, which are critical for cell growth. Not only has it been shown that UV radiation can lower concentrations of folate in the bloodstream, it is well established that folic acid deficiency during pregnancy leads to neural tube defects and resulting adverse birth outcomes [27,28].

Although it is yet to be investigated, it is important to consider another mechanism of action might involve UV and sunlight-induced production of maternal serotonin. Serotonin is a neurotransmitter and hormone known to be involved in fetal brain development; several studies suggest the use of serotonin reuptake inhibitors during pregnancy to be linked with an increased incidence of autism spectrum disorder after birth [29,30]. Moreover, in conditions like seasonal affective disorder, seasonal changes, including lower amounts of sunlight and cold weather, could deplete levels of serotonin in the brain leading to depression and other psychological effects. Maternal depression is a known risk factor for detrimental socio-emotional and cognitive development of children and depression in adulthood [31,32]. It is therefore possible for birth outcomes to depend on the action of sunlight and/or UV exposure to act on any or a number of these pathways. Future studies exploring these pathways are warranted to gain more insights for the development of alternative therapeutic strategies during pregnancy, especially for women living in regions where access to sunlight is limited.

Epidemiological considerations

Epidemiological factors such as environment, time, and demographics must also be considered. While most of the original studies have been performed in industrialized countries in both the Northern and Southern Hemispheres, we determined that the numbers of studies performed in developing regions of the world on UV exposure are vastly limited, and to date, no studies have investigated the association between sunlight exposure during pregnancy and offspring outcomes in Canada. Meteorological differences in Northern continents can affect levels of exposure received, when compared to Southern latitude countries. In fact, Canadian cities, such as Iqaluit, have average hours of sunlight reach lows of 0.4 hours per day as well as an average UV index of 0 in the winter months [33]. There are also racial, socioeconomic, and geographical differences, as observed by Thayer et al. [16]. In this study, in addition to higher birth outcomes in those living in the North versus the South, there was a lower incidence of low BW and prematurity observed for non-Hispanic black women compared to non-Hispanic Caucasian women. Ngueta et al. hypothesize that these outcomes may not directly be linked to racial differences but rely instead on the closely associated maternal fat mass [34]. According to this hypothesis, there is a lower bioavailability of vitamin D due to its lipophilicity, which causes it to be trapped in fat masses and unable to act to prevent adverse birth outcomes.

Nonetheless, these individual-level differences are particularly important in multicultural and diverse countries such as Canada, where policymakers must take into consideration social determinants of health. Moreover, with varying exposures to sunlight in different regions coupled with differing methodologies to measure exposure effects in settings with a range of resource availabilities, it becomes difficult to make inferences about UV exposure without intricate epidemiological analysis. With genetic differences between ethnicities, individual behavioral differences, and distinctive exposure responses and capacities, another layer of complexity is added and must be accounted for when designing public health policies and recommendations. This also suggests interventions must be more personalized rather than assuming a “one-size fits all” strategy.

Practical considerations for policy implementation

Before policy implementation, further clinical trials comparing UV exposure to vitamin D supplementation for pregnant women with vitamin D deficiency are imperative. Though limited in terms of regional representation and consistent methodology, current literature suggests a therapeutic benefit in implementing health recommendation guidelines for sunlight exposure during pregnancy. Moreover, existing evidence suggests the level of benefit depends on various genetic, environmental, and behavioral factors. As a result, it is necessary for policy recommendations to be developed after consultation with an interdisciplinary collaborative of atmospheric science experts, healthcare professionals, medical scientists, public health officials and policymakers. Due to geographical variations in sunlight exposure, recommendations should be designed at the provincial or regional level considering for the intensity, duration, and other anticipated meteorological factors. Existing regional policies on environmental exposures, such as the 2006 British Columbia Reproductive Care Program Guideline for Tobacco Use in the Perinatal Period [35], which provides recommendations as the current standard for prevention and management of tobacco use and second-hand smoke exposure during pregnancy, can be used as a guide in developing novel recommendations for sunlight exposure.

Conclusions

Though scarce, the majority of available evidence suggests low sunlight exposure is associated with adverse fetal growth-related birth outcomes and long-term health outcomes. One study showed a conflicting association between sunlight exposures and birth outcomes, while two other studies demonstrated none. Exposure was implicated in long-term health outcomes including skeletal system development and reducing the incidence of MS, pneumonia and asthma after birth. This work has summarized and evaluated the main findings of the current body of evidence, identifying key limitations and implications to inform considerations for public health policy. In particular, we recognized limitations of comparing findings obtained through diverse methodologies and variable factors (i.e., geography, racial differences, inherent genetic variations,

Table 1 | Summary of existing literature on the effects of ultraviolet exposure on fetal growth-related, neonatal and long-term outcomes. Studies identified using the search strategy presented in this review are displayed. Abbreviations: UV, Ultraviolet radiation; IGF-1, insulin-like growth factor; GH, growth hormone; MS, multiple sclerosis.

First author, year	Setting/ Population	Sample size (n)	Exposure and comparison		Study design	Outcomes
			Exposure	Comparison		
Tustin, 2004 [12]	New Zealand maternal birth cohort	8,516	Seasons with peak sunlight over 5 year period	Seasons with trough sunlight over 5 year period	Longitudinal	Peak sunshine exposure during first trimester was associated with higher birth weight infants compared to trough levels of sunshine in the same trimester IGF-1/GH may be involved in an indirect UV exposure pathway during fetal development
Waldie, 2000 [13]	New Zealand maternal birth cohort	20,021	Months with higher sunlight exposure	Months with lower sunlight exposure	Longitudinal	Prenatal exposure to sunlight can increase birth weight and height after birth Melatonin-growth hormone pathway may be involved in an indirect UV exposure pathway during fetal development
Gustafson, 2018 [14]	Norwegian Caucasian maternal birth cohort	855	Darker seasons (winter-time)	N/A	Longitudinal	Darker seasons of pregnancy were associated with lower birth weight and poorer outcomes in this study Attributed this finding to lower vitamin D production, which has direct or indirect effects on the fetus
Zhang, 2020 [15]	Chinese maternal birth cohort	637,033	Longer duration of sunlight exposure	Shorter duration of sunlight exposure	Retrospective cohort	Prenatal exposure to sunlight was associated with healthy birth weights and lower incidence of small for gestational age infants The strongest association to positive birth outcomes was seen for sunlight exposure in the second trimester
Thayer, 2014 [16]	United States maternal birth cohort	2,825,620	High UV exposure	Low UV exposure	Cross-sectional	Average annual UV index was correlated with low birth weight and higher preterm birth rates The analysis revealed both racial differences and income disparities had a stronger association with differences observed with both outcomes
Elter, 2004 [17]	Turkey maternal birth cohort	3,333	Greater hours of sunlight	N/A	Retrospective cohort	When individual birth weights were compared to mean birth weights, there was no significant difference observed between either exposure or comparison
Pereira, 2012 [18]	Western Australia maternal birth cohort	147,357	Greater hours of sunlight and higher temperature	N/A	Retrospective cohort	Birth weight effect sizes observed for sunlight exposure were small and statistically non-significant
Balogun, 2019 [19]	African maternal birth cohorts	703	Higher self-reported sunlight exposure score	Lower self-reported sunlight exposure score	Cross-sectional	Birth weight, gestational age and Apgar scores showed no significant difference between high sunlight exposure and low sunlight exposure scores
Staples, 2010 [21]	Australian maternal birth cohorts	1,524	Ambient UV exposure per region	N/A	Longitudinal	Lower exposures to ambient UV during the first trimester of pregnancy was associated with an increased risk of multiple sclerosis in offspring Vitamin D may be implicated in genetic mechanisms, to increase interactions with a locus determining susceptibility to MS

Table 1 (continued)| Summary of existing literature on the effects of ultraviolet exposure on fetal growth-related, neonatal and long-term outcomes.

First author, year	Setting/ Population	Sample size (n)	Exposure and comparison		Study design	Outcomes
			Exposure	Comparison		
Vio Streym, 2013 [22]	Denmark maternal child cohort	236,424	Season of birth	N/A	Retrospective cohort	No effect of season of birth on risk of type 1 diabetes, cancer, schizophrenia and ischemic heart disease Season with greater sunlight exposure lowers risk for pneumonia and MS
Wernerfelt, 2014 [23]	United States national survey cohort	264,701	Number of hours of sunlight exposure	N/A	Cross-sectional	Increasing exposures to sunlight during pregnancy resulted in a lowered risk for the development of asthma in later life Sunlight exposure in the second trimester showed a significant reduction in the risk of asthma incidence
Wernerfelt, 2014 [23]	United States birth cohorts	2,119,857 (3,036 cohorts)	Sunlight intensity and duration per region	N/A	Retrospective cohort	Sunlight exposure during pregnancy was associated with a lowered risk for the development of asthma Sunlight exposure in the second trimester was significant associated with a reduction in asthma incidence
Sayers, 2009 [24]	South West England county maternal child cohort	6,995	Maternal UVB exposure during third trimester	N/A	Prospective cohort	Maternal UV exposure is associated with bone size during later childhood UV-induced vitamin D status in pregnancy may exert direct effects on periosteal bone formation in subsequent childhood

socioeconomic factors, etc.) in these studies. We have also incorporated considerations based on current understanding of exposure effect at different stages in pregnancy, different mechanisms of action, epidemiological factors, and practical considerations prior to policy implementation. Nevertheless, more research is necessary and future avenues should examine a way to quantify the threshold level of healthy exposure, personalized therapeutics to account for the effectiveness of sunlight exposure per individual, and therapeutic interventions through non-UV-vitamin D mechanisms.

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Reflecting on environment to understand diversifying health perspectives: My journey to researching strength-based approaches

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Abstract:

People hold health conceptions that are shaped by their environments. In Canada, these ideas and subsequent research approaches are often developed further through academic training. Current public health perspectives and approaches are largely focused on Western worldviews of health. I share my reflections on my environments, and continued journey as a student in academia that led me to question the current standard of teaching uniform health perspectives. Fostering a singular-worldview learning environment translate to future scholars missing opportunities to learn promising discourses – such as strength-based approaches – that may be more effective in application, including in Indigenous health research. I suggest ways in which environments that foster the appreciation and comprehension of diverse health perspectives can be built.

Before entering post-secondary and studying health science, students hold conceptions of health that are shaped by their environments. Generally, in Canada these ideas are developed further through academic training that focuses on Western worldviews of health, which stem from Eurocentric values. In turn, students are inspired to similarly model these worldviews in their research approaches. My journey through academia however, led me to question this process: would things positively change if academic environments were purposively organized for students to reflect on their own health constructs and share and consider diverse approaches to health?

Environments shaping our health perspectives

Most would agree that our health conceptions are constructed through our environments and experiences from an early age. In Canada, we typically learn about health through our family, school, communal, recreational, and work environments. We take these environments of experiential learning for granted. When we enter post-secondary institutions to study in our various health silos to become "experts" in different knowledge areas, we find ourselves as students "jumping into the work." We may not question our perspectives or may not be encouraged to seek alternative health perspectives, unless we are indisputably confronted with contrasting viewpoints.

Before I entered a Master of Science program in public health, I was working in a holistic health and education program for youth within my northern Canadian First Nation community. I returned home after completing my undergraduate degrees and gained a new appreciation for the way wellness and education programs were delivered for community members. It gave me space to reflect on practitioners, researchers, and students that I had worked with in the health field. I became cognizant that most of my former non-Indigenous colleagues were very excited to learn from our community, because – as they expressed – there were few opportunities to learn about Indigenous health approaches during their schooling.

I felt that the lack of articulation of Indigenous health worldviews in a system designed to teach about health was peculiar. For me, Indigenous wellness approaches were the norm for our homeland. Preceding colonization, Indigenous Peoples had a highly effective tradition of practicing holistic medicine and public health that intertwined with the environment [1]. For example, Indigenous health approaches emphasize a balance of spiritual, mental, physical, and emotional wellbeing of the individual, family, community, and environment [2, 3]. Indigenous approaches tend to utilize existing resources and be solution oriented. Through my first-hand experiences, I saw multiple examples of the validity of these approaches, such as smoking cessation, increased physical activity, increased prenatal care, and injury prevention. I was

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puzzled as to why the highest level of learning would not adequately teach Indigenous health perspectives and wondered how this translated into approaches to health research.

Current public health perspectives and practices

Differentiating Western and Indigenous health approaches

Attending classes as a new graduate student in Public Health, I was excited to hear about foundational ideas that led to promising health research. I was somewhat discouraged however, to learn that most best practices, particularly in Indigenous health, were largely driven by Western concepts of health. The European arrival privileged a major shift in health ideology to a Western illness-orientated, individualistic approach [2]. Today, despite efforts to promote reconciliations, Western approaches dominate in research – including public health [4] – allowing little room for the recognition of "other" health approaches [1, 5], particularly Indigenous approaches [2, 4]. For example, in a review of mental health interventions in Arctic Indigenous groups, it was concluded that although many studies described the Indigenous populations and living environments related to their health interventions, they failed to apply any of that information in their methods [6].

Western public health approaches stem from the bio-medical model, where health equates to absence of physical or mental disease, [2] and has expanded to include health as a state of well-being [7]. A Western worldview is based on linearity and hierarchy, singularity concepts, static thinking, and objectivity that are secured through physical measurement and observation [8]. In research, these approaches are revered for eliminating personal opinions and relationships [9] and are usually top-down in terms of community engagement [10]. Western approaches value individual ownership and progression [11], wherein patients or communities are the problem and researchers are the solution.

Although rooted in the bio-medical model, most health scholars have recognized a socio-ecological perspective by utilizing the "social determinants of health model" in the last few decades. This model identifies the social circumstances and contexts that play a role in health inequities and inequalities between populations [12]. For example, it is widely noted that Indigenous populations uphold cultural and social identities distinct from mainstream society [13]. The traditional "social determinants of health" model considers individuals living and working conditions, income, disability, education level, race, and food security [12, 14]. Scholars that use the social determinants of health acknowledge the influence of cultural components. However, in Western systems there is little recognition of broader Indigenous holistic models that incorporate not only social determinants, but also determinants beyond the social [15].

Indigenous scholars recognize determinants of Indigenous health and well-being that do "not typically… fall under the category of 'social' – for example, spirituality, relationship to the land, geography, history, culture, language, and knowledge systems" [15, p.xii]. Underlying all the determinants is a history of colonialism and persisting neocolonialism [16, 17]. An Indigenous healing perspective considers the structural determinants and underlying causes related to the historical, political, cultural, and societal factors [18, 19]. In contrast the "social determinants of health" are largely based on quantitative epidemiological evidence that endorse implicit associations and suggestive interventions, which lacks considerations for intervention appropriateness and effectiveness [20], such as accounting for colonialism or Indigenous perspectives [15]. Differences in worldviews of health lead to variances in defining and approaching health goals.

Differentiating deficit-based and solutions-based health discourses

From what we were taught in graduate school, Western health models are the building blocks for most health research. Common public health research is expert driven, top-down, and deficit-oriented, while Indigenous health research approaches regard more than physical health and use a holistic balance, solutions-based approach [19]. Deficit discourse is defined as an approach "that frames and represents Aboriginal identity in a narrative of negativity, deficiency, and disempowerment" [21 p.1]. Western health research typically uses a pathologizing lens, with a focus on pathos and deficiencies [22] as a rationale for interventions, resource redistribution, and systematic reorganization [11]. Typically, research on Indigenous Peoples is "damage-centered," using harm and pain as means to convince an outside entity or government funding agency that something has to be "fixed" and compensated [23]. However, this often leads to the stereotyping of Indigenous Peoples in society [24], and underlying perceptions of "native problems" [21, 25] that disseminate a false Indigenous health history and reproduces inequities [11]. Researchers using this approach often miss the opportunity to engage locals as knowledgeable sources; this is because expertise is only accepted by outside help to "fix" the problem [11].

In contrast to a deficit-based approach, the relationality tenet in Indigenous health research involves researchers interpreting participants' talents and experiences as valid and being solutions-focused [26]. One recognized form of a solutions orientated practice is a strength-based approach built on the salutogenic theory that recognizes elements that contribute to and prolong health [27]. Employing strength-based approaches entails working directly with members in a study and supporting their "voice" and power in research decisions (25). A strength- or asset-based approach emphasizes relevant and appropriate ideas for the future that are constructed on what is working and has worked well within a community (28). Strength-based approaches empowers those involved and promotes social change (29). Utilizing these approaches does not minimize or disregard issues [30], but rather identifies the multilayered strengths of individuals, families, and communities, and engages those strengths to prevent and overcome challenges [11].

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I was familiar with using a strengths-based lens for wellness from my community experiences. I had seen multiple examples in action; the most eminent example being our original community afterschool program: the *Chekoa Program* for children and youth. This program was created to address education and health issues holistically from a First Nations lens. As a child, I attended and later volunteered at the *Chekoa Program* and learned in-practice, the intricacies of strength-based approaches to wellness. This program tackled a multitude of issues by building on our community strengths: the involvement of parents and grandparents, the pedagogy of older youth with younger youth, and existing educational resources in our culture and language. It was a successful community health program that helped shape my health perspective. During graduate school however, I was unsettled by my observation that Indigenous perspectives were missing.

Where do we go from here? Building an environment to appreciate diverse health perspectives

As I stumble through graduate school and my rolodex of outside resources increase from learning opportunities in different countries, conferences, and communities, I am impressed by the different perceptions on health and health-related research approaches. While navigating public health courses, I kept searching for health perspectives outside of a Western worldview. Within my limited required course load in Canada, these never emerged. That led me to consider how I could contribute, and what recommendations I could support to foster academic environments that promote diversifying health perspectives and approaches.

Following my experiences with university classes, I knew that a deficit-based, individualistic research approach was unethical for me to conduct in a First Nations community. I immersed myself in Indigenous research literature and decided to bring Indigenous approaches to the forefront, including strength-based approaches, within my health research. Although strength-based concepts are common in the fields of socio-psychology, education, and business, calls for strength-based research approaches in Indigenous health continue. In the last few decades, "health promotion" research has emerged in public health and in theory, aligns with a strength-based approach [31]. Although this lens moves away from a pathogenic approach and towards a salutogenic model that stresses constructive factors to endorse people's health [32, 33], in practice there remains a tendency for solutions to come from "outside experts." This approach is far from holistic as it targets only individuals, disregards the strength of a population, and uses culture superficially [34, 35]. Health promotion, although with limitations, holds promise for future collaboration with Indigenous approaches to health. Mechanisms for defining, applying, and evaluating strength-based Indigenous health research approaches, however, are limited and understudied. There is a lack of research utilizing the strength of Indigenous knowledge, and approaches aimed at Indigenous wellness, despite many Indigenous communities incorporating strategies that build on their assets in health programming. Understanding concepts of strengths from a non-Western perspective is under-researched [36]. Furthermore, there is insufficient empirical research on the effectiveness of strength-based research approaches [36]. I hope to address these knowledge gaps in my research.

Future directions

Beyond my own research, I look forward to supporting environments that promote multiple definitions and applications of health research. When given the opportunity to learn about them, future scholars may become more amenable to using non-Western health approaches, such as using strength-based approaches. Ultimately, a research approach should not only be dictated by the researcher, but also by what is most effective for a population. This can only happen when environments that foster diverse approaches exist. My recommendation is to begin with the establishment of health classroom environments built on multi-epistemological concepts of health. This can occur through current and future professors encouraging student reflection on experiences that shaped their health perspectives, biases, and approaches. I acknowledge that my view is limited by my experiences based on a handful of health programs in North America, and this may be the norm in some health classrooms. However, only when we critically reflect on and share our own experiences, can we consider and hopefully appreciate alternative perspectives to our own.

This standpoint coincides with part of an Indigenous research agenda to not dismiss Western knowledge, but to rewrite and "re-right" the collaboration between Indigenous and Western ways of knowledge in research [25]. There is value in welcoming public health Indigenous approaches [37] as supported by various scholarly allies [2, 4, 24]. Indigenous strength-based approaches may serve as one method to be adopted in health research. Willie Ermine describes what this ethical space would look like, "…a cooperative spirit between Indigenous peoples and Western institutions [that] will create new currents of thought that flow in different directions and overrun the old ways of thinking" [38 p.203]. I hope my research journey reflections encourage others to reflect on their research approaches, lack of perspectives, and ways to create a space where "new currents of thought" can flow in the field of health.

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Vaccines in the 21st century: Clarifying the factors that promote vaccine hesitancy, delay, and rejection

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Abstract:

Vaccines have been crucial in reducing mortality and morbidity around the world, particularly in low- and middle-income countries. Furthermore, vaccinations have also resulted in a considerable amount of economic savings. However, there are a growing number of individuals who express a strong skepticism of vaccine safety and effectiveness. These "vaccine-hesitant" individuals choose to reject or delay vaccine administration. A number of strategies have been developed to address the various socioeconomic and cultural circumstances of each vaccine-hesitant individual. However, there is a need to clarify the various factors that promote vaccine acceptance, delay, and rejection. In this article, we discuss the factors that promote vaccine hesitancy from recent research, describe some of the interventions we know to be effective in reducing hesitancy, and develop an agenda for researchers and students interested in vaccine hesitancy research.

Introduction to vaccines, vaccination, and vaccine hesitancy

Vaccines are the backbones of health care systems. They are among the most effective public health interventions; widespread vaccination has dramatically reduced disease burden worldwide, especially in low- and middle-income countries where vaccine-preventable diseases have slowed socioeconomic progress [1]. Research has demonstrated that vaccines have reduced mortality and morbidity, and contributed to a considerable amount of economic savings. For example, Ray and colleagues estimated that the meningococcal vaccine alone saved the United States government $1.5 billion in direct and indirect costs from 1993 to 2002 [2].

Despite successes, there is a growing group of individuals with an increasing skepticism of vaccines. In particular, there are more and more parents who are choosing to forego vaccines today, which has given rise to an increasing number of cases of vaccine-preventable diseases such as measles [3]. There is a continuum of attitudes towards vaccines ranging from full acceptance to full rejection (i.e., "anti-vaxxers"). The SAGE Working Group on vaccine hesitancy defines vaccine hesitancy as the "delay in acceptance or refusal of vaccination despite [the] availability of vaccine services" [4]. The decision to delay or reject vaccines depends on a compendium of factors including negative interactions with healthcare providers and an orientation towards natural living.

Some may incorrectly believe that vaccine hesitancy is a 21st century phenomenon; however, there are instances in our history that say otherwise. In the 1920s, an anti-vaccination group in a United Kingdom county appealed to make the smallpox vaccine optional [5]. Although these appeals were rejected, this example illustrates that vaccine hesitancy has existed since the advent of vaccines, even though we know it allows people to live healthy and productive lives. What is new are the far-reaching implications that vaccine delay or rejection has on children's health, and the cultural and lifestyle factors that promote it.

Due to the novel implications of vaccine hesitancy on public health today, there is a need to develop interventions tailored to the socioeconomic and cultural circumstances of each parent's vaccine hesitancy. However, to develop and test such interventions, healthcare professionals require clarity on the various factors that promote vaccine acceptance, delay, and rejection. To address the lack of clarity in the literature, in this article we: 1) discuss the factors that promote vaccine hesitancy, 2) describe interventions that have been effective in reducing hesitancy, and 3) develop an agenda for researchers and students interested in vaccine hesitancy research.

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Reviewing the factors that promote vaccine hesitancy in parents

Recently, Dube and colleagues published a systematic review of 22 qualitative studies to clarify the determinants of vaccine hesitancy at multiple levels of society (i.e., individual, community, and policy levels). The determinants include experiences, emotions, ways of thinking, information sources, family and friends, perceptions of disease risk, and trust in healthcare systems [6]. The majority of factors pertained to individual, interpersonal, and community attitudes and behaviors. They found few primary studies that have examined the determinants at the organizational and public policy level, representing a significant gap in research. Although this work is helpful to conceptualize the different levels at which vaccine hesitancy operates, it does not illustrate the mechanisms through which these factors encourage or discourage vaccine hesitancy beliefs. For this reason, we conducted an interpretive review of 34 qualitative studies on parents' decision-making process with regards to childhood vaccines using a qualitative research integration approach [7]. We identified overlaps and relationships between 7 factors that promote vaccine hesitancy: previous experiences; "natural" and "organic" living; perceptions of other parents; experiences interacting with healthcare providers; information sources, challenges, and preferences; distrust in health system players; and mandatory vaccine policies. These factors can be conceptualized using the metaphor of a gear train from the physics discipline. The gear train metaphor illustrates that while a parent may prioritize up to two factors to make their vaccine decision, the parent still considers all other factors but to a lesser degree. Previous works have also explored parents' rationale behind vaccine hesitancy. For example, in a systematic review of qualitative studies on the reasons why parents in the United Kingdom vaccinate their children or reject vaccines, Forster and colleagues found two types of decision-making: *non-deliberative* (i.e., parents felt that they had no choice, were happy to vaccinate their child, and/or relied on the social and cultural norms of their community) and *deliberative* (i.e., parents sought information from a variety of sources to weigh the risks and benefits of vaccinating, as well as considering others' advice and experiences) [8]. Additionally, a study by Brunson generated a grounded theory of the vaccine decision-making process of 15 mothers and 3 couples which comprises the following components: awareness, assessing, choosing, stasis, and ongoing assessment [9]. Brunson's work illustrated that vaccine-hesitant parents make the decision to not vaccinate for each individual vaccine rather than all vaccines as a whole. For this reason, parents' decision to not vaccinate is susceptible to change based on their environment and as new information is made available by trusted sources for each vaccine [7].

Findings from the Forster and Brunson both illustrated the dynamic nature of parental vaccine-hesitancy. These studies demonstrate that every vaccination decision is considered separately by parents and their stance on vaccination is subject to change according to the information available to them by trusted sources of information [7].

Strategies for addressing vaccine hesitancy

When designing and implementing interventions to address vaccine hesitancy, researchers and decision-makers need to understand that there is a compendium of reasons and combinations that uniquely position each parent in their rationale to delay or reject vaccines. Reasons may also differ between vaccines; all reasons must be considered together when determining which interventions will be effective.

We have found that parents' expectation of shared decision-making – a component of informed consent whereby patients and healthcare providers make collaborative health care decisions [10] – in vaccine decisions conflicts with healthcare providers' orientation towards vaccines. Parents may enquire about the benefits and possible health risks of vaccines to make an informed decision. However, allopathic healthcare providers may perceive this enquiry to challenge their knowledge, expertise, and experience, especially when providers report a lack of up-to-date knowledge about recent vaccine research [11]. As a result, healthcare provider behaviours may conflict with parents' needs for specific information about vaccines before making a decision. For a considerable number of parents, this conflict may entrench them in their vaccine-hesitancy beliefs which may cause some parents to discontinue their relationship with allopathic medicine [12]. Parents may then seek information from the media or internet, or complementary and alternative providers [13].

Previous research has found a scarcity of evidence-based approaches to address vaccine hesitancy [14]. Existing interventions that have been somewhat successful in improving vaccine acceptance are multicomponent- and dialogue-based (e.g., social media, mass media, and information-based tools for healthcare providers) [15]. While Walling and colleagues' systematic review found 2 informational interventions, 18 behavioural interventions, and 31 environmental interventions to improve vaccine uptake [16], Dube and colleagues identified no strong evidence supporting the effectiveness of any specific vaccine uptake promotion strategy in their survey of 15 literature reviews [14]. These findings illustrate that there is a need to focus attention and resources to develop newer and more innovative interventions tailored to the compendium of reasons and rationales that parents use to delay or reject vaccines.

A three-part agenda for future vaccine hesitancy research

Based on our discussion, we suggest three directions for future vaccine hesitancy research:

1. Focus on interventions targeting vaccine-hesitant parents instead of vaccine rejectors

There will always be groups who will reject vaccines for various reasons, and we do not need 100% acceptance for all vaccines. As long as vaccination rates are sufficiently high, herd immunity may still be achieved; this is a phenomenon where an immune subpopulation slows the spread of a disease, indirectly protecting unvaccinated individuals [17]. Although we do need high acceptance for some vaccines in order to achieve herd immunity, our efforts will be more efficient if we target those who are most likely to seek new information and try to address their beliefs. Therefore, resources should be dedicated to better understanding partial acceptance, partial rejection, and delay of vaccines. Understanding which factors are more influential for which parents under certain circumstances will clarify the elements of interventions that will most likely improve outcomes.

2. Focus energy and resources on tailoring existing interventions and testing the effectiveness of these interventions in different contexts

We have a reasonable amount of effectiveness research on interventions to address vaccine hesitancy. We need to continue testing their validity and applicability in different contexts (e.g. countries, populations, and reasons for vaccine hesitancy). We also need a more robust understanding of how to tailor existing interventions for different values and beliefs regarding vaccine hesitancy. Tailoring is an effective strategy to improve the impact of interventions, particularly when considering the behaviour, belief, population, and demographic variables [18]. The assumption is that since there is a multitude of reasons and rationales that promote hesitancy, interventions need to be tailored for each parent; for example, we have found that vaccine-hesitant parents are more likely to have the financial capacity to not vaccinate (i.e., placing their children in more expensive private schools that do not mandate vaccination, or creating a healthier and more "natural lifestyle" for their children). However, developing a different intervention for each parent is impractical. There is a need for research to identify how we can balance an intervention's ability to target a wide range of vaccine-hesitancy beliefs while simultaneously be effective in addressing the unique rationales of each parent.

3. Develop robust continuing medical education that promotes shared decision-making in vaccine discussions

Negative experiences with allopathic health providers are among the most commonly cited reason for parents to entrench in their vaccine hesitancy beliefs [7]. Shared decision-making is uncommon for vaccine discussions because it is more relevant for *preference-sensitive decisions*, where there are multiple treatment options each with their pros and cons. Vaccination is not a preference-sensitive decision because vaccines have important benefits when administered and deleterious risks otherwise. However, since the parents' expectation of shared decision-making is increasing [19], it is important to identify which elements of shared decision-making are most appropriate, and train healthcare providers to incorporate these elements in their discussions with vaccine-hesitant parents. In this way, vaccine hesitant parents may feel more welcomed and invited, and as such, be more amenable to accepting vaccines for their children.

Vaccine hesitancy is a complex phenomenon; parents express a compendium of reasons and rationales for rejecting or delaying vaccines. As the number of vaccine hesitant parents increase worldwide, the values and assumptions that ground public health is being challenged. In the face of such challenges, healthcare professionals might consider not reacting with judgement or ignorance; rather, healthcare providers need to identify why vaccine hesitancy persists and how they can tailor interventions to address or alleviate such beliefs for the goal of improving public health. This article provides an overview of vaccine hesitancy research to promote better and more relevant research.

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The gut-brain axis and microbial therapeutics: The future of personalized medicine for psychiatric disorders

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Abstract:

Given the vast personal and economic burdens of psychiatric disorders, specifically mood and anxiety disorders, finding appropriate treatments for all those affected is critical. Due to the various presentations of psychiatric indications, no one treatment method is efficacious in all patients. Thus, a more personalized, but feasible treatment method is necessary for properly treating and preventing these disorders from becoming refractory and more burdensome. In recent years, there has been a growing appreciation for research in the field of the "gut-brain axis" (GBA), specifically as a target for psychiatric disorders. Researchers have found the gut to be influenced not only by similar determinants to that of psychiatric indications, but also highly modifiable using GBA treatments such as probiotics and fecal microbiota transplant (FMT). This is compelling evidence for the use of the GBA as a target for disorders such as depression and anxiety and for development of personalized treatment methods.

Mental illness can be considered similar to other physical illnesses in that it has a wide variety of causes and symptoms; however, it's not quite as straightforward in its etiology. Mental illness refers to a broad range of mental health conditions that affect feelings, thoughts, and as a result, behaviour. On average, 1 in 5 Canadians experience a mental illness or addiction problem, with 70% of the mental health problems beginning in childhood or adolescence [1]. Mood and anxiety disorders are among the most prevalent mental illnesses and due to overlapping symptoms and causes, they can often be comorbid with one another, further complicating disease presentation and course. In addition to psychiatric symptoms – such as depressed mood, loss of interest, and excessive worry – mood and anxiety disorders are characterized by significant functional impairments in affected individuals [2]. There are great personal and economic burdens associated with these indications, yet effective treatments that work for all those affected remain unknown. This is partly due to high individual variability in symptoms and course, comorbidity with other psychiatric and non-psychiatric disorders, and the influence of genetic and environmental factors.

Traditionally, we have been drawn to the physiological causes of illnesses, however understanding mental health requires condering both the physiological and environmental causes in conjunction with one another. The main physiological cause of mood and anxiety disorders is believed to be an imbalance of neurotransmitters, such as serotonin and norepinephrine. Serotonin and norepinephrine are both involved in the regulation of emotions and cognition, among many other functions [3,4]. This explains the theory behind selective serotonin and serotonin-norepinephrine reuptake inhibitors as treatments for many psychiatric disorders as they enhance neurotransmission of serotonin and norepinephrine by increasing their availability in the brain by delaying their reuptake [5].In addition to these physiological mechanisms, there exists a wide range of environmental determinants that may also influence the development of psychiatric disorders, such as socioeconomic status, diet, traumatic life events, and adverse childhood experiences; however these factors are not always considered when developing treatments. Given the heterogeneity that exists in mental disorders, efforts to comprehensively understand, prevent, and treat mental illness will require a more holistic approach – perhaps one that explores multiple targets for treatments on a case-by-case basis.

Current treatments for psychiatric illness

Standard options for treating most psychiatric illnesses include antidepressant medication and/or psychotherapy. Other treatment methods, such as electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), and ketamine are also options. Although ample amounts of research have been conducted on antidepressant treatment options to unveil highly efficacious pharmacological interventions, as it stands, they tend to have many side effects, unwanted pharmacological actions, and are not as easy to personalize [6,7]. This can

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therefore make antidepressants a poor first-line treatments for some individuals [8]. As for psychotherapy, although also highly effective and more personalized to focus on the individual's thoughts and actions, it can be rather expensive and often associated with long waitlists to receive care. Further, treatments such as ECT, TMS, and ketamine are often administered in later stages of depression, to those that are often resistant to pharmacotherapy, making them less of a preventative treatment method. ECT also requires hospital equipment and anesthesia and may be associated with side effects such as cognitive impairment [9]. Ketamine, although also highly efficacious, can cause dissociation, may have high addictive potential and is often abused as a recreational drug [10]. This highlights a need for more preventative, personalized, and feasible treatment methods.

Gut-brain axis: A novel target for mood and anxiety disorder

In recent years, there has been a growing appreciation for research in the field of the "gut-brain axis" (GBA), specifically as a target for psychiatric disorders. The GBA consists of bidirectional, biochemical, and neural signalling between the gastrointestinal (GI) tract and the brain [11]. The GI tract is colonized by over one hundred trillion commensal bacteria that exist symbiotically with our bodies and is largely influenced by mode of delivery (c-section vs. vaginal birth) and through breast feeding [12].

The human gut microbiota is known to have substantial individual variability in bacterial abundance and diversity and is influenced by a variety of factors such as genetics, diet, metabolism, age, geography, antibiotic treatment, and stress [13]. Although similarities exist in the gut microbiome of different individuals, no two individuals have the same gut microbiota composition [14]. However, in recent studies, individuals with psychiatric disorders have been shown to have a significantly dissimilar microbiota composition compared to healthy individuals, due to decreased diversity and abundance of the healthy gut microbes [15].

The gut microbiota is able to modulate the GBA both directly and indirectly via endocrine, neural, metabolic, and immune pathways; these pathways can become compromised in disease- or stress-states resulting in intestinal dysbiosis; changes in mood, behaviour, and cognition; and altered inflammatory levels [16]. During stress states, our hypothalamic-pituitary-adrenal (HPA) axis is activated and a release of hormones – such as corticotropin releasing factor, adrenocorticotropic hormone, and cortisol – ensues in response to stress. Beginning at the HPA axis, communication between the brain and intestinal lumen of the GI tract is facilitated by the GBA. The gut microbiota alters the availability of nutrients and release of peptides. Galanin, a neuropeptide that is involved in sleep/wake regulation, feeding, mood, and nociception is an example of one of these peptides. Via HPA axis stimulation, galanin influences the release of the above mentioned hormones, suggesting a potential role in stress modulation [17]. The release of cortisol can affect immune cells, alter enteric muscles and gut permeability, and change microbiota composition [10].

The immune pathways consist of immune cells located in the gastrointestinal tract to facilitate proper functioning of the gut. One of their functions is to release signaling proteins known as cytokines (such as the interleukins IL-10 and IL-6). During disease-states, cytokines interact with other immune cells to regulate the body's immune response. When the gut microbiome is altered, the number of inflammatory cytokines can be affected, leading to dysregulated enteric nervous system, increased gut epithelial permeability, and activated pain sensory pathways. These disruptions can trigger low-grade inflammation, commonly seen in stress-related psychiatric illnesses [17].

The neural pathway of the GBA involves the vagus nerve, enteric nervous system, and the activity of the neurotransmitters. The afferent nerve fibers of the vagus nerve, gather information from metabolites of the microbiota, immune cells, and enteric muscles and communicate it to the central nervous system [16-18]. The central and peripheral changes that occur as a result of this communication are hypothesized to improve psychiatric symptoms.

Finally, the metabolic pathway mainly involves metabolites produced by gut microbiota via fermentation of non-digestible carbohydrates. These metabolites are known as short-chain fatty acids (SCFA). Though indigestible, these SCFAs are integral for the gut to carry out various roles through interactions with the gut microbiome. In particular, they influence the synthesis of the rate-limiting enzyme tryptophan hydroxylase which synthesizes serotonin produced by enterochromaffin (EC) cells [19, 20]. Approximately 90% of the body's serotonin is produced by EC cells [21]. In the gut, SCFAs also influence the expression of anti-inflammatory markers, such as IL-10, in macrophages and intestinal dendritic cells [22].

The interaction of the gut with the aforementioned environmental determinants of psychiatric illnesses – such as diet and early life stress and the pathways connecting the gut and brain – indicate that the gut microbiome may be a good target to prevent and treat psychiatric symptoms.

Gut-repopulation treatments: Potential for personalization

In current research, repopulating and strengthening the gut with the use of GBA treatments are being explored to determine the influence of the gut microbiome on the gut-brain axis. There exists two distinct GBA treatment methods that are more heavily explored than others – probiotic treatments and fecal microbiota transplants. While probiotic treatments are used to supplement the gut with one or two healthy bacterial strains, fecal transplant is the transfer of many strains of fecal bacteria from a healthy donor to a recipient [23]. These treatments aid in upholding the bacterial balance and function. Other variations of this treatment, such as Microbial

Ecosystem Therapeutics-2 (MET-2), are also currently being explored in psychiatric indications such as Generalized Anxiety Disorder and Major Depressive Disorder. MET-2 consists of gut bacteria from a healthy donor, chosen for its safety profile, that is then purified from stool samples and lab-grown prior to being lyophilized and ingested orally by patients [24]. Current research, particularly studies exploring the use of FMT for psychiatric illness, suggest an improvement in mood or anxiety symptoms in both preclinical and clinical populations[25]. A recent review by Chinna Meyyappan et al. systematically weighs the pros and cons of FMT [25]. Though every study found an improvement in psychiatric symptoms which may be mediated by gut repopulation and improvement of GI symptoms, there are limitations. These include transiency of treatment effects; unknown costs and associated stigma; and lack of large-scale, double-blind, placebo-controlled trials, given the novelty of the treatment method. The studies also differed in many aspects including FMT administration protocols, main indications (chronic stress, anorexia, depression), and underlying GI conditions, which makes it hard to draw overarching conclusions [25]. Probiotics studies, have also found positive results with similar drawbacks [26, 27].

A therapeutic advantage to the link between psychiatric disorders and the gut microbiota is the accessibility and modifiability of the gut. Prior to administering aforementioned GBA treatments, stool samples are often obtained from patients. These samples are analyzed for diversity and abundance of bacteria and can show the dissimilarities between healthy patients and patients with psychiatric disorders. As we learn more about what makes a "healthy" microbiome, we can use this baseline data to personalize treatments such as MET-2 to include bacterial strains that are lacking in ill participants when compared to what we define as a healthy microbiome. Although studies looking into the efficacy of microbial ecosystem therapeutics in alleviating mood and anxiety symptoms have yet to be published [24], ongoing research exploring the use of other GBA treatments, such as fecal microbiota transplant (FMT) and probiotics, suggest there is great potential for personalization [25, 26].

Due to the many influencers of gut microbiome and as a result incredible variability between individuals, the gut may be a good representation of individual history. Given the connection between the gut and psychiatric symptoms, detailed analyses of the gut could therefore explain the differences in risk of illness, disease course, and response to treatment. Additionally, the similarity between the environmental determinants of gut composition and psychiatric disorders indicate that the GBA may be an excellent target for treatments. Due to the varied presentations of these indications, personalized medicine approaches are critical for not only treating and managing them, but also for preventing the illnesses from becoming refractory. Thus, the modifiability of the gut using GBA treatments, such as MET-2, shows its potential as a personalized treatment method for psychiatric symptoms.

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Untangling complexity as a health determinant: Wicked problems in healthcare

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Abstract:

As the healthcare system has modernized, it has also become rich with complexity. This complexity continues to foster the creation of *wicked problems* that, at first consideration, appear inherently insoluble. To compound matters, policy and decision-makers continue to view the healthcare system in a reductionistic and linear manner. The following article advocates that all stakeholders within the system (policy-makers, providers, and patients) become comfortable with complexity as a determinant of health, and offer tools for productively working with complexity, instead of trying to solve it. These tools include: complexity heuristics, adjusting to an emergent decision-making paradigm, and easing anxiety associated with ambiguity and paradox by becoming antifragile. By adopting these methods, complexity, as a health determinant within the Canadian healthcare system, can be effectively handled, thus leading to sustainable and scalable interventions, strong patient-partners in care, and efficient use of monetary and human resources.

Introduction

The structure of healthcare in Canada appears to balance on a precipice as successive provincial governments restructure the delivery of health care and providers grapple with multiple macro-level challenges. Since the beginning of the century, large scale challenges such as an aging population [1,2], tighter fiscal constraints [3,4], and disruptions to service provision [5] have been abundant. These challenges have contributed to the spiralling cost of healthcare in Canada (at a cost of $264 billion in 2019, and forecasts of even higher costs in 2020) with middling patient outcomes [3]. In addition, the cyclical political environment and high expectations from the public means that there is no catch-all solution. As the layers of data, technology, and administration have accumulated, so too, has the complexity of the healthcare system [6,7]. At the heart of this complexity are so called *wicked problems* [8]. First formally described in *Management Science* in 1973 by Horst Rittel and Melvin Webber, wicked problems contain several aspects which makes them unsolvable including: connection to other problems, range and variety of stakeholder opinion regarding proper action, economic burden, and imperfect or paradoxical knowledge for best action. Consequently, the operating environment of healthcare provision has created a strained system at every interface – from reducing wait times, to constraining operations costs [3] – ultimately, wicked problems have significantly hindered our ability to provide healthcare to Canadians.

We believe that a key to untangling these problems is not only recognising them, but also by accepting complexity as foundational to the healthcare process to enable the system to perform and meet the additional strain it will face in the 2020s. To do so requires adopting certain tools and heuristics to ease the transition of moving from a linear and stable environment to a complex and ambiguous one.

Health determinants primarily focus at the individual-level, with a neo-liberal assumption of individual responsibility, ignoring the role of systems [9]. This individualistic approach is even evident in the implementation of the social determinants of health, where public health messaging places responsibility for change at the local-level. In this short article we assert that positioning our discussion of health determinants within a framework of complexity will allow for adoption of new ideas, new approaches, and new solutions to the myriad of challenges facing current health systems [10,11].

Procedural vs. conceptual problem-solving

Evidence-based policy has long been the gold standard for constantly improving and informing service provision under the Canada Health Act. Systematic reviews and randomized control trials are commonly referred to when amending health policy or crafting novel health strategy, as rigorous methodology is a backbone of the evidence-based approach

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[12]. Once enough evidence has accumulated, rules are dictated for best practice, which are then applied in a linear fashion (outcome Y is solved by intervention X, with measurable indicators Z and W [12]). Rules help turn a conceptual problem into a procedural one – where the solution can be executed by simply following a proscribed methodology; and not worrying about the accompanying context. Healthcare policy, as well as implementation techniques, have tried to capitalize on this linear way of thinking [13,14]– assuming the healthcare system operates in a bounded, rule-driven environment [15]; this is not the case.

The healthcare system operates in a much more fluid environment. This "zone of complexity" (see Figure 1; [16]) fosters the creation and growth of wicked problems, as the rules of operation in the interdisciplinary healthcare system are constantly changing, and it is not immediately clear how rules relate to outcomes [6]. A great example of policymakers' failure to understand the important difference of working in a zone of complexity is the $20.6 billion-dollar implementation of the National Programme for Information Technology (NPfIT) by the NHS in England [15]. While this example is borrowed from a British context, there are many interesting parallels to the contemporary Canadian system. The largest being the similar guiding principles of healthcare provision within a universal healthcare paradigm. Secondly, following the COVID-19 pandemic, the interest in virtual care and clinical information systems has since exploded. Implementing pan-national electronic health initiatives is difficult, in part due to lack of precedent. Canadian implementors would be wise to study this case as interest in electronic health begins to yield tangible interventions. Lastly, this is a pre-emptive example of policy-makers sticking to an evidence-based, linear approach even in the face of failure and complexity which can also be seen in the limited large-scale Canadian eHealth projects, such as Nova Scotia's MyHealthNS [17].

The NPfIT was implemented from 2003 to 2010 and saw limited overall success (largely measured by the uptake of clinical information systems in small, disjointed private practices). The entirety of the implementation process was rife with technical, operational, economic, and political complexities which resulted in poor uptake of electronic health initiatives under the national program. Despite this, those at the helm of the implementation process continued to defend – and fund – the program, believing there was an invisible "tipping point" in which the entirety of the system would unexpectedly apply the changes they were advocating. This change never came, and the implementation debacle of the NPfIT was a major point of contention heading into the 2010 UK elections. Ultimately, the election resulted in a hung parliament, and required the coalition of the Conservative Party and Liberal Democrat Party – two polar political entities. Even with the rhetoric of altering or abolishing unpopular aspects of the NPfIT, the coalition did nothing. Further evidence that even at the highest levels of leadership, and with massive monetary stakes, not appreciating the complexity of the healthcare environment, and adjusting the tools to make decisions within it, leads to unmitigated collapse [15].

Continuing to engage in rational decision-making while not acknowledging the complexities of large-scale implementation was flagged as a contributing factor for the relative failure of the NPfIT. Figure 2 [16] explores an appropriate paradigm for decision-making while working in a zone of complexity: emergent decision-making. Emergent decision-making requires individuals to acknowledge that paradox and ambiguity are common in a complex adaptive system, and allow for the engagement of wicked problems in a

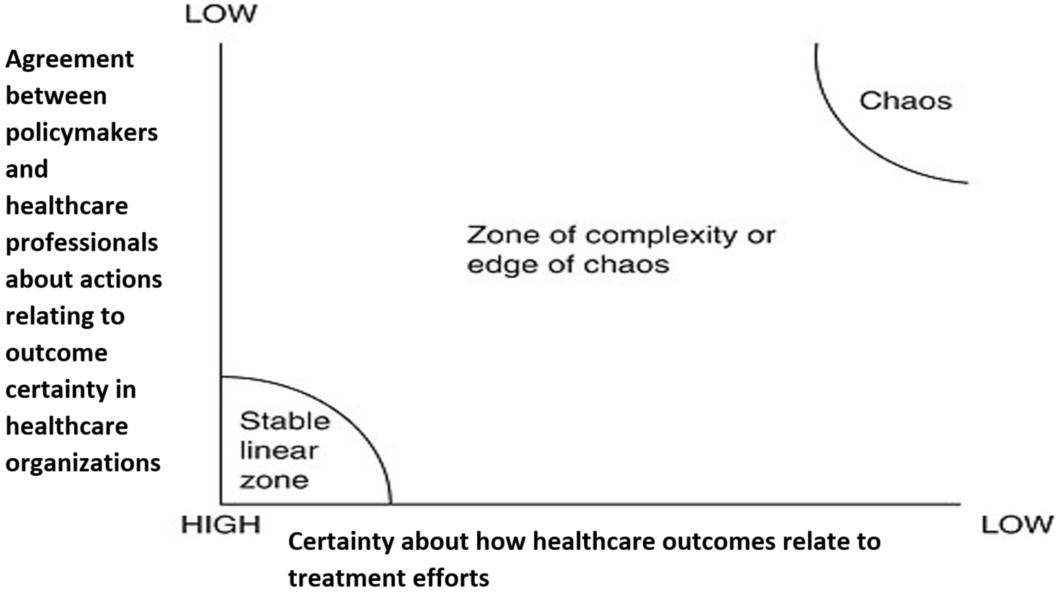

Figure 1 | A representation of organizational categories as a function of certainty of outcomes and inputs and agreement of decision-makers. Adapted from Stacey et al.

productively holistic manner, rather than the positivist method of attempting to break them down piecemeal. These methods have been shown to be impactful when used in smaller settings, such as clinicians deciphering medication dosage [18], and has even been shown to occur naturally within cell signalling pathways [19].

Rational decision-making is decidedly linear. It posits that intervention X will address outcome Y, and be measurable by some variable Z. Using this type of logic has contributed to Canada being a "nation of pilot projects" [20], with a vast majority of programmes failing to scale up and become sustainable at a broader level of healthcare organization. At a time where all resources (both monetary and human) need to be maximized, it is a tragedy that so much time, money, and effort is wasted in the pilot project stage of the healthcare arena. Utilizing emergent decision-making could help implementors and policymakers adjust their beliefs while working in an interdisciplinary, complex environment [21] such as the healthcare system.

Grappling with wickedness: Tools for dealing with complexity

There has been a steady increase in the study of wicked problems and complexity across a diverse range of disciplines [22], and decision-makers within healthcare are starting to take notice as well. To thrive in the complex and dynamic environment of healthcare policy, provision, and front-line treatment, behaviour and attitudes require a fundamental shift. This shift will not occur all at once - akin to the "tipping point" policymakers sought with the NPfIT – but gradually, and with great effort [23].

One of the ways we can become more comfortable with complexity and wicked problems is developing heuristics which can be relied upon in unfamiliar situations. In his book, *Thinking, Fast and Slow*, Daniel Kahneman lays out two systems humans rely upon to reason [24]. Heuristics are a portion of thinking generally referred to as "system one". This system is distinguished by its quick, emotional, and intuitive foundation. The second system is characterized by slower, more deliberate thought, necessitating the analysis of several streams of information, and rectifying that with internal values and morals. While heuristics have their downsides (no shortcut is right with 100% accuracy), they are still incredibly useful in everyday life, and many people use them without realizing [25]. A potential drawback of heuristics includes stereotyping [26], thus, guarding against this is important in maximizing the development of heuristics to approach wicked problems, making them more easily digestible for both the public, practitioners, and policymakers.

Rogers et al. offered some insight on complexity heuristics in 2013. They highlighted three "habits of mind" which individuals should practice in order to engage productively with complexity and complex systems [27]. The first

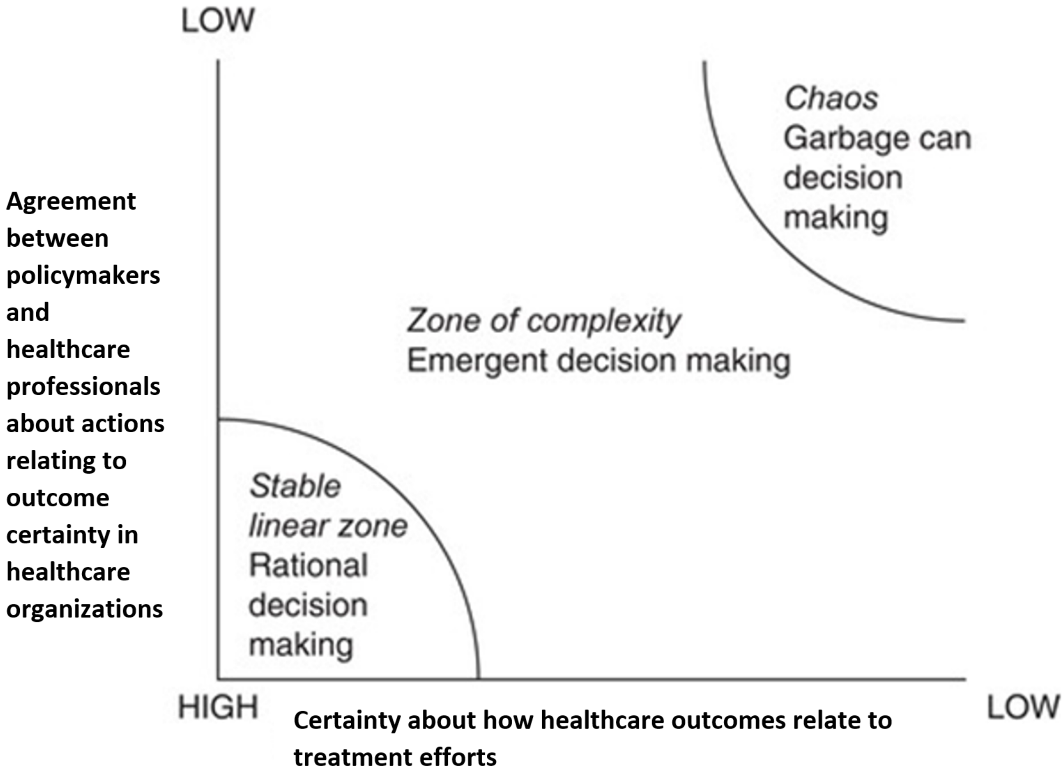

Figure 2 | Decision-making paradigms of each organizational category. Garbage can decision-making is truly random, rational decision-making is truly linear. Emergent decision-making exists in between. Adapted from Stacey et. al.

habit of mind, or heuristic, is *openness*. To be open, hold your strong opinions lightly [and encourage others to do the same], embrace emergence, expect ambiguity and paradox, and value diversity – among a long list of other contributing factors. The second is *situational awareness*, or the ability to assign appropriate appreciation to scale and context. To improve your situational awareness one can consider the importance of relationships between entities (not just the entities onto themselves), reflect often (individually, collectively, formally and informally), and cultivate diverse feedback mechanisms [avoiding echo-chambers and group think]. Lastly, a *healthy respect for the restraint/action paradox* is a heuristic characterized by the ability to act small and local [avoiding large system wide interventions], not being afraid of intelligent mistakes (as they lead to learning), and avoiding the paralysis of uncertainty – accepting that an action undertaken in a certain context has its risks and rewards and act accordingly.

The above heuristics offer basic behaviours which can help navigate complex systems. Many of them go against the contemporary norms seen in mass media and social media. Advocating for strong listening, loosely held opinions, and embracing ambiguity seem out of place in the urgent, partisan, and absolute environment we find ourselves in in 2020; this, of course, has had it's influence on policy, and by extension healthcare. The saying "patience is a virtue" has never rung more true – and should be recited *ad nauseum* as we wait to see if the above habits of mind can help the healthcare system meet the rigorous needs of Canada's future.

Working downstream instead of swimming upstream

Another way to tackle these wicked problems is to actively work *with* complexity, rather than trying to *solve* it. One potential avenue to explore this is by creating components of the system, both people and interventions, more antifragile. Antifragile entities stand to gain stability from volatility, rather than be harmed by it [28]. Antifragility has been used in other disciplines as a guiding principle in project design [29], as well as in healthcare [33]. It is intuitively appealing because it aligns with the holistic, realist approach to health implementation advocated by some academics to help an overburdened healthcare system meet demands. Interventions are antifragile by capitalizing on different functions at the project design level (such as starting small, ensuring optionality, and non-linear evaluation), and maximizing the probability they will thrive in a given healthcare environment. Thriving projects may also have an easier time scaling to other contexts and proving sustainable within these new spaces. The reputation Canada has of a nation of perpetual pilot projects could gradually change as stale and deterministic initiatives are replaced by more agile and innovative interventions.

Besides developing policy and projects, which can help unravel these wicked problems, the people within the system (known as *agents*) must become antifragile as well. Mentioned in the heuristic of openness, one must be comfortable with ambiguity and embrace emergence. Patients also must find their voice and push for a patient-partnered system where they have just as much power as the physician or nurse in their treatment. In his book, *Range*, David Epstein posits that generalists fair much better than specialists, even though the world is generally specialized [30]. This is especially true in healthcare, as specialization is evident at all levels of the healthcare system. Patients, providers, and policymakers need to have significant breadth of knowledge when interacting with one another to create a system where paradox, if not understood, is at least tolerated and worked with. Sufficient knowledge, habits of mind, and advocacy help smooth a system smothered in complexity.

Conclusion

An ignorance of wicked problems and system complexity by policy-makers, planners, and politicians have contributed to an unsustainable healthcare system and a misunderstanding of how to appropriately address the foundational determinants of health. In order to improve how health systems respond to macro-level (global, national, regional) and micro-level challenges (institution, community, individual), a complex systems approach is necessary. Wicked problems must slowly be unwrapped, allowing a breath of fresh air into a labouring healthcare system and a re-orientation away from linear-thinking and one-size-fits-all approaches to major issues. To do so will not be quick, nor easy, but there are some clear and simple practices we propose to facilitate that change.

First, moving policymakers from a rational decision-making paradigm [31], most suitable for linear systems, to an emergent one tailored for the inherent complexity in healthcare system is an essential start. A good example is the response to potential pandemic threats. In the early days of the transmission of a novel virus, policymakers and health professionals must make critical decisions with limited knowledge. Decisions pertaining to transmission method, incubation rates, and effective drug regimens are not overtly apparent – and instead practitioners must settle for being vaguely right instead of precisely wrong. Emergent decision-making in this case is the only available pathway, and it has performed well in the face of SARS, MERS, and NCoV-2019 [32].

Second, establishing habits of mind such as openness, situational awareness, and respect for the restraint/action paradox can help policy-makers and planners become more comfortable in a complex environment. For example, as medicine moves from a patient-centered model into a patient partnership one, this necessitates greater transparency and communication between a care team and the patient. In order to productively engage in patient partner techniques, practitioners would be wise to keep the habits of mind discussed close at hand to create a reciprocal relationship with their patient-partner.

Third, working with complexity instead of against it could increase the uptake of initiatives and pilot projects to improve the system. This example can be seen in the world of

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electronic health, where eHealth projects in rural communities that are designed to be inherently antifragile – or account for complexity within the design phase – have a greater chance of scaling and sustaining in multiple rural contexts [26].

Essential to the implementation of the above practices is the necessity to include the basics of complexity in graduate education programs, whether in medicine, public health, or foundational health science research. The tension for change is high in Canada, and the tools outlined above could help bring it about. One thing is for certain: 2020 and beyond will test the healthcare system to it's limits – how it responds is up to us.

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Hand hygiene: A simple strategy for health care-associated infection prevention and control with implications for control of the current COVID-19 outbreak

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Abstract:

The World Health Organization (WHO) defines Health Care-Associated Infection (HCAI) as an infection a patient acquired in health care settings. In Canada, more than 220,000 patients are infected by HCAIs annually, with 8,500 to 12,000 of these patients resulting in death, thus becoming the fourth leading cause of death for Canadians. Hand hygiene practice is the most critical measure to prevent HCAIs, however, research indicates that in hospitals worldwide, just 40% of health care workers abide by the advised hand hygiene guidelines. A new effective HCAI control and prevention program is needed to sustain benefits, building on prior interventions such as including hand hygiene education that stresses the necessity of this practice in the protocol, providing factual proof of the effectiveness of hand hygiene, the acknowledgment by senior staff of their responsibility as role models for all staff, innovative technological methods, and regular auditing/feedback. With the current outbreak of coronavirus disease (COVID-19) that has infected millions around the world, a new HCAI control and prevention program can increase the compliance rate of handwashing with alcohol-based hand rub/sanitizer amongst healthcare professionals thus aiding in prevention and control of spread within the community.

The WHO defines HCAI as an infection acquired by a patient during the process of health care in various settings, including and not limited to hospitals, long-term care, family medicine clinics, home care, and ambulatory care and are not present or incubating at admission. The WHO identifies HCAIs as the most harmful and recurrent event in healthcare delivery worldwide [1]. HCAIs appear within 2 to 30 days following health care [6]. This infection can then spread from the health care environment to society upon contact outside these settings, being detrimental to human health. HCAIs also include occupational infections among healthcare staff, such as doctors, nurses, and administration. Factors including advanced age, underlying illness, the prevalence of antibiotic-resistant organisms, and international travel lead to an increase in the risk of developing HCAI's [6].

Moreover, HCAIs alone constitute a significant burden, causing significant morbidity and mortality in hospitalized patients. HCAIs are now the fourth leading cause of death for Canadians, whereas two decades ago, it was the eleventh leading [7]. Although preventable, in Canada, HCAIs remain persistent with more than 220 000 patients infected annually, and an estimated 8,500 to 12,000 deceased while receiving healthcare [2]. HCAI's also constitute a significant financial burden on society, with Canada's annual direct costs estimated to be one billion dollars [2].

However, this significant mortality, morbidity, and financial burden caused by HCAIs can be reduced and are often preventable. About 80% of common infections are spread by health care workers, patients, and visitors [7]. Through infection prevention and control strategies, researchers estimate that 70% of HCAI's can be prevented [7]. Employing the best strategies for preventing HCAI's can reduce HCAI risk significantly. Antibiotics are the most common treatment for HCAIs, but this increases antibiotic-resistant organisms and requires extended health care stays, resulting in a lack of efficient hospital systems, possible disability, and mortality in some cases. The often neglected and poorly performed hand washing practice is the most critical measure to prevent HCAIs [8].

Nonetheless, research indicates that in hospitals worldwide, just 40% of health care workers abide by the advised hand hygiene guidelines [3]. Depending on the type, mi-

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croorganisms can survive on hands from 2 to 60 minutes after contact with patients and contaminated environments such as patient gowns, bed linen, and bedside furniture [9]. Poor hand hygiene can be the result of using an inadequate amount of product or limited duration of hand washing, which increases the likelihood of microbial transfer. Health care workers' contaminated hands due to poor hand hygiene have been linked to endemic HCAIs and numerous HCAI outbreaks [9]. Hand hygiene is the primary proven measure effective in HCAI prevention and antimicrobial resistance spreading, and effective interventions exist to improve compliance [9]. However, low compliance rates among health care workers have been reported from both developed and developing countries, with an overall average of just 38.7% [9].

In the past, there have been HCAI epidemics called nosocomial outbreak (NO), but most occur sporadically. In some cases, during an outbreak investigation, once the NO has been identified, the source may be traced to a single health care worker. Danzmann et al. (2013) conducted a systematic review evaluating outbreaks caused by healthcare workers [10]. A total of 152 NOs in 26 countries from 1958 through 2006 were included in the review, finding pathogens Hepatitis B virus, *S. aureus* bacteria, and *S. pyogenes* bacteria to be predominant [10]. Transmission of pathogens mainly occurred via direct contact with patients, with 41.5% of outbreaks deriving from physicians and 39.4% outbreaks deriving from nurses [10].

Currently, Coronavirus Disease 2019 (COVID-19), a new viral illness that is part of the same family as the severe acute respiratory syndrome (SARS) coronavirus, has globally infected millions of people. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is the strain of coronavirus that causes COVID-19, can survive up to 72 hours on plastics, 48 hours on stainless steel, 24 hours on cardboard, and 4 hours on copper [11]. These are all surfaces found in hospitals that can contaminate hands due to poor hand washing practice if the coronavirus virions are not thoroughly removed from the hospital setting [11]. Enveloped viruses, such as coronaviruses, are generally more susceptible to handwashing detergents and the use of alcohol-based sanitizers due to lysis or the solubilization of the lipids and proteins of their cell membrane [12,13]. For this novel coronavirus, the WHO advises that standard practices still hold for this outbreak: regular and thorough hand washing with alcohol-based hand rub/sanitizer will aid in killing any possible viruses on the hand [5]. With the current outbreak of COVID-19 that has infected millions around the world, a new HCAI control and prevention program can increase the compliance rate of handwashing with alcohol-based hand rub/sanitizer amongst healthcare professionals thus aiding in prevention and control of spread within the community.

At present, hand hygiene interventions include health care staff education, handwashing performance feedback and audits, verbal reminders and signs, improvement of water and soap availability, automated handwashing machines, and introduction of hand sanitizer. The WHO Multimodal Hand Hygiene Improvement Strategy and guidelines were developed by informed literature on spread methodology, implementation science, behavioral change, diffusion of innovation, and impact evaluation [9]. Wearable hand hygiene products such as hook-on alcohol-based hand rub dispensers that allow staff to disinfect while mobile are now available and research has shown an increase in the rate of handwashing from 37% to 49% [8]. This wearable dispenser would be convenient and easily accessible and thus can help form a habit of washing.

Nevertheless, further measures for the prevention of HCAI during the current COVID-19 pandemic are essential. Research indicates that multi-modal education and behavior interventions increase hand hygiene compliance, and if not implemented, benefits cannot be maintained, and prior interventions cannot be built on [14]. Trajtman et al. (2013) found ultraviolet, visible markers to be useful as an audit tool in evaluating surface cleaning compliance, which could prevent contamination on hand [15]. Storey et al. (2014) found increased hand hygiene compliance by providing electronic badges for hospital staff that displays immediate hand hygiene status to colleagues and patients [16]. Dalziel et al. (2017) found that continuous monitoring of the volume of alcohol-based hand rub used is a valid indicator of compliance [17]. Thus, technology-enabled observation of actual practice can help to sustain hand hygiene compliance [14].

Although these current interventions enable hand hygiene, there seem to be barriers to handwashing for healthcare workers. First, when recognizing Hawthorne effects where a performance improvement occurs due to the awareness of being observed, these interventions would likely result in positive changes in compliance and perhaps are not sustained [14]. Further, researchers investigated the reason behind low rates of hand hygiene compliance among healthcare workers. Hand hygiene knowledge varied among staff, junior staff followed poor hygiene examples from senior staff, there was a belief of lacking effectiveness in good hygiene, and hand hygiene were not found to be integral. For the stated interventions to be successful and sustained, these further measures need to be coupled with existing methods. Improved awareness of the evidence across good hand hygiene is required to improve ownership of those behaviors. There is also a need for senior staff to acknowledge their responsibility as role models in developing the culture of hand hygiene practices within the workplace [4].

Also, as of May 5, 2020, Public Health Ontario reported 292 outbreaks, with 16.1% of health care workers infected with COVID-19 since April 21st, 2020, in public hospitals and long-term care [18,19]. A NO of COVID-19 is unnerving as the Centers for Disease Control and Prevention reports that infection with SARS-CoV-2 is associated with a mortality rate currently estimated to be 0.2% [20]. In health and congregate care settings, the Ontario Coalition reported 4951 patients/residents infected with COVID-19, an increase of 155.7%, and 1878 patients and residents deceased in outbreaks, an increase of 333.7 % [21]. Older patients/residents and those with chronic conditions would be at higher risk of infection, along with those who work in these settings. Health care workers can be infected since they are in close contact with those infected with COVID-19 and the community, thus transmitting to hospitalized patients if infected.

Currently, in Wuhan, SARS-CoV-2 was found to be extensively distributed on object surfaces in a hospital, indicating a possible high infection risk for health care workers and patients [22]. Respiratory droplets and close contact are found to be the primary transmission routes for this virus [23]. Handwashing with alcohol-based hand rub/sanitizer by healthcare workers will be essential to protect against coronavirus infections in healthcare settings due to the high possibility of infection from object surfaces and close contact with patients. An increased handwashing compliance rate among hospital staff is essential in achieving control during this pandemic. It prevents contraction from infected patients and, thus, transmission to the community and uninfected patients.

To conclude, the acknowledgment of the factual proof surrounding COVID-19 is vital for controlling infection and prevention during this pandemic due to the dangerously low hand hygiene compliance rate among health care workers [9]. Future studies that analyze the impact of an increase in hand hygiene compliance during the current COVID-19 outbreak will help improve patient care and safety. A new and effective HCAI infection control and prevention program is needed to sustain benefits. Hand hygiene education included in existing interventions will stress the importance of this practice in the protocol. Factual proof of the effectiveness of hand hygiene, senior staff acknowledging their responsibility as role models for all staff, innovative technological methods, and regular auditing/feedback are required [4]. It is likely that including these measures into the program will increase and, most importantly, sustain hand hygiene compliance of healthcare workers, and thus control the spread of the COVID-19. It is unfair for uninfected patients hospitalized for other conditions as well as health care professionals to be more likely to contract this disease due to poor hand hygiene. With this current COVID-19 outbreak that has infected millions worldwide, an increase in healthcare worker compliance of a common and simple practice such as handwashing with alcohol-based hand rub/sanitizer can make a difference [5]. The difference is as follows: a reduction in the likelihood of nosocomial infection in hospitals, thus helping in decreasing the probability of patients and healthcare workers becoming infected by this viral infection, which in turn will control and prevent spread to the community.

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Digital health in a broadband land: The role of digital health literacy within rural environments

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Abstract:

The rapid rise and widespread integration of digital technologies (e.g., smartphones, personal computers) into the fabric of our society has birthed a modern means of delivering healthcare, known as digital health. Through leveraging the accessibility and ubiquity of digital technologies, digital health represents an unprecedented level of reach, impact, and scalability for healthcare interventions, known as digital behaviour change interventions (DBCIs). The potential benefits associated with employing DBCIs are of particular interest for populations that are disadvantaged to receiving traditional healthcare, such as rural populations. However, several factors should be considered before implementing a DBCI into a rural environment, notably, digital health literacy. Digital health literacy describes the skills necessary to successful navigate and utilize a digital health solution (e.g., DBCI). Given their limited access to high-speed internet, higher cost associated for similar services, and poorer development of information and communication technologies (ICTs), most rural populations likely report lower digital health literacy – specifically, computer literacy, the ability to utilize and leverage digital technologies to solve problems. Hence, DBCIs should address this 'digital divide' between urban and rural populations before implementation. Practical solutions could include evaluating rural communities' access to ICTs, needs assessments with rural community members, as well as integrating rural community stakeholders into the design of digital literacy education and interventions.

Consumer digital technology is a ubiquitous element of modern life. A recent report from Statistics Canada in 2018 estimates that 88% of Canadians own a smartphone and use the internet [1]. Healthcare services and providers looking to leverage digital technologies have given rise to the field of 'digital health,' which according to Lupton, "refers to a wide range of technologies directed at delivering healthcare, providing information to lay people and helping them share their experiences of health and illness, training and educating healthcare professionals, helping people with chronic illnesses to engage in self-care and encouraging others to engage in activities to promote their health and wellbeing and avoid illness" [2]. Digital health encompasses previously used concepts to describe the merge of technology with healthcare. For our purposes, digital health covers the concept of eHealth, which describes the application of information and communication technologies (ICTs) in the health sector [3] and the more specific concept of mobile health (mHealth) which refers to the use of wireless mobile devices, like smartphones, that have the computing power, built-in sensors, and internet connectivity to facilitate and monitor healthcare interventions [4]. Utilizing digital health as a tool for digital health interventions offers numerous advantages over traditional means of healthcare delivery and interventions [5-7].

The term digital health intervention describes a "discrete functionality of the digital technology to achieve health sector objectives" and can be aimed at clients/patients, health care providers, health system or resource managers, or data services [8]. Within the context of our commentary, we will be focusing on digital health interventions aimed at improving the health outcomes of clients/patients, also referred to as persuasive systems [9] or digital behaviour change interventions (DBCI), [10].

DBCIs symbolize an enormous potential for promoting health behaviours, such as healthy eating and physical activity [11], due to the widespread uptake of smartphones which allows for an unprecedented level of reach and scalability of high-quality healthcare. Ambient sensors (e.g., accelerometer, location tracking) and the ability to prompt notifications/reminders and evaluate collected data in response to real-time events (a.k.a., ecological momentary assessment) highlight the unique adaptive capabilities of DBCIs. For example, the Carrot Rewards app aims to improve physical activity through offering small monetary incentives (points)

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based upon smartphone sensor tracked step counts, as well as education and social competition elements [12]. Emerging work involving DBCIs report efficacy for a variety of health behaviours include physical activity [13], diet [14], and medication adherence [15].

In order to fully reap the benefits of DBCIs adequate digital health literacy should be considered. Norman and Skinner define digital health literacy as “the ability to seek, find, understand, and appraise health information from electronic (e.g. mobile and internet) sources and apply the knowledge gained to addressing or solving a health problem” [16]. In particular, digital health literacy consists of analytical skills (i.e., traditional literacy & numeracy, information literacy, media literacy) and context-specific skills (i.e., health literacy, computer literacy, science literacy), [16]. Current evidence describes an association between digital health literacy and healthy behaviours, such as exercise, healthy eating, and sleep behaviour [17]. Similarly, a lack of digital health literacy may lead to adverse outcomes, such as chronic illness, lower perceived self-management skills, and lower self-perceived understanding of health status, symptoms, and optional treatments [18]. Additionally, recent conceptual frameworks highlight the direct influence of computer literacy on engagement with DBCIs [19]. Thus, digital health literacy skills should be qualified as part of the DBCI research design process. Digital health literacy warrants particular attention among digitally underserved or disadvantaged populations, such as those residing in rural areas. Hence, the purpose of our commentary is to discuss the role of digital health literacy [1] in relation to the effectiveness of DBCIs, specifically for rural populations; [2] as an outcome of disparity among rural and urban areas; [3] and as the focal point for proposed strategies in rural areas.

Rural populations experience unique barriers related to their physical environment that impede the delivery of and access to traditional healthcare services. Canada’s rural population, defined by Statistics Canada as those who live in outside settlements of <1,000 inhabitants with a population density of <400 inhabitants per square kilometre [20], are often subject to barriers to health care services and interventions including: geographic barriers (e.g., increased travel to receive healthcare services), limited availability of health care personnel and services, and cultural factors (e.g., unfamiliarity with the healthcare system), [21]. As a result, rural Canadians report poorer health outcomes and cite greater unmet health care needs, compared to their urban counterparts [22-23]. Given that 16.8% of Canada’s total population, as of 2016, lives in a rural area [24], DBCIs, through the use of ICTs, represent a potentially transformative solution to addressing the distinct healthcare barriers of this population. Yet, at present, DBCIs have typically been run in urban centres, such as university settings [25], or recruit through convenience sampling in cities [5]; results obtained in these environments may not be replicated in rural areas, in large part due to a gap in digital health literacy.

We propose that the uptake and effectiveness of DBCIs in rural areas would likely be limited or hindered based, in part, on a poorer digital health literacy of these communities, specifically computer literacy [16]. Computer literacy is the ability to utilize and leverage digital technologies to solve problems [16]. In the context of digital health, computer literacy describes the ease and aptitude for individuals to navigate and engage with health care services and interventions through modern digital technologies such as computers, smartphones, mobile applications, and peripheral technology (e.g., Fitbit, smart assistant). For example, computer literacy impacts if, how, and the extent to which an individual may be able to: navigate a digital health application and its features on their specific device, self-monitor their daily step count through an application on their smartphone, manage their personal data through privacy settings, and engage in the participative and social features of the web, including social media platforms.

Although strengthening individuals’ computer literacy is foundational for successful DBCI implementation, rural communities likely struggle with achieving equity in computer literacy for a number of reasons. Rural communities lack access to the same high-speed internet services as their urban counterparts. This dearth of options is attributed mainly to the limited and rudimentary internet infrastructure within these areas. While 96% of urban Canadians in 2016 had access to broadband internet speeds of 50 megabits per second (Mbps) of download speed and 10 Mbps of upload speed, only 39% of rural and remote Canadians had access to the same services [26]. Lack of broadband development, compared to urban areas, further hinders access to similar ICTs in rural regions [27]. Even if rural Canadians have access to ICTs, they are often cost-prohibitive. Not only do rural Canadians have fewer choices of Internet Service Providers (ISP) nation-wide, compared the price for similar speeds of internet offered in urban centres, rural areas are often much more expensive, with fewer affordable options [28]. Lower-income rural households are therefore further disadvantaged, with lower household income being associated with both lower use of ICTs and lower digital literacy [29]. This disparity in access and affordability to ICTs, or “digital divide” [26] creates fewer opportunities for Canadians living in remote or rural areas to explore and familiarize themselves with digital health solutions. A recent survey in the US reported nearly a quarter of rural adults do not access the internet on a daily basis, and 15% report never going online (compared to 9% of urban respondents), [30]. Taken together, lack of access, development, and affordability of ICTs in rural areas act as barriers to the acquisition of digital health literacy skills, and consequentially reinforce the divide of computer literacy and health knowledge [31].

Taken as a whole, successful DBCI implementation must account for the potential computer literacy inequity among rural and urban populations. To this end, we propose several practical strategies that should be considered prior to implementing a DBCI in a rural/remote community.

Foremost, the access to ICTs of a population must be determined, since the principle of DBCIs hinges upon the use of these digital devices. This could be done through questionnaires via mailed letters, calling, and/or snowball recruitment. If a population has access to the appropriate ICTs, then the subsequent step should be to evaluate the digital health literacy of the population. This can be achieved through a community needs assessment [32] which aims to identify local challenges of a target population and implement recommended solutions. A multitiered, targeted community needs assessment model uses quantitative (e.g., Digital Health Literacy Instrument) [34] and qualitative methods [e.g., focus groups with rural residents] to collect data from multiple sources (e.g., rural residents, community leaders, healthcare practitioners, ISPs) in order to highlight various health needs. This needs assessment process could be guided by rural health research-specific guides [34] with questions informed by conceptual models, such as the model for mHealth readiness [35], which assesses the readiness of a community towards mHealth initiatives.

Finally, consideration should be taken when designing digital health literacy material for rural populations. Formative work has recommended that digital health literacy content be made relevant to remote and rural communities "in order to foster their inclusion" [29]. Hence, the creation of digital health literacy educative materials should involve collaboration between knowledge users (i.e., rural community members) and experts (e.g., clinicians, health behaviorists, researchers). This integrative process aligns with the principles of integrated knowledge translation, allowing for "deeper understanding of contextual circumstances which, in turn, enhances the usefulness of the research findings" [36]. Embedding rural community stakeholders in the research and development process, by way of town hall meetings and community representatives within research teams, for instance, will help in tailoring and modifying digital health literacy education to address the unique barriers among rural areas.

There are, of course, limitations to how well these solutions can be implemented. The lower adoption and usage of ICTs among rural Canadians presents the biggest barrier to improving digital health literacy, since access to digital devices predicates improving digital literacy [37] in much the same way that access to reading material is necessary for improving literacy. This digital divide is shrinking, however, as Canadian policies specifically targeting broadening ICT infrastructure to rural areas are enacted, such as the Connecting Canadians program [38]. Yet, even with access to ICTs, the sheer heterogeneity in digital technologies (e.g., brand, operating systems, features, user interface) may make it difficult to standardize educational materials or resources aimed at improving digital health literacy. For example, a separate walkthrough for how to download, navigate, and/or utilize features of smartphones may be required for iOS devices vs. Android devices. Recruitment of rural community members also poses a barrier as it is more difficult when compared to urban communities – even when dealing with digital health. Assessing outcomes such as access to ICTs means recruitment methods must reflect participants potential lack of access to ICT, necessitating analog means of advertisement, recruitment, and study communications [e.g., face-to-face, mailed letters, posters], which can be slow in remote or rural areas [39]. Finally, given the relative nascency of DBCIs, little work has been done examining the impact of digital health literacy within a rural-focused DBCI.

In sum, digital health represents a potentially transformative and modernized means of healthcare. The ability to adapt traditional health care interventions to DBCIs has potential for an unprecedented level of reach, impact, and accessibility. However, applying DBCIs to a rural environment requires consideration for the digital divide and resultant inequality in computer literacy. Evaluating the digital health literacy landscape through needs assessments and embedding stakeholders in digital health literacy development are practical steps to bridging the divide.

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Examining chronic pain through the lens of the socioeconomic gradient

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Abstract:

Longstanding evidence reveals the existence of a gradient of health running along the socioeconomic spectrum. This is denoted by a graded association between health and levels of socioeconomic status, including factors such as gender, income, education, and occupational roles. This gradient is found across many chronic diseases including heart failure, arthritis, type 2 diabetes, ulcers, and certain cancers, all of which commonly possess debilitating pain diagnoses. Here, I examine chronic pain and its severity through the lens of this socioeconomic gradient across three perspectives along with their potential limitations. First, I discuss how this gradient represents risk factors for greater pain severity, disability, and comorbidity. Then, I explore potential underlying health determinants and how one's position on this spectrum may predetermine their chance of receiving optimal care for their pain. Finally, I end with the prospect of better clinical and biological understanding of chronic pain severity with the inclusion of this socioeconomic gradient.

Introduction

Pain is the leading utilization of health care resources and the most important source of disability among working adults in both Canada and the United States. In Canada, we estimate chronic pain to affect nearly 20% of the general population. The estimated cost of chronic pain to the Canadian society is $6 billion/year in medical treatments and $37 billion/year in loss of productivity [1]. Given its high prevalence and important societal cost, chronic pain has evolved from a common comorbidity to a prominent health concern of its own.

Unfortunately, the underlying etiology behind most chronic pain conditions, along with the mechanisms behind the transition from acute to chronic status, remains poorly understood [2]. The traditional injury model is not enough to explain pain and its chronicity. For patients suffering from low back pain, one of the most prevalent forms of chronic pain, only a small portion of patients (<5%) report a traumatic event or fracture that could have contributed to their pain development [3]. This is not specific to back pain as most chronic pain types do not present a single specific etiology, but rather a mix.

This poor pain-injury correspondence has led to research targeting common mechanisms behind chronic pain conditions. Pain is a complex process including both a sensory-discriminative and an affective-motivational dimension, relying on detection mechanisms, reactive nociception, and reinforcement of avoidant behavior toward any pain or injury. This has motivated further research toward a biopsychosocial model of pain, acknowledging the synergic contributions from biological, psychological, and social factors to the development or maintenance of chronic pain [4]. While research has increasingly started to combine biological and psychological measures to better understand chronic pain, social factors remain most often ignored. Researchers may control for social factors, but do not typically examine them despite the various health outcomes associated with socioeconomic status (SES).

The socioeconomic gradient and its role in chronic pain

The World Health Organization refers to SES as the social gradient of health, running from the top to the bottom of the socioeconomic spectrum. Denoted by a graded association between health and all levels of SES, this measure includes factors such as income, education, profession, and more. Additionally, demographic factors such as one's gender, age, and ethnicity also play a role in the socioeconomic gradient of health as they contribute to one's overall status and position in society.

Interestingly, this gradient is also found across many chronic diseases including heart failure, arthritis, type 2 diabetes, ulcers, and certain cancers, all of which present common debilitating pain diagnoses such as chest pain, osteo-

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arthritis, diabetic neuropathy, burning stomach, and cancer pain. In parallel, extensive literature describes low SES as a strong potential risk factor for chronic pain. Population-wide studies reveal large socioeconomic disparities in pain across gender, education, and income. Pain levels are lower for men than women and decrease across increasing education and income quartiles [5]. A study examining the experience of pain showed that lower SES was associated with a higher prevalence of severe pain, including a greater number of painful body sites, greater pain intensity, and/or greater feelings of being disabled by pain. Even at the same intensity of pain and the same number of painful body sites, the study reported that participants at the lowest as compared to the highest SES were two to three times more likely to feel disabled by their pain [6]. This is in addition to the greater risk of developing multiple psychiatric comorbidities: generalized stress disorder, panic disorder, depression, and post-traumatic stress disorder along with their pain [7], also commonly observed in lower SES populations [8].

Importantly, demographics also contribute to the effects mentioned above within this socioeconomic gradient, with pain typically being more pronounced in women [5]. Pain-related disparities between men and women are both biological (sex) and socio-cultural (gender) in nature. Strong biological evidence indicates that males experience stronger opioid analgesia [9]. Yet, these differences are also the recipient of social influences. For instance, questionnaires assessing the gender role in pain expectation reveal that even after controlling for sex, self-identified gender still predicts pain tolerance [10]. It remains unclear, however, the extent to which we can dissociate the contribution of SES from gender, as women typically present lower SES compared to men.
A very similar case can be made with ethnicity, where pain is found more prevalent and disabling among non-Caucasian ethnicities [5]. However, a study suggests that this race effect appears to be strongly mediated by socioeconomic disparities. While non-Caucasian populations are typically the first targets of this socioeconomic gradient, presenting lower income, education, and occupational role, non-Caucasian individuals living in neighborhoods of greater SES do not seem to present the same pain severity as those of lower SES [11]. However, little research has explained the potential biological role behind race in chronic pain, and it still requires further investigation.

Health determinants of chronic pain and likelihood for optimal care

Linking this socioeconomic gradient to chronic pain may not be enough to provide potential avenues towards understanding disease or treatment outcomes. One must understand the mechanisms driving this gradient that impact the subjective experience of pain. This is especially important given that these mechanisms may be overlapping across many chronic pain conditions.

One well-recognized determinant of health is health behaviors, including smoking, alcohol use, physical inactivity, poor sleep, and malnutrition, all of which have also been independently observed as predictors for greater prevalence or severity of chronic pain [12]. Another determinant of health, probably the most specific to lower SES and more impactful for chronic pain patients, is the access in health care and the related expenditure for successful treatment.

Populations on the lower end of the socioeconomic gradient have been found to be misrepresented in clinical trials [13], limiting the extent to which a given successful treatment is generalizable. The reported efficacy may thus be over-optimistic, as it doesn't account for the additional severity and comorbidities typically reported in these populations. Furthermore, these populations report increased prevalence of pain in the chronic (> 6 months), rather than acute (< 3 months) phase. This suggests that SES may not play a role in the occurrence of pain, but instead in the transition from acute to chronic pain [14], potentially reflecting suboptimal treatment in these populations.

The poor understanding of chronic pain etiology has also led to multidisciplinary treatment approaches which are found to work best in reducing pain. In addition to opioid-derived medication, this includes an array of off-label medications (anticonvulsants, antidepressants, and others) paired with other forms of interventions (physical therapy, relaxation techniques, cognitive behavioral training, among many others). However, this approach must be done early in the acute phase (< 3 months) in order to be effective [15]. While individuals are in the acute-to-chronic transition phase (3-6 months), they are at greater risk of developing psychiatric comorbidities as a result of their pain and will typically become less responsive to traditional treatments in the future.

Unfortunately, this approach, now considered standard to chronic pain care, is costly in time and money. For individuals on the lower end of the socioeconomic gradient who often have less-accommodating work environments, their economic well-being suffers due to the cost of treatment and lost productivity. This is in addition to a variety of complementary and alternative medicine (CAM) treatment forms typically recommended during the multidisciplinary treatment approach not accessible due to their extraneous cost. CAM therapy users are typically younger, more highly educated, and have a higher income [16]. Patients presenting lower SES are also less likely to be prescribed traditional opioid treatments due to being at higher risk for substance abuse disorders, despite it being the most effective treatment for pain management in the acute phase.

One major limitation in the interpretation of the determinants of health towards this socioeconomic gradient is directionality. On one hand, socioeconomic factors may predispose individuals to turn to different coping mechanisms (e.g. smoking, alcohol use, malnutrition) for their pain dependent upon their affordability. These coping techniques, although potentially beneficial to cope with pain in the short-term, can lead to further morbidity or mortality in the long-term. This is in addition to other health behaviors that

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may reflect reaction mechanisms to intolerable pain (e.g. poor sleep and physical inactivity). On the other hand, one may suggest that poor health behaviors may predispose a given individual to experience greater pain, as each of these behaviors is essential to optimal health and pain tolerance. The relationship between health behaviors and chronic pain may be bidirectional, and therefore self-reinforcing in the maintenance or worsening of chronic pain.

Similarly, the directionality also applies to access to health care. Patients who develop chronic pain following a traumatic event may be more likely to transit toward a lower socioeconomic status as a result of their pain. The exorbitant health care cost along with their inability to sustain the type of work they normally engage in may lead to unemployment, decreased income, and an inability to pursue further education. A careful interpretation is therefore needed before declaring specific directionality of these health determinants with chronic pain.

Understanding chronic pain etiology & biology through SES

Investigating the socioeconomic gradient and its health implications is an important, yet often overlooked component in our understanding of pain and its chronicity. Human neurobiological research has so far presented very few models that reliably reflect pain severity in patients, mostly limited to modeling chronic pain as a dichotomous outcome in patients (i.e. present or absent). These measures, including brain imaging, biological sampling, and genetics among many more, typically present poor correlates of pain severity (i.e. as a continuous variable) in comparison to psychosocial variables [17].

In this case, the lack of ecological consideration may be hindering biological understanding, ignoring the various health determinants contributing to the maintenance, worsening, or potential resilience of chronic pain. This idea for ecological or holistic consideration, however, is not new nor specific to chronic pain. There has been a growing trend toward moving away from small, carefully selected, and homogeneous cohorts toward larger-scale cohorts presenting richer and more diverse phenotyping, potentially more representative. This has also been accompanied by an interest toward normative modeling of populations, acknowledging disease heterogeneity and potential transdiagnostic similarities in treating these conditions as a spectrum rather than discrete categories. This approach seems ideal for the study of chronic pain.

Fortunately, the prospect of integrating this socioeconomic gradient within our biological understanding of chronic pain may be currently possible. A population-wide study that has enrolled nearly one million adults in the United Kingdom Biobank (i.e. the UK Biobank) will investigate the contribution of biological [brain imaging, biological sampling, and genetic], environmental (demographics and socioeconomic), and various health outcomes (pain, sleep, nutrition, and more) in the development of diseases. This represents by far the largest sample ever studied of chronic pain patients and an exciting prospect for understanding chronic pain across diseases along with their interactions with SES. Furthermore, the researchers intend to contact participants five to ten years following the initial assessment, providing an opportunity for the study of the combination of these socioeconomic and biological factors in the acute-to-chronic pain transition.

While socioeconomic factors may contribute to providing a better understanding of pain severity, it may lead to further consideration for factors contributing uniquely to each of these chronic pain diseases. Although the common sociodemographic mechanisms behind chronic pain are conceptually similar, distinct mechanisms of health are also occurring. For instance, chronic back pain is most prevalent in blue-collar workers while painful diabetic neuropathy is more prevalent in populations suffering from malnutrition and obesity. The effect of gender may also differ depending on the disease. Chest pain is typically more common in men, while widespread pain is more common in women. This also applies to biological mechanisms, where some chronic pain conditions present well-established markers. This is the case for a rheumatoid factors test that can help track the number of autoantibodies in the blood and help pinpoint a diagnosis for rheumatoid arthritis. Although it may correlate poorly with pain, it may be essential in tracking the disease progression.

Conclusion

Here, we denote that chronic pain severity appears to be intimately related to one's position on the socioeconomic gradient. Given that many key determinants of pain are the social and economic conditions in which people work and live, research must be directed at the root of those socioeconomic factors shaping pain and suffering. This is true for the whole spectrum, including why individuals on the higher end of the spectrum present less pain severity. What factors do patients with higher SES present that alleviate their pain, beyond these health determinants? Could they be targeted specifically?

On one hand, there is great potential for furthering our understanding of pain severity and the common biology among chronic pain conditions. On the other hand, this gradient of health also entails a clear need for the development of a comprehensive healthcare plan based on a patient's socioeconomic profile and may force us potentially redefine what we think of as minimal health coverage. This may be a crucial step toward more accessible pain management which will become increasingly important in our aging society.

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The information theory of aging: Hacking immortality?

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Abstract:

Humans have sought to cheat death for as long as we have been cognizant of our mortality. History's early explorers of the frontier of immortality include alchemists in the pursuit of an elixir of life and emperors who, ironically, hastened their own death from the consumption of mercurial concoctions. Scientifically grounded approaches to the extension of the human lifespan emerged in the 20th century and were based on hormonal rejuvenation, calorie restriction, and most recently, the consumption of supplements with purported anti-aging effects. A combination of three "longevity drugs" has recently been championed by Dr. David Sinclair, co-discoverer of the lifespan-regulating sirtuin enzymes, and author of the epigenetics-focused Information Theory of Aging (ITA). In this work, we investigate the evidence behind Sinclair's ITA, highlight concerns related to his regimen, and reflect on the possibility that we are at a nexus in time preceding a dramatic increase in human healthspans. Promisingly, if the ITA holds true, individuals will be uniquely empowered to "hack" their own immortality.

Introduction

For at least as long as recorded history, the realization of life's finitude has provoked unease among some people. Mortality is a major theme in the earliest known work of literature, the Epic of Gilgamesh, in which the death of his friend Enkidu prompts Gilgamesh to undertake a quest at whose conclusion he makes peace with his own eventual death [1]. Accepting mortality (or some concept of continued survival in the afterlife) has not proven satisfactory for everyone, however, and practical efforts at achieving immortality have been attempted throughout the centuries.

Perhaps the most notable pre-scientific endeavors are those of alchemists, both in Western esoteric and Daoist traditions. In a famous example, the first Chinese emperor, Qin Shi Huang Di, so feared death that he imbibed various purported elixirs of life which is believed to have hastened his death due the toxic effects of mercury, a key ingredient in the concoctions [2].

In the late 19th and early 20th centuries, the rise of professional science and increasing biological understanding enabled the development of the first scientifically-grounded anti-aging interventions, which were based on the inferred rejuvenating power of hormones (reviewed in [3]). Although such interventions were unsuccessful, several practical approaches to extending both lifespan and healthspan (the period of one's life when in generally good health) have become prominent among later 20th and 21st century longevity enthusiasts, including caloric restriction and anti-oxidant supplementation. [4]

One particular pharmacological cocktail of three drugs has recently gained attention when Dr. David Sinclair, one of the discoverers of the role of sirtuins in lifespan regulation, revealed in a LinkedIn post [5] (posted on June 25th, 2018) and later in his book [6] (published September 19th, 2019) that he was taking these "longevity molecules" every day. The combination consists of the anti-diabetes medication metformin, the mTOR inhibitor rapamycin/resveratrol, and nicotinamide mononucleotide (NMN), a precursor to nicotinamide adenine dinucleotide (NAD^+), an essential co-factor of sirtuin function. Here, we examine the justification for taking these three drugs in context with Dr. Sinclair's mechanistic theory of aging, which he calls the "Information Theory of Aging" (ITA).

Epigenetic control of aging — The Sinclair theory

Biological theories of aging can be divided into two types: *evolutionary* theories aim to explain why aging exists as a phenomenon, while *mechanistic* theories aim to describe the proximal cause of senescence, or age-associated decline in function.

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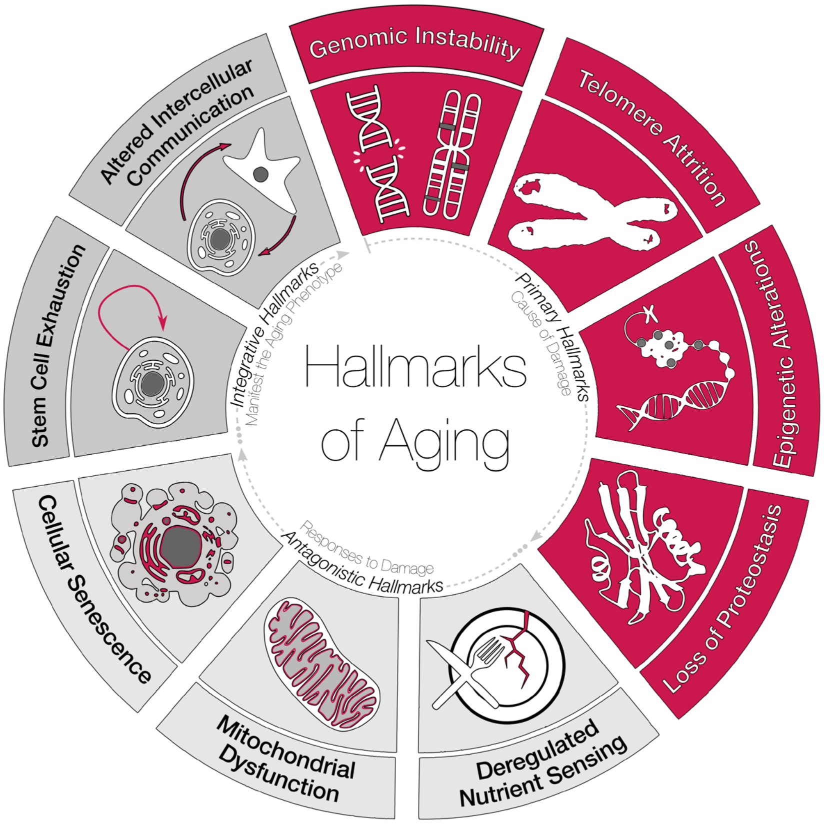

Figure 1 | The nine hallmarks of aging and their functional interconnections. The primary hallmarks (red) are responsible for initial cellular damage which manifests the antagonistic hallmarks (light grey) as a response to mitigate that damage. Together, these hallmarks contribute to the manifestation of the integrative hallmarks (dark grey) which, ultimately, are responsible for the aging phenotype. Figure adapted from [10].

Here, we use the terms aging and senescence interchangeably to signify the functional decline of an organism as a function of calendar time. Senescence, in this sense, is distinct from cellular senescence, which is a narrower term signifying terminal cell cycle arrest and stereotypical phenotypic changes in the cell [7].

The most influential evolutionary theories (reviewed in [8]) have in common the idea of aging as an outcome of specific selective force interaction patterns, but discuss the molecular and cellular mechanisms with a high level of abstraction.

Mechanistic theories, by contrast, suggest specific causes of senescence at the molecular, cellular, and organismal levels. Important mechanistic theories can be further divided into programmed aging theories, which consider senescence a programmed response (examples include the endocrine and immunological theories), and damage theories, which explain it as a consequence of accumulated errors or damage (examples include oxidative stress theory, somatic mutation theory, and telomere shortening theory) [9].

The concept that aging is not necessarily inevitable is evidenced by several multicellular taxa (including plants, invertebrate, and vertebrate animals) which do not exhibit an age-dependent increase in mortality, a phenomenon which Caleb Finch termed *negligible senescence* [10, 11]. Thus, it appears that senescence is neither evolutionarily inevitable, nor impossible to overcome at a mechanistic level. To be overcome, however, it must first be understood.

An influential review in 2013 by several leading scientists in the field of aging biology has proposed a list of nine hallmarks of aging: genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication [7], illustrated in Figure 1. Of these nine, four are proposed as the "primary hallmarks", or the ultimate causes: genomic instability, telomere attrition, epigenetic alterations, and the loss of proteostasis. The rest are considered either "antagonistic hallmarks" which are responses to damage, or "integrative hallmarks", which are the proximal causes of organismal decline [7] (Figure 1). In other words, the primary hallmarks are biochemical events that trigger local (cellular) responses in the form of antagonistic hallmarks, which in turn result in tissue- and organ-level dysfunction (the integrative hallmarks). This tissue and organ dysfunction is the most proximal (immediate) cause of the phenotypes observed in aged individuals.

In the ITA as proposed by Sinclair, there is one principal cause of aging: loss of epigenetic (non-DNA-encoded gene regulatory) information. In this framework, the aging process is represented by a linear sequence of events, depicted in Figure 2 [6]. While genomic instability, caused by DNA breaks, does precede and cause the epigenetic dysregulation, the ITA considers the loss of epigenetic information as the central cause of aging. In other words, any genetic alterations (mutations) that result from DNA breaks and genomic instability are irrelevant to the downstream events: only the disruption to the epigenome counts.

Today, epigenetics has come to signify non-DNA-encoded heritable information, but it retains much of its original meaning

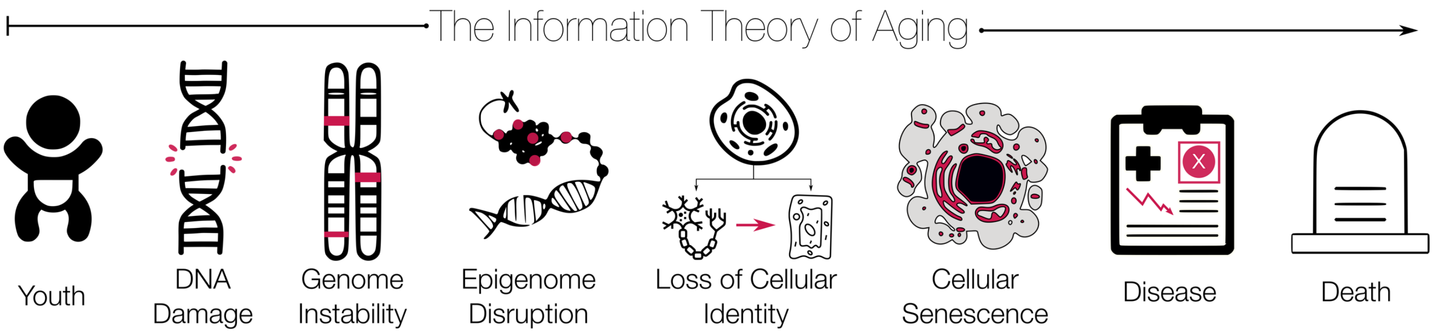

Figure 2 | Illustration of Sinclair's information theory of aging. Adapted from [5].

proposed by Conrad Hal Waddington as the causal mechanisms of multicellular development [12]. Epigenetic mechanisms, it is now understood, control the spatio-temporal patterning of gene expression, which allows cells to maintain a specific identity and coordinate the events of organismal development and later maintenance. Loss of cellular identity, according to the ITA, is directly downstream of the loss of epigenetic information, and is ultimately responsible for organismal breakdown. If the loss of epigenetic information can be either prevented, or the lost information recovered, the ITA predicts that cellular identity can be maintained *in perpetuo*, which would result in negligible senescence.

What constitutes epigenetic information? What are some of the specific hallmarks of epigenetic aging? In a narrow sense, epigenetic information in the nuclear genome is represented by histone marks (chemical moieties present on histone tails) and DNA methylation. Nuclear DNA is tightly wound around nucleosomes-octamers of histone proteins. The number, location, and nature of histone marks (such as acetyl, methyl, ubiquityl, and other functional groups) control the accessibility of DNA to the cellular environment, which has direct consequences for gene expression (when transcription is switched "on" or "off") as well as DNA damage and repair [13]. Typical epigenetic hallmarks of senescence include the loss of histones, the loss of balance between various histone marks, changes in chromatin architecture and the pattern of euchromatin and heterochromatin ("open" and "closed" conformations of DNA and histones), changes in DNA methylation patterns (global hypomethylation and local hypermethylation), and as a result of all these changes, transcriptional dysregulation (reviewed in [14]).

Dr. Sinclair has played a pivotal role with the discovery that the histone (and non-histone) deacetylase SIR2 (Silent Information Regulator 2), which lends its name to the sirtuin enzyme family, is a regulator of lifespan in budding yeast (later confirmed in other animals, including mammals [15]). It is therefore not unexpected that the ITA would elevate epigenetics above the other hallmarks of aging. But what evidence supports this contention?

One stream of support comes from so-called "epigenetic clocks", which is a term that refers both to mathematical estimators of chronological and biological age on the basis of cytosine methylation in the DNA, as well as the cellular processes themselves which give rise to age-related DNA methylation patterns (reviewed in [16]). Three such epigenetic estimators—Hannum's, Horvath's, and Levine's clocks—correlate well with chronological age and other age-related conditions, consistent with the idea that biological aging results from developmental and maintenance programs that generate the characteristic DNA methylation patterns [16].

The second line of evidence comes from Dr. Sinclair's recent work on "ICE" (inducible changes to the epigenome) mice and cells lines, which is currently deposited on a pre-print server [17, 18]. ICE mice and cells contain a tamoxifen-inducible endonuclease I-*PpoI*, endogenous to the slime mold *Physarum polycephalum*, that recognizes approximately 20 sites in the mouse genome. Tamoxifen treatment of ICE mice or cultured cells induces I-*PpoI* expression, resulting in DNA double strand breaks (DSBs). In the experiments reported in the pre-print publications, tamoxifen was added to the food of 4-6 month old ICE and control mice of both sexes for a period of 3 weeks to induce I-*PpoI* [18]. Compared to tamoxifen-treated control mice, tamoxifen-exposed ICE mice display numerous signs of premature aging (decreased weight, increased frailty, pronounced kyphosis, progeroid features in several organs, and neurological impairment). Additionally, the ICE mice were 50% "older" than age-matched controls, according to blood and muscle tissue-validated DNA methylation clocks [18]. Crucially, for the argument that the progeroid phenotypes are caused by epigenetic alterations downstream of DSB induction, neither ICE mouse tissues nor cultured ICE cells display telomere shortening or an increased mutation rate at I-*Ppol* cut sites, off-target sites, or 100,000 random genomic loci [17, 18].

However, questions remain about the mutagenic potential of I-*PpoI* activation. It has been noted on the BioarXiv discussion board that previous work using this system has shown that while I-*PpoI* does not cause point mutations, it has the potential to cause large deletions (up to 1Mb) and generate chimaeric DNA by joining two different I-*PpoI* sites during repair [19]. It is not clear whether ICE mouse tissues are affected by such large deletions. Furthermore, tamoxifen-treated ICE cells show increased levels of LINE-1 retrotransposon RNA [17]. LINE-1 retrotransposition events have been associated with at least 65 disease-causing mutations in humans [20] and it is unclear whether the increase in LINE-1 activity may contribute to mutagenesis on genomic sites other than the I-*PpoI* sites or the 100,000 random sites (the mouse genome includes 2.5 billion nucleotides).

Even if the conclusions drawn from ICE mouse experiments are correct and the epigenetic alterations are the sole cause of progeroid phenotypes in this setting, it does not follow that loss of epigenetic information is the sole possible cause of aging in the wild type setting, where somatic mutations, proteostasis, and telomere attrition may play a role together with or independent of the epigenetic alterations. Somatic mutations, in particular, are dismissed by Dr. Sinclair as not important on the argument that the largely normal lifespan of animals created by somatic cell nuclear transfer (SCNT) shows that irreversible genetic changes cannot be the cause of aging [17, 18]. However, the extremely low efficiency of SCNT (<2% per reconstructed oocyte) and the documented role of genetic abnormalities associated with aging phenotypes in several cloned pigs make this a premature conclusion [21].

Regardless of whether the ITA is correct in all particulars, it represents an advance in the understanding of aging biology. Armed with this increasing knowledge, we are on a better footing today than early 20th century hormone researchers or elixir-imbibing ancient emperors to discover pharmacological interventions to combat or reverse the effects of aging.

The Sinclair regimen

The popularity of Sinclair's ITA is due, in part, to its emergence as a promising mechanistic theory of aging. However, the ITA enjoys a widespread acclaim that can be attributed to its marketing as an *actionable* theory of aging. That is, Sinclair himself advocates for a self-prescribed regimen based on his ITA in both his book and in public lectures. Sinclair describes the regimen he developed and adheres to is an effort to extend his own healthspan with an emphatic admission that he is not a medical doctor and offers no assurance that his self-prescribed regimen will result in dramatically improved healthspans. He does, however, disclose that his brother, father, wife, and family dogs each adhere to a version of this regimen and, anecdotally, all have enjoyed improved health outcomes since. Table 1 outlines Sinclair's regimen, augmented with the longevity-related rationale.

As introduced, various stripes of "immortality-hackers" have existed for as long as we have been cognizant of our inescapable mortality. A plethora of supplements and lifestyle interventions of varying degrees of scientific validity exist today, each presenting trade-offs with other comforts of life. One notable example is periodic self-imposed starvation (*i.e.* intermittent fasting) to enforce caloric restriction. Sinclair's regimen presents a paradigm shift in his claims that the stimulation of NAD^+-dependent sirtuin pathways through the consumption

Table 1 | Sinclair's Longevity Regimen, as Outlined in [6].

Type	Intervention	Dose	Specification	Rationale
Chemical	NMN	1,000 mg/daily	Morning (tablet)	Based on ITA
	Resveratrol	1,000 mg/daily	With yogurt; soluble in fat	Correlated with longevity
	Metformin*	1,000 mg/daily	Morning (tablet)	Hypoglycemic effect
	Vitamin D	Daily recommendation	Morning (tablet)	Improves protein homeostasis
	Vitamin K2	Daily recommendation	Morning (tablet)	Linked to decreased mortality [22]
	Aspirin	83 mg/daily	Preventative dosage (tablet)	Cardio-protective
Lifestyle	Limit high carb. intake	Reduced/Eliminated	Specifically: sugar, bread, pasta, and desserts	High carb. food lead to increased blood pressure and heart rate
	Modification of meal number/size	1x daily, reduced size or eliminated	Typically: skipped lunch	Enforces caloric restriction
	Plant-based diet	Meat intake reduced/ eliminated	Exception: meat consumed when exercising	Associated to multiple health benefits
	Regular exercise	Walking/stairs daily, gym on weekends	Mixture of weight training, cardio, and cold-shock therapy	Associated to multiple health benefits
	Toxin/radiation avoidance	N/A	Specifically: non-smoker, avoid UV, X-rays, CT scans, certain plastics	Reduces DNA damage
	Cold exposure	Keep cool daily, nightly	N/A	Hormetic effect
	Maintain BMI	N/A	N/A	Ideal to maintain optimal healthspan

* Typically prescribed, possibly replaceable with over-the-counter Berberine for which studies demonstrate comparable hypoglycemic effects at similar dosages [23]. Note: Sinclair mentions a phlebotomist visit every few months to have his blood drawn and evaluated for several dozen biomarkers to inform adjustments to his diet and exercise.

of NAD$^+$ or its precursors can not only slow the progression of aging, but ultimately reverse it based on experiments in mice. Since sirtuins are activated when in a calorie-restricted state, boosting sirtuin activity through the consumption of an NAD$^+$ precursor, in theory, should provide health benefits without the necessary starvation. Moreover, Sinclair claims that, at a high level, the maintenance of one's epigenome will prevent or delay the onset of many of the most common diseases and causes of death among the geriatric populations (*e.g.* heart disease, diabetes, cancer, *etc.*), thereby extending individual healthspans.

Evidently, a supplement-based anti-aging approach accompanied by minimal commitment to exercise and dietary changes is attractive among the immortality-DIYers and broader public, alike. While the concept of translating senescence-reversing laboratory research into an actionable regimen that enables individuals to mitigate their own aging is certainly widely attractive, a number of weaknesses in the ITA-based regiment must first be addressed.

Hasty generalization from studies in model organisms

Ground-breaking medical research is conducted using model organisms for which genetic makeup and environmental factors are tightly controlled; a reality in stark contrast to the genetic diversity and chaotic environments of *Homo sapiens.* Sinclair himself acknowledges that all aging-related therapies lack the rigorous long-term clinical studies required to understand the breadth of possible health outcomes. Nonetheless, Sinclair claims that the imminence of death justifies this hasty, and possibly detrimental, generalization; ironically echoing a view shared by Qin Shi Huang Di and history's prematurely demised alchemists who pursued the elixir of life.

"N=1" study of regimen efficacy

While many of the sirtuin activating compounds depicted in Figure 3 are undergoing human clinical trials, the anecdotal evidence in support of Sinclair's regimen is derived from a form of "N=1" self-experimental study, where the efficacy of his regimen is concluded from his claimed rejuvenated youthfulness. Ignoring the numerous confounding factors introduced from other longevity-related interventions (*e.g.* intermittent fasting, regular exercise, temperature regulation), an anecdotal, uncontrolled, and possibly biased account of improved healthspan violates the scientific method. Furthermore, the ITA itself focuses on conserving epigenetic health (one hallmark) to prevent a detrimental biological cascade, however the Sinclair regimen incorporates a number of interventions derived from research focused on other aging hallmarks. While the regimen itself is not an explicit test of the ITA, it would be fallacious to attribute its successes solely upon the ITA-based interventions [24].

Commercial conflicts of interest

Finally, Sinclair is integrally involved in the commercial development of therapeutics based upon his research. While several of his affiliated companies are still active, a number of them have terminated for a variety of reasons. His laboratory webpage reports these affiliations [25] and the industry connections which have been disclosed to the National Institute of Health are highlighted in Table 2. As a biotech entrepreneur, Sinclair's extensive commercial involvement presents a two-sided coin: on the one hand, Sinclair's faith in his research justifies significant investment in the pursuit of therapies that hold the potential to dramatically improve the

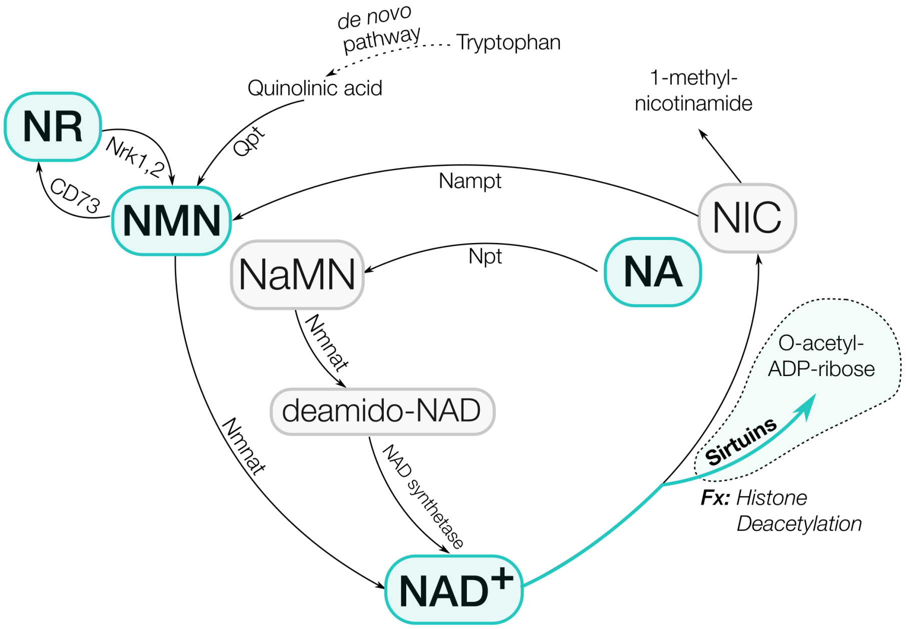

Figure 3 | The NAD+ biosynthetic pathway emphasizing the consumable molecules in support of Sinclair's regimen. The green molecules represent over-the-counter, commercially available molecules in the form of supplements aimed at increasing the production of NAD+ to promote sirtuin histone deacetylation activity. This activity helps to preserve the epigenomic health of an individual and may result in an increased healthspan, as purported by ITA. Abbreviations: NMN, nicotinamide mononucleotide; NR, nicotinamide riboside; NA, nicotinic acid; NAD+, nicotinamide adenine dinucleotide; NaMN, nicotinic acid mononucleotide; NIC, nicotinamide. Adapted from [24].

Table 1 | Sinclair's ProPublica Reported Conflicts of Interest to the NIH.

Company	Brief Description	Affiliation(s)
OvaScience	Biotechnology company focused on female infertility, based on Jonathan Tilly's research on mammalian oogonial stem cells Sinclair's work on mitochondria.	I
Cohbar, Inc.	Development of mitochondrial-based therapeutics to treat age-related diseases.	F,E,A
Life Biosciences	Parent company for eight daughter companies, each developing commercial solutions for one of the hallmarks of aging (excl. Deregulated Nutrient Sensing).	F,I,E,A,B,IP
Senolytic Therapeutics	Life Biosciences company focusing on the cellular senescence hallmark of aging by developing senolytics: small molecules targeting and inducing death in senescent cells to improve human health.	F,I,E,A,B
Spotlight Biosciences Inc.	A Life Biosciences company developing proteomics services.	F,I,E,A,B,IP
GlaxoSmithKline (acq. Sirtris Pharmaceuticals)	Global healthcare organization that acquired Sirtris Pharmaceuticals, a biotech company co-founded by Sinclair to develop molecules targeting sirtuins.	A,IP
Jumpstart Fertility	Life Biosciences company focusing on restoring egg quality in women of advanced age or experiencing premature infertility.	F,I,E,A,B,IP
Jupiter Orphan Therapeutics	Develops a delivery system for a reformulated resveratrol to alleviate central nervous system symptoms associated with rare diseases and Alzheimer's.	E,A
Liberty Biosecurity	An EdenRoc company developing a variety of biosecurity-related health products based on discoveries in medical genomics.	F,I,E,A,B
Metrobiotech East/Midatlantic, LLC	An EdenRoc company developing NAD+ pharmaceuticals.	F,I,E,A,B

Affiliation Abbr. | F: Founder; I: Investor; E: Equity; A: Advisor/Consultant; B: Board of Directors; IP: Inventor on licensed patents; L: Funding for laboratory

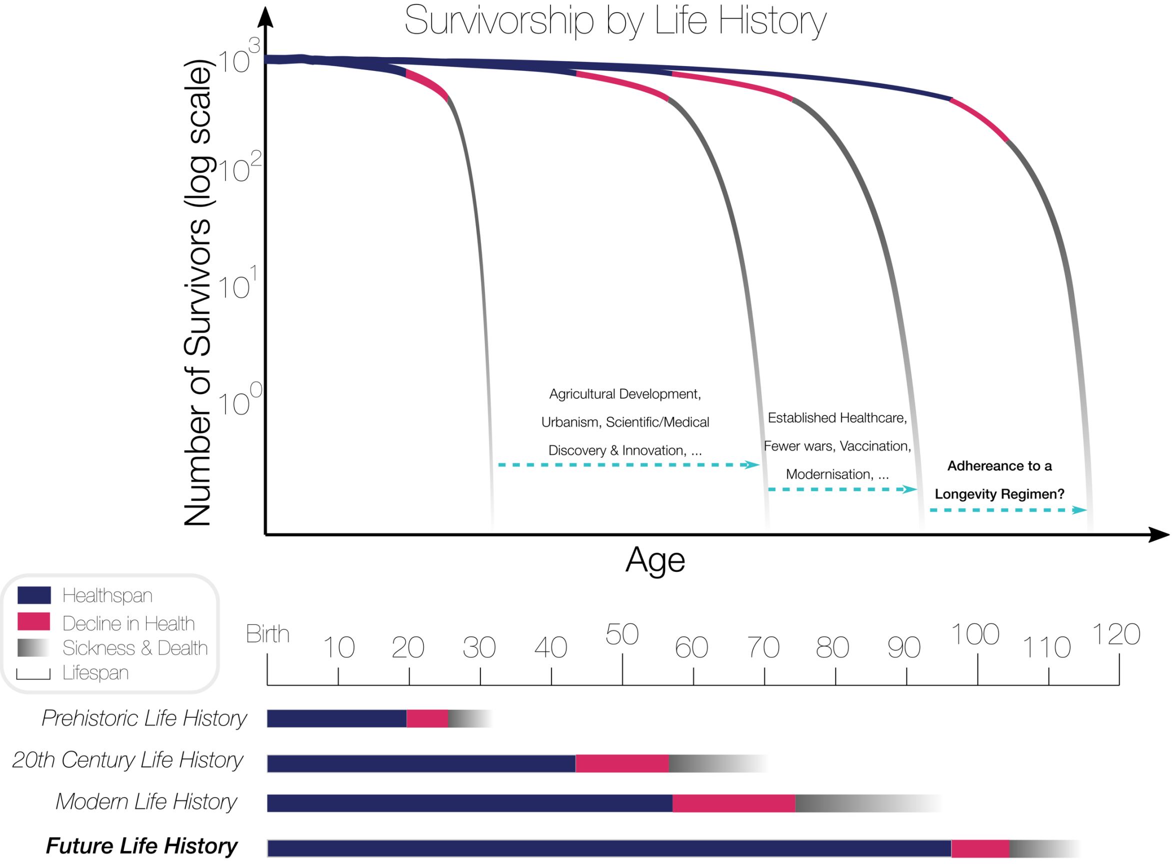

Figure 4 | Simulated survivorship curves for various stages of human life histories.

lives of millions of people; conversely, these commercial interests represent potential biases that challenge the objectivity of the scientific foundation of these studies. While these conflicts of interest themselves are commonplace in the field of biotechnology and are not a weakness of the presented work, the mitigation of potential biases requires rigorous experimental methodology, complete transparency, evidence of reproducibility, and continued disclosure of commercial conflicts of interest.

Contemplated at a high level and ignoring the minutiae, we can theorize whether or not a drastic (or even modest) extension to human lifespan is theoretically possible. Historically, *Homo sapiens* have seen a gradual increase in average life expectancy over the past centuries due to a mixture of technological, social, scientific, and medical innovations. As large mammals, humans exhibit a Type I survivorship curve, characterized by a long lifetime with a low death rate and high survivorship rate, followed by a dramatic increase in death rate. Figure 4 illustrates this concept and highlights the various developments that resulted in considerably improved average life- and healthspans of human populations at various stages in history. However, to date, there is no definitive evidence that the *maximum* human lifespan has increased despite the increase in average lifespans. Sinclair posits that adherence to a longevity regimen that maintains one's epigenomic health will dramatically reduce or prevent the onset of major illnesses prevalent later in life, which ultimately leaves us with the question: do these lifespan increasing methods affect *aging* (*i.e.* achieve negligible senescence *in perpetuo*) or just lifespan (*i.e.* we endure longer with the same kind of "damage")?

Conclusions

In summary, there remains much to investigate and reconcile en route to a fully understood mechanism of aging and the development of efficacious and evidence-based life-extending regimens. A reflection of our shared history reveals dramatic increases in the average human life- and healthspans as a result of scientific innovations; we may now be at the cusp of the next. Much in the way that the development of vaccines eradicated diseases that plagued humanity prior to the 20th century, essentially eliminating diseases that killed the majority of the population, it is not inconceivable that anti-aging regimens might do the same for the major diseases of the present day, improving and extending millions of currently lived lives. Future generations may balk at the idea that humanity ever lived in ignorance of the resultant new limits on lifespan. Unlike the cessation of wars, breakthroughs in medicine, and the implementation of social innovations, this ability to dramatically affect one's own longevity resides with the individual; we have the power to contemplate this emergent research and choose to hack our way to immortality.

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Nutritional psychiatry: A solution for socioeconomic disparities in access to mental health care?

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Abstract:

As in all sectors of healthcare, socioeconomic status (SES) affects an individual's ability to benefit from psychiatric care. Mood and anxiety disorders are the most common mental illnesses for which psychiatric care is sought, and while there are options for effective treatments available, they often have accompanying costs. Further to costs, issues with the heterogeneity of mental illness have led resarchers to explore other options for psychiatric care. Nutritional psychiatry is an emerging field that uses dietary and nutritional approaches to target the gut-brain axis for the prevention and treatment of mental illness, including mood and anxiety disorders. Nutritional psychiatry has been promoted as being an advantageous alternative to classic mental health treatments due to its broader accessibility, given the lower costs associated with lifestyle changes than medication and psychotherapy. At a glance this may appear accurate, but upon closer examination, may not be entirely true. Factors surrounding healthy eating, food deserts, the supplement industry, and adherence to lifestyle changes are all barriers present in nutritional psychiatry that are accompanied by additional costs. These costs likely contribute to the disparity between low SES and high SES individuals benefitting from nutritional psychiatry approaches in a similar way to standard treatments. This commentary reviews these factors and suggests that while there are certainly benefits, nutritional psychiatry may not be the accessible treatment option it is purported to be. The importance of clinical researchers' awareness of these disparities in the field is also discussed.

It should come as no surprise that socioeconomic inequalities plague our healthcare system and prevent individuals with lower socioeconomic status (SES) from obtaining care. SES continues to affect health even once care is received by limiting the ability to benefit from treatment options. This includes mental health care, with access and costs of treatment being the primary barriers with which patients with mood and anxiety disorders struggle. Mood and anxiety disorders such as depression affect approximately 11% of Canadians and are the leading disorders for which people seek mental health care [1]. Standard options for the treatment of depression include antidepressant medication and/or psychotherapy. In Canada, antidepressant medication costs between $30 and $200 per month, and while some counselling and therapy can be provided at no cost within universities or other institutions, private psychotherapy costs between $50 and $220 per one-hour session. In most cases, these treatments require a prescription from a physician. While most provincial drug plans and formularies cover a portion of the cost for prescription drugs and psychotherapy, there are often outstanding costs still to be paid out of pocket such as dispensing fees.

Depression is a complex psychiatric disorder characterized by both psychological and physiological symptoms that impair daily functioning. Like most mental health disorders, it is highly heterogeneous; the etiology, pathophysiology, symptomatology, and response to treatment vary widely between patients [2]. This has made mood disorders difficult to treat using standard medication. For these reasons, other approaches for alleviating symptoms associated with mood disorders are being explored by researchers, several of which involve targeting the microbiota in the gut. The connection between the brain and the gut was established long ago, as early as the eighteenth century [3]. With recent advances in techniques and an increased appreciation for the depth of the connection, research on the relationship between the brain and the gut has broadened and is now termed the "gut-brain axis" [4].

The gut-brain axis can be targeted to help improve mental health by applying techniques from the field of nutritional psychiatry. Nutritional psychiatry is an emerging field studying how diet and nutrition may be used in the prevention and treatment of mental illness. Nutritional psychiatry can be broken down into three approaches: 1) using specific nutrient supplements, such as vitamins, polyunsaturated fatty acid supplements, and probiotic supplements; 2) consuming functional foods, or foods that are fortified in specific nutri-

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ents; and 3) altering whole dietary patterns. The nutrients we obtain through our diet and supplements alter our gut microbiome. These changes in our gut microbiome affect brain development and function via several interconnected biophysiological pathways encompassing the gut-brain axis, including the autonomic nervous system, the enteric nervous system, the neuroendocrine system, and the immune system [4]. This is true for both healthy and unhealthy eating behaviours. Nutritional psychiatry functions on an evidence-based premise of consuming foods and supplements that, through the gut-brain axis, aid in regulating neurotransmission critical for mood and anxiety regulation. Currently, research indicates that adhering to a Mediterranean-type diet, consisting of plenty of fresh produce, whole grains, lean proteins and healthy fats, may be effective in alleviating mental illness symptoms [5, 6]. Several specific nutrients such as probiotics are under investigation as potential standalone supplements as well [7]. These approaches remain in the exploratory stage and are not yet considered an approved treatment for mood and anxiety disorders, making the prevalence of their clinical application in the field unknown. However, the potential benefits they offer are numerous.

Nutritional psychiatry approaches may be preferential to standard treatments for alleviating mental illness symptoms for several reasons. These approaches do not carry the same stigma common to standard treatments, which often leads to poor treatment adherence. There is also lower risk of contraindications with other medications, making them safer and more tolerable options, and they may be more suitable for people who are reluctant to take medications. Further, they are not accompanied by distressing side effects. In fact, the beneficial effects of nutritional psychiatry approaches may indeed extend into other aspects of physical health and lead to the adoption of further health behaviours.

Given the socioeconomic barriers to standard mental health care, perhaps one of the most appealing aspects of nutritional psychiatry is the idea that anyone, regardless of SES, can reap its benefits. Targeting the gut-brain axis using nutritional psychiatry approaches has been promoted as being a more accessible alternative to standard treatments for mental health disorders, such as medication and psychotherapy. To make nutritional psychiatry-based lifestyle changes, it is not essential to see a specialist or even a general practitioner, nor budget for prescription or therapy costs. Thus, ostensibly there should be no socioeconomic disparity in using nutritional psychiatry approaches to alleviate depressive symptoms. However, this is not invariably true, and this caveat requires serious consideration as nutritional psychiatry becomes increasingly mainstream. While nutritional psychiatry undoubtedly has its benefits, accessibility may not be one of them. There exist several significant socioeconomic barriers to having nutritional psychiatry approaches universally accessible. First, a significant financial investment is required for healthy eating. Second, there is a distinct lack of availability of healthy food in many geographical areas. Third, the supplement industry has driven up costs in response to popular culture trends. Finally, adherence to lifestyle changes such as diet is notoriously difficult. These barriers will be reviewed here and discussed in the context of how nutritional psychiatry does indeed have many benefits, but universal accessibility may not be one of them.

Eating healthy is expensive

While there is no precise definition of a ‘healthy diet’, dieticians generally recommend dietary patterns that include a variety of fresh fruits and vegetables, whole grains, lean proteins, and healthy fats. This is consistent with what is being studied and appears promising for mental health [5, 6]. A 2013 meta-analysis that critically evaluated data from studies across 10 countries found that consuming these healthier foods costs approximately US$1.50 more per person per day than eating an unhealthy diet [8]. The costs for basic healthy foods are not the only things that are more expensive: functional foods, or foods that are fortified in a given nutrient are often pricier as well. These costs add up quickly, and grocery stores do not accept prescriptions for healthy eating, nor is there insurance coverage for a filet of salmon and a bundle of kale. To make things worse, these healthy choices are often not only out of reach financially, but geographically as well.

Food deserts persist

Food deserts are geographical areas with limited access to fresh, healthy foods. This is due to a lack of supermarkets that offer a larger variety of affordable, healthy, and better-quality foods compared to smaller convenience stores that stock more expensive and less healthy prepackaged foods or fast-food chains [9]. Food deserts are also often located in low-SES areas [9]. This is seen most notably and on a large-scale in Northern Canada where there is very limited fresh food supply, and what is available has been documented as being up to 81% more expensive than the rest of the country [10]. To access healthy foods, those who live in food deserts must have access to a vehicle or pay for public transportation. Since people tend to make food choices based on availability, this leads to individuals in food deserts consuming more unhealthy foods [11], or having to spend more money travelling to access healthier foods. This further adds to the disparity of being able to access nutritional psychiatry-based mental health care approaches. When considering alternatives, longer-lasting and shelf-stable nutritional supplements that may replace vital nutrients are unfortunately not a viable option due to their own drawbacks.

The supplement world is designed to make a profit

The supplement industry is an ever-growing multi-billion-dollar industry. Nutritional supplements are undeniably effective in the case of a deficiency, such as iron supplements for anemia, or when additional supplementation is required, like folic acid during pregnancy to support the growing fetus

[12]. However, despite recent evidence suggesting that nutritional supplements like a multivitamin have no added benefit for those who are otherwise healthy [13], the supplement industry has grown as a result of rising popularity in 'wellness culture'. Wellness culture is an industry with good intentions of achieving overall physical, emotional, spiritual, intellectual, and social wellbeing, but one which is plagued by pseudoscience and is driven by profits. A cornerstone of 'wellness culture' is the use of nutritional supplements. It has driven up the cost of supplements, including vitamins, botanicals, minerals, proteins and amino acids, fibers, and specialty carbohydrates, polyunsaturated fatty acids, and more, making it expensive and less accessible to purchase these over-the-counter supplements.

Diet is a hard habit to change

Nutritional psychiatry approaches are largely based on lifestyle modification. While this may seem like a more viable option than taking a daily medication or attending therapy sessions, maintaining dietary habits is notoriously one of the most difficult lifestyle changes to adhere to. Rates of non-adherence to chronic illness treatments can be as high as 80%, with up to 60% of patients prematurely abandoning healthy behaviour changes [14]. Individuals who use a diet regimen for a specific health issue, whether it be physical or mental or both, will need to be rigorous with their adherence to get the desired outcome. This may require added expenses: regular follow-up appointments with a healthcare professional, habit-tracking apps on a smartphone, or support groups, to name a few. These additional financial commitments may not be possible for those with low SES.

Given the factors considered above, SES may indeed affect individuals' access to nutritional psychiatry-based approaches just as much as their access to classic treatments for mental illness, limiting their ability to benefit from these approaches. Nutritional psychiatry offers many advantages, and while these approaches are not yet considered an approved and prescribable course of treatment, research continues to advance in this direction. Clinical studies are currently underway examining both the effectiveness of this proposed new approach as well as strategies for treatment. These clinical studies will inform us on how to proceed with the best course of action for intervention, but clinical researchers must also be cognizant of the socioeconomic impact of these interventions. Should the research support nutritional psychiatry as an evidence-based treatment option for mental illness, informed researchers can then help to make recommendations to policy makers for nutritional psychiatry strategies that will reduce associated costs. This will allow those across the socioeconomic spectrum to have equal opportunity to choose a nutritional psychiatry approach to alleviate their symptoms and be able to equally reap the benefits of this proposed new approach to mental health care.

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Exploring obesity through diet-gene interactions

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Abstract:

The increasing prevalence of obesity is becoming a global health concern due to its association with chronic diseases including type 2 diabetes, non-alcoholic fatty liver disease, and cardiovascular diseases. Obesity occurs when energy intake outweighs energy expenditure, leading to a conventional intervention strategy being "eat less and move more." However, this strategy does not consider the influence of genetic factors and their interactions with environmental factors (diets and physical activity), making obesity prevention and management inefficient. To better understand obesity, research in nutrigenetics and nutrigenomics seek to explore the influence of genetic variations on dietary responses, and how dietary components alter gene expression in obese individuals. Current evidence suggests that variations in genes involved in lipid regulation, carbohydrate metabolism, and energy homeostasis are strongly associated with the risk of obesity and its related metabolic syndromes. In addition, diet-gene interactions influence intervention effectiveness for obesity management. By examining obesity-related metabolic pathways, we can reveal the functional basis of diet-gene interactions in relation to obesity risk. Although limitations exist within the current literature, emerging evidence indicates that obesity risk and intervention can be affected by diet-gene interactions, and continued research is needed for further exploration.

Obesity is a trending global health concern that affects over 35% of the world population, and 60% of adults in Canada [1, 2]. Obesity is more than just excessive fat in our body; it is a medical condition that contributes to the development of chronic diseases including type 2 diabetes, non-alcoholic fatty liver disease (NAFLD), cardiovascular diseases, and some cancers [3]. Most pressingly, emerging evidence revealed that obese individuals faced increased risk of intensive care admission for SARS-CoV-2 infection (commonly known as COVID-19) [4, 5], implicating obesity as a potential risk factor in COVID-19 severity that requires increased clinical attention. The cause of obesity has been well-recognized as a long-term unbalanced energy status in our body, which means higher energy intake coupled with lower energy expenditure for an extended period of time [6]. The old adage "you are what you eat" highlights the role that one's diet plays in preventing disease and improving overall health. Therefore, conventional population-based intervention strategies used to combat obesity often include reduction and modification of food/energy intake (e.g. caloric restriction, low-fat/low-sugar diet, etc.) [7]. However, the number of obese individuals around the world per year continues to increase, especially amongst children and young adults [1], indicating the lack of effective interventions for the prevention and management of obesity. With increasing awareness of individual differences, we now realize this conventional "one size fits all" strategy to weight reduction does not always work [8, 9]. The reason behind an unbalanced energy status is more complicated than "eating too much and moving too little." Past studies have recognized that people respond differently to certain foods [10], thus researchers are now attempting to tailor dietary components to a person's genetic profile for a better understanding of individual differences in obesity, promising a personalized intervention strategy for obesity management [11].

The ongoing research exploring the interactions between genome and diet are termed nutrigenetics and nutrigenomics. Nutrigenetics aims to identify and characterize gene variants associated with differential responses to diets, whereas nutrigenomics aims to determine the influence of dietary ingredients on changes to gene expression and cellular response in biological systems [11, 12]. Evidence from current studies suggest that interactions between one's genetic makeup and environmental factors (diets and physical activity) play more important roles than environmental factors alone [11, 13, 14]. The most well-studied example showing the significance of the diet-gene interaction is caffeine consumption. Nutrigenetics studies revealed that the individual differences in response to caffeine consumption are caused by genetic variations in the *CYP1A2* gene. This gene encodes the enzyme CYP1A2 which metabolizes over 95% of caffeine in our

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body [15]. Variations in the *CYP1A2* gene can alter CYP1A2 enzyme activity, leading to a "faster" or "slower" metabolism of caffeine amongst individuals [15]. Recently, more studies have applied the same research strategy from studying caffeine-gene interactions to explore diet-gene interactions in obesity and its associated chronic diseases [14]. With an increased appreciation for precision medicine (personalizing drugs and therapies to a patient's genetic profile) in recent years [16], and the emerging link between diet-gene interactions and obesity, current research now seeks to answer the following questions: why are some individuals more susceptible to obesity-related risk factors, while others are not? Why do individuals respond differently to the same dietary intervention? And how big of a role do diet-gene interactions play in obesity and its associated diseases? Various scientific approaches have been applied to this field including clinical research, molecular biology, genetics, and bioinformatics, to help obtain a comprehensive understanding of both nutrigenetics and nutrigenomics perspectives[14, 17].

A nutrigenetic persepctive: how genetic variations affect dietary responses involved in obesity

Genetic variation is the difference in DNA sequences between individuals within a population [18]. Major advances in genome sequencing techniques and the formation of large global collaborative networks (e.g. Genome-Wide Association study and the International HapMap Project) have led to the comprehensive knowledge of genetic variations in the human genome [18, 19]. Interestingly, genetic variation between individuals are minimal. Despite the fact that 99% of our genetic makeup is identical, the remaining 1% of genetic variation leads to large variability in health outcomes [20]. Common forms of genetic variation include single nucleotide polymorphisms (SNPs: substitution mutation in a single nucleotide) and copy number variations (CNVs: change in gene copy-number) [18]. In recent studies, several SNPs have been found to be corelated with obesity risk or its associated metabolic syndromes through interactions with dietary intake [21-24]. For example, a three-year study of 479 men and women in Finland revealed that a SNP in the fat mass and obesity associated (*FTO*) gene is associated with higher body mass index (BMI) in individuals consuming a high fat diet [21]. Likewise, another study found that SNPs in the *FTO* gene are associated with an increased risk of obesity amongst Asian-Indian individuals with high-carbohydrate diets [22]. Moreover, when consuming a Western diet high in refined grain products, sweets, and processed meats, individuals with certain genetic variations in *APOC3, APOC1* (encoding lipid-binding proteins for lipid transportation), and *MC4R* (encoding a key regulator for energy homeostasis) showed a higher risk of developing obesity-related metabolic syndromes [23, 24]. In addition to SNPs, studies on CVNs also found a significant association between low copy numbers of the salivary amylase gene (*AMY1*) and increased BMI and obesity, indicating a genetic link between carbohydrate metabolism and obesity risk [25].

SNP-diet interactions have also been investigated in differential responses to dietary interventions. An early study conducted in 1990 set a milestone in the field. 12 pairs of sedentary monozygotic (identical) male twins between the ages of 19 and 27 were overfed by 1,000 kcal/day for 6 days a week for a total of 84 days during a 100-day period. At the end of the study, researchers found that overall weight gain was three times more similar amongst twin pairs than between non-twins [26]. This indicates a critical role for genetic factors in dietary intervention. Recent studies found that several SNP-diet interactions were also associated with different responses in weight loss, insulin resistance, and serum lipid levels. Notably, high protein diet interventions induced greater weight loss in individuals with SNPs in *FTO*, and less weight loss in women with SNPs in *MTNR1B*, which encodes a receptor for melatonin [27, 28]. These nutrigenetics studies provide evidence that genetic variation is associated with obesity risk and dietary intervention, suggesting that individual genetic differences interact with dietary factors and can result in different responses to obesity management.

A nutrigenomic perspective: how diets/nutrients change gene expressions involved in obesity

In contrast to nutrigenetics studies, nutrigenomics studies provide evidence that diet and/or nutrients have direct impact on gene expression and metabolic pathways involved in obesity and its related metabolic syndromes, leading to differences in health risk [29-33]. For example, diets high in fat and sugar increase the expression of *LEP, SREBF1*, and *PLIN* (genes encoding regulators for lipid synthesis and uptake), resulting in an increased risk of obesity [29]. High saturated fatty acids have also been shown to induce obesity and inflammation through increased expression of proinflammatory cytokines such as *TNF* and *IL6* [30]. Diets deficient in choline and folate have also been associated with increased risk of non-alcoholic fatty liver disease (NAFLD) through the dysregulation of genes involved in lipid metabolism, such as *APOE, FOXA1,* and *PPARGA* [31, 32]. On the contrary, studies have also suggested that some dietary components have beneficial effects on obesity management through the regulation of gene expression. For example, diets high in polyunsaturated fatty acid (PUFA) modulate the expression of genes involved in energy balance, such as *POMC* and *GALP*, and lead to obesity prevention [33]. Moreover, apple polyphenols were found to reduce the risk of obesity by modulating the expression of lipid metabolic genes: decreasing the expression of *LEP, SREBP1* and *PLIN*, and increasing the expression of *PPARGC1A* and *AQP7* [29]. Results from nutrigenomics studies indicate that different dietary components can differentially affect obesity management through modulating the expression of genes involved in obesity-related metabolic pathways, providing insights into the functional basis and causal relationships involved in diet-gene interactions in obesity.

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Limitations and future directions

Despite emerging evidence in recent years that suggest diet-gene interactions have significant impact on obesity and its related metabolic diseases, gaps and limitations in the knowledge still exist. Given that approximately 700 SNPs have been found to be directly or indirectly associated with obesity [34], and that the field of nutrigenetics is relatively new, there is little replicated evidence to show the relationship between obesity-related genetic variations and diet [35, 36]. The only exception is the *FTO* gene [36]. Since the first genetic variation associated with obesity risk was found in *FTO* in 2007 [37, 38], a wide range of replicated studies have emerged [35, 36]. However, controversial results exist among them. Some studies found a strong association between *FTO*-diet interactions and obesity risk [21, 22, 27], whereas some found no significant associations [39, 40]. The opposing conclusions may be explained by differences in study settings and sample populations. Some studies [39, 40] were cross-sectional and had long-term lifestyle exposures, whereas other studies [21, 22, 27] were prospective with a relatively short intervention time. Additionally, different populations with varying samples sizes were used in different studies, which may cause bias and influence whether interaction effects could be readily detected [36]. Therefore, more studies with refined standardization are needed to verify and extend the current evidence. While nutrigenetics studies provide association-based evidence between diet-gene interactions and obesity risk, further exploration into the functional basis of diet-gene interactions and causal relationships is needed because association-based evidence alone is not sufficient to support a clinical decision [41]. Ultimately, more nutrigenomics research on mechanisms of actions is needed to support the evidence coming from nutrigenetic studies.

In addition to the limitations of current nutrigenetics/nutrigenomics studies, limited evidence has also been found regarding psychological issues raised by genotype-based intervention strategies. The success of personalized dietary intervention largely depends on whether individuals consider genetic testing results as a destined fate or a motivation for lifestyle changes [42]. One study showed that individuals who received genetic testing results were more likely to respond to dietary recommendations than those without genetic testing [43], whereas another study found no changes in lifestyle behaviors following a genetic test result [44]. These contradictory conclusions highlight the need for greater investigation into psychological aspects that shape the acceptance of, and adherence to, genetic-based intervention strategies for obesity management.

In conclusion, emerging evidence from current studies indicate that the diet-gene interaction plays a role in obesity risk and dietary intervention outcomes. The old adage "you are what you eat" is still a golden rule when it comes to health improvement and disease prevention, especially obesity management. However, with increasing awareness of individual differences and a rapid expansion of nutrigenetics and nutrigenomics research [8, 9, 11], the health determinant focus is shifting from "you are what you *eat*" to "you are what *you* eat." Despite the existence of inconsistent conclusions and the need for greater mechanistic studies to support current evidence, the rationale behind exploring obesity through diet-gene interactions remains strong and continues to motivate research in this field [11, 36, 41].

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Assessing the efficacy of Canada's food guide and the barriers of use

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Abstract:

The landscape of nutrition advice is vast and full of misinformation. A primary source of nutrition advice in Canada comes from the Canadian Food Guide, however, many questions remain regarding the reach and accessibility of the food guide. Specifically, is the population most likely to receive and use this information, the population that needs it the most? Are there barriers to following this guide that Health Canada has failed to address? Is there evidence supporting the efficacy of this food guide in populations at risk for nutrition misinformation or diet-related preventable diseases? This commentary reviews the past research regarding efficacy of previous food guides and highlights potential barriers preventing equal and accessible use of Canada's Food Guide.

Dietary guidelines as a primary source of nutrition information

The landscape of nutritional advice is vast and full of misinformation. For example, celebrity Gwyneth Paltrow's Netflix show "The Goop Lab" claims to provide scientifically backed advice on topics including fasting and veganism, but researchers and medical professionals have debunked many of their health claims [1]. Gwyneth's show is one among many other media outlets criticized for spreading misinformation, specifically in the area of nutritional advice [2,3]. Nutritional advice is abundant in internet blogs, lifestyle magazines, and from celebrities and self-claimed social media 'health experts,' many of whom do not have an equal standard of nutrition accreditation [2–4]. One study found that 54% of health information given out on social networking sites contained inaccurate content [5]. This spread of misinformation contributes to the increasing public confusion regarding nutritional eating choices, which can negatively impact perceptions or behaviours [6].

Globally, governments play a large role in regulating public health through nutritional recommendations in the form of food guides. Canada's Food Guides are created with expert input from dieticians, public health nurses, teachers, and physical activity specialists, and may help to counter the spread of misinformation by providing evidence-backed and fact-checked information [7]. Health Canada released the new, long-awaited Canada's Food Guide in March 2019, 12 years after the previous version was released in 2007. The new Food Guide adopts a plate-centric style, which includes sections on a plate of various food groups to represent qualitative intake proportions, and veers away from the past numeric formats where certain food groups were allotted a specific number of servings to have per day [8]. In addition to providing a variety of food options, the new Food Guide includes qualitative advice on how to eat across different life stages, and behavioural advice for healthy eating habits (i.e. eating with others). This supplementary information supports the idea that nutrition and healthy eating are not black and white concepts that require strict rules to follow.

Efficacy and reach of Canada's food guide

Canada's Food Guide is diligently backed up with reliable research, however, there is a lack of knowledge regarding the efficacy of its use or the use of government-backed nutritional guidelines in general. More specifically, is the population most likely to receive and use this information the population that needs it the most? Are there barriers to following this guide that Health Canada has failed to address? Is there evidence supporting the efficacy of this Food Guide in populations at risk for nutrition misinformation or diet-related preventable diseases such as diabetes? Although most of the research presented herein was conducted before the release of the current Food Guide, the reach and use of past Canadian Food Guides can be used to predict the efficacy of the current guide.

Data from the 2012 Canadian Community Health (CCH) survey revealed that while most Canadians were aware of the Food Guide, less than one-third of respondents had a copy in their homes, of which most were women. Out

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of the sources used for healthy eating information, ~50% of respondents selected “no sources,” followed by ~20% for both “general research,” “family and friends,” and a mere 8.7% said they consult the Food Guide [9].

Preliminary data from a new survey (n=1017) conducted by Dalhousie University and the University of Guelph revealed that 52% of Canadians face barriers to adopting the new Food Guide [10]. More than 25% of respondents cited that the new Food Guide would not be affordable to adopt, but calculations showed that on average, a family of four would save 6.8% more if they adopted the new Food Guide. However, with the push to increase fruit and vegetable consumption, the demand in produce over the next few years may increase which could in turn reduce the affordability of the Food Guide if fruit and vegetable prices were to spike [10].

Similar to the 2012 CCH survey, participants placed the Food Guide 6th for sources of healthy eating advice, behind family and friends, general research, social media, cookbooks and magazines, and TV programs, and less than 30% of Canadians had viewed the 2007 Food Guide in the past 12 months [10]. The lack of use in that year highlights the minimal impact the guide had on Canadian food choices. Detailed participant demographics were not revealed, except that they were above 18 years old and had lived in Canada for more than 12 months. Therefore, we cannot be confident the sample population represents the variety of ethnic and socioeconomic backgrounds present in Canada.

Research has shown that socioeconomic status (SES) is a predictor of diet quality [11,12]. SES is a measure of social status or class, and is often calculated as a combination of education, income, and occupation. With this is mind, it is speculative to state that lack of awareness, education, and use of national food guides is a potential contributor to low diet quality in those with a lower SES. Geographical barriers are also a large issue to people with low SES; in the United States, there are typically fewer chain grocery and more convenient stores in lower SES areas as well as in predominantly African American neighbourhoods in comparison to Caucasian and high SES ones [12]. There is also an intersection of low SES and racial minorities in certain geographic locations, and this may further contribute to the reduced chain-grocery store abundance in both these areas [13]. Poor access to supermarkets and an ensuing dominance of convenience stores with mainly energy dense and nutrient lacking foods is an inevitable set-up for poor adherence to nutritional guidelines [14]. If barriers are not removed to allow for healthy food choices, then a national food guide cannot confidently expect to impact the population that may benefit from these recommendations the most.

Notable advancements and future directions

Arguably, the government’s simplified plate approach, with no quantitative food recommendations, is flexible and adaptable. Individuals can swap the marketed fresh fruits and vegetables with frozen counterparts, instead of using canned forms, which often contain excess sugar or salt. The Food Guide also contains over 30 diverse recipes, posted on the online Canada’s Food Guide website, from a variety of cuisines that are in line with the recommendations. Perhaps these recipes could have alternate instructions on how to prepare using frozen, canned, or dried ingredients to increase accessibility for the variety of SES backgrounds.

Healthy eating is just as important for ones’ mental health as it is for physical health, and arguably one’s psychological attitude towards food (e.g. having anxiety towards eating) can impact their food choices [15]. There are associations linking a diet high in refined sugars with increased mental illness symptoms, further backing the need to address the psychological factor of healthy eating [16,17]. The emphasis on food behaviours including “eating with others” or “cook your own meals” is an acknowledgeable component of the new food guide and highlights the psychological component of healthy eating. A statement from the Community Food Centres Canada described this guidance as “a critical step forward is the inclusion of advice not only on what we eat but how we eat – cooking more at home, enjoying food, and eating with others – which, taken together, encourage a more communal and healthful approach to eating.” [18]. These behavioural changes in eating habits may be more easily implemented irrespective of SES and cultural background.

The efforts of the government should not go unnoticed and the 2019 Food Guide is a move in the right direction. In order to maintain a level of inclusivity expected from such a governing body, we need evidence-based research concerning the use and accessibility for people of lower SES and various cultures. The past studies conducted on the use of the 2007 food guide should be repeated with the new food guide to assess whether the food guide itself or it’s updated marketing tactics (i.e. advertisements on social media) can influence consumer use. Additionally, there needs to be organized programs in place to increase nutrition awareness and educate on reliable sources for nutrition information, as well as resources on how to use the guide on a budget. Future research should aim to address if the past or current Food Guide has been associated with beneficial health effects such as reducing type 2 diabetes incidence across Canada and if there is potential benefit of increased food guide marketing to at-risk populations. Canada’s Food Guide has the potential to play an important role in the lives of Canadians but there is more work to be done to ensure optimal use and its role in countering the spread of nutrition misinformation.

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