



RIPPLE EFFECTS

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Addressing the
Needs of Pregnant
Individuals During
the COVID-19
Pandemic

Indirect Effects
of the COVID-19
Pandemic on
Reproductive
Health

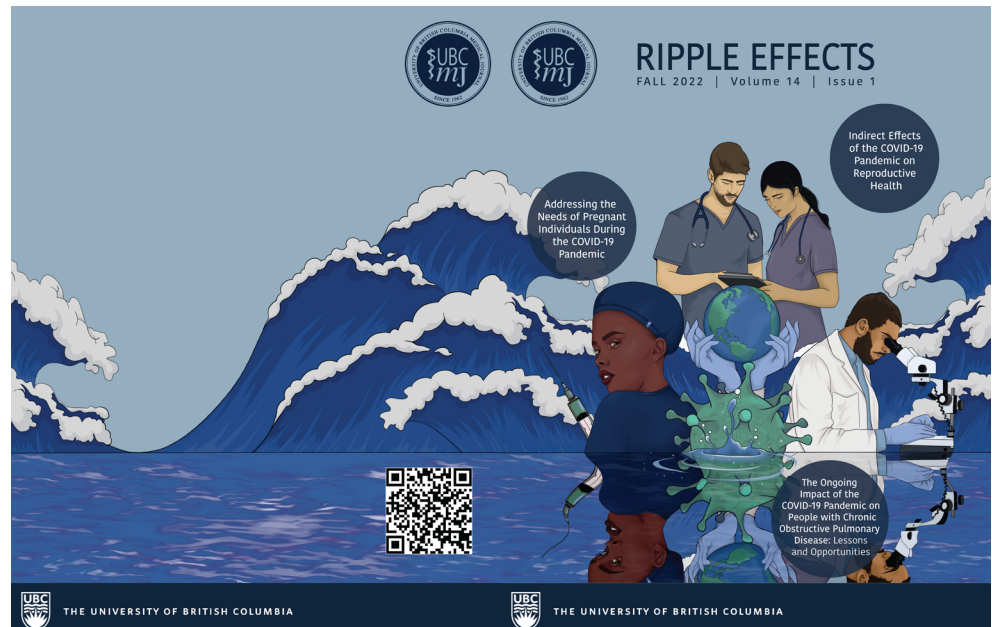
The Ongoing
Impact of the
COVID-19 Pandemic on
People with Chronic
Obstructive Pulmonary
Disease: Lessons
and Opportunities



THE UNIVERSITY OF BRITISH COLUMBIA

The University of British Columbia Medical Journal (UBCMJ) is a peer-reviewed, student-driven academic journal with the goal of engaging students in medical dialogue and contributing meaningful discourse to the scientific community.

On the cover



In this issue, we explore the ripple effects of the ongoing COVID-19 pandemic. Several entries in this issue investigate newly arising challenges due to COVID-19-related effects on our healthcare system. The cover art for this issue reflects the genesis and propagation of these challenges through the metaphor of a raindrop falling into water, with SARS-CoV-2 at its epicentre. As society gradually transitions back to pre-pandemic conditions, this issue serves to remind that COVID-19-related challenges are certain to last.

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Ripple effects

Brendan Tao¹, Chia-Chen Tsai¹

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Since March of 2020, the coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) has disrupted the functions of society to unprecedented levels. For many, the transition to a “new normal” under pandemic restrictions continues to wreak havoc in every sector of our lives, with those facing systemic barriers often bearing the heaviest burden. Now over two and a half years into the pandemic, it may feel as though the end is drawing near with recent relaxations to COVID-19 restrictions in British Columbia (BC). Yet due to the immense stresses inflicted on our healthcare system, the ripple effects of the pandemic continue to generate new challenges. In this editorial, we discuss a select few of these ripple effects to contribute to the ongoing dialogue of managing these novel society-level stressors. Although there is some end in sight, there is no better time than the present for proactive intervention.

One pandemic ripple effect is the growing prevalence of “long COVID”, otherwise known as “long haulers” or “post COVID syndrome”, following acute COVID-19 infection. As of August 6th, 2022, there have been over 4.1 million confirmed COVID-19 cases in Canada.¹ However, when accounting for cases unconfirmed by testing, the Institute for Health Metrics and Evaluation estimates that 65% of Canadians have been infected at least once as of July 11th 2022.² Thus, this substantial group of Canadians stand risk of developing “long COVID”. Long COVID describes the persistence of symptoms from acute infection and/or the development of novel symptoms that last weeks to months.³ A recent review reports that approximately 35% of COVID-19 patients treated in outpatient settings retain residual symptoms following an acute infection, with the prevalence among hospitalized patients reaching about 87%.³ According to a systematic review and meta-analysis, the most prevalent symptoms after at least 12 months of follow-up include fatigue (28% of patients), dyspnea (18%), arthromyalgia (26%), depression and anxiety (23% and 22%, respectively), and memory and concentration difficulties (19% and 18%, respectively).⁴ Other evidence from severe cases implicate additional damage to other organ systems.⁵ The pathophysiology of long COVID is still under investigation but is hypothesized to involve consequences of concerted viral infection and autoimmune or inflammatory responses.⁵ While anyone with previous infection is susceptible to long COVID, current evidence suggests that female sex, older age, severe acute infection, obesity, and healthcare worker status are additional risk factors for developing long haul symptoms.⁶ Of additional concern are the ripple effects of long haul symptoms, which correspond to hindrances in people’s social lives and return to work. These impedances can negatively impact patients’ mental health and confer substantial economic ramifications extending all the way to the societal level.⁶ Preliminary evidence is beginning to implicate long COVID symptoms with reduced economic productivity. Reductions in labour supply constitute one economic outcome of long COVID, with one American survey reporting that 44% of respondents with long COVID exited the

labour force while 51% worked fewer hours.^{5,7} As it stands, long COVID is a lasting ripple effect of the COVID-19 pandemic, and despite active investigations into this condition, it is too early to fully understand its long-term health and economic outlooks.³

Since the pandemic’s onset, the Canadian healthcare system has strained to accommodate a substantial volume of patients presenting with acute COVID-19 infection. Yet this rapid rise in case volume is expected to elicit a lasting and rippling effect on healthcare accessibility for the foreseeable future.⁸ During the COVID-19 outbreak, healthcare workers had already expressed overwhelming sentiments of burnout, with reports of between 25% to 44% of healthcare workers experiencing at least one of following: anxiety, depression, and sleep disorders.⁹ One Canadian report describes the rate of burnout as being as high as three in four physicians.¹⁰ These figures are not helped by the perceived stigma and career threat against healthcare workers who show signs of burnout. Indirectly, the cumulative effects of burnout can lead to clinicians’ poorer communication and adherence to guidelines, thereby increasing the potential for lower quality care and compromised patient safety.⁹ To date, across Canada, pandemic-induced stresses on healthcare workers have elicited a resultant staffing shortage, at least in part, due to insufficient work incentives coupled with an exodus of burnt out practitioners from the labour force.^{10,11} Given these dire circumstances, healthcare accessibility will remain a troubling issue for Canadians.

Another pandemic ripple effect involves the substantial buildup of unmet healthcare needs that now face an already strained healthcare workforce. As a result of efforts to mitigate short-term infection spread, jurisdictions across Canada transiently decreased the performance of non-emergent and elective treatments. For instance, in 2020, the surgical backlog in Ontario was estimated to be 148,364 surgeries, requiring an average increase of 11 413 surgeries per week to satisfy this unmet need.¹² Treatments may also be time-sensitive to optimize patient outcomes, yet this Ontario study estimated a wait time of over 1.5 years to clear this estimated surgical backlog.¹² Other areas of patient care are also experiencing service backlogs. For example, one Canadian study during the pandemic onset reported a 21% reduction in cancer care services, corresponding to a 42.4% reduction in cancer screening.¹³ As well, related surgical cancer treatments were reduced by 14.1% while radiation treatments dropped by 21%.¹³ Regarding the domain of mental health, the pandemic has instilled a lasting detriment to Canadians’ mental health. For instance, one Canadian study during the pandemic reports that the prevalence of Canadians screening positive for major depressive disorder had doubled since pre-pandemic times.¹⁴ However, such demand for mental health services is quickly outpacing the healthcare system’s ability to meet this need. Unfortunately, this ripple effect of decreased access to healthcare services disproportionately affects minority populations. Several reports describe unequal access to care among Indigenous, female, immigrant, and racialized populations.¹⁵⁻¹⁸ Overall, these unmet healthcare needs are resultant ripple effects of the COVID-19 pandemic, which hold potential to worsen patient outcomes, increase healthcare costs, and disadvantage vulnerable populations.

From a public health perspective, the pandemic has evoked ripple

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effects on three domains: health protection, health services, and health improvement.¹⁹ In the domain of health protection, COVID-19 introduced sanitation measures, such as hand hygiene, social distancing, and mask wearing, to prevent disease spread.²⁰ For instance, initiatives supporting access to water, sanitation, and hygiene (WASH) have been implemented across 84 countries worldwide during the advent of the pandemic.²¹ Despite achieving target vaccination coverages, sanitation methods, such as mask wearing, have become commonplace practices and continue to be recommended.²² Regarding the health services domain, ripple effects have led to the widespread use of telemedicine. Prior to March 2020, telemedicine was poorly integrated into the healthcare system with implementation complexities.²³ However, when telemedicine was reintroduced to decrease COVID-19 transmission, telehealth visits skyrocketed from 840,000 in 2019 to 52.7 million in 2020.²⁴ Telehealth has decreased healthcare spending, increased access to care to patients from remote areas, and improved the efficiency of care provision.²⁵ Although there are disadvantages, such as technical difficulties and privacy breaches, telehealth remains essential in healthcare delivery.²⁵ In July 2022, the United States House of Representatives passed a bill to continue certain Medicare telehealth policies enacted at the start of the pandemic.²⁶ However, in the health improvement domain, ripple effects have led to misinformation. During efforts to provide education on disease prevention and vaccinations, medical misinformation became widespread through social media.²⁷ The spread of misinformation undermines healthy practices, such as vaccinations and handwashing, and encourages measures that heighten the risk of COVID-19 infection, resulting in increased disease spread and poor health outcomes.²⁸ For instance, a study in the United States predicted that medical misinformation would cause a 20% decrease in vaccine uptake across the country and 67% increase in hesitancy rates across Democratic regions.²⁹ Ultimately, the positive and negative ripple effects of the pandemic will continue to have a significant impact on future health outcomes, infection prevention and control practices, and health promotion and education strategies worldwide.

In “Ripple Effects”, we at the UBC Medical Journal focus attention on the ongoing work being conducted by healthcare leaders to target our system’s most critical challenges. This issue’s first feature article is written by Dr. Sarka Lisonkova, MD, PhD, an associate professor in the UBC Department of Obstetrics and Gynaecology, in which she discusses the indirect effects of the COVID-19 pandemic on reproductive health. Our second feature article is written by Dr. Elisabeth McClymont, PhD a postdoctoral fellow in the UBC Department of Obstetrics and Gynaecology, who writes on the needs of pregnant individuals during the COVID-19 pandemic. The final feature article is written by Dr. Stephen Milne, BBiomedSc, MBBS(Hons), FRACP, PhD, a postdoctoral fellow in the UBC Centre for Heart Lung Innovation and division of respiratory medicine, who discusses the impact of the COVID-19 pandemic on patients with chronic obstructive pulmonary disease.

While there have been tremendous efforts to manage the COVID-19 pandemic since its peak, its aftermath continues to propagate a new set of challenges that necessitate societal attention. As we transition into the next phase of living alongside SARS-CoV-2 and mending its ripple effects, it is ever clearer that these challenges distribute especially to those facing systemic barriers. That is to say, no matter our background, the responsibility lies with all British Columbians to support one another in collaborating against these issues. No doubt, the

prospect of repairing our province and healthcare system depends on it.

Conflict of interest

The authors have declared no conflict of interest.

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Indirect effects of the COVID-19 pandemic on reproductive health

Sarka Lisonkova¹

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Since early 2020, the rapid spread of SARS-CoV-2 and its variants^{1,2} has significantly impacted global health, including reproductive health. Studies have repeatedly shown that comorbidities, including overweight and obesity, diabetes, hypertension, and chronic respiratory illnesses, increase risks associated with COVID-19.³⁻⁷ Current evidence suggests that pregnancy does not increase susceptibility to SARS-CoV-2 infection, however, the clinical course of COVID-19 is worse compared with nonpregnant women.^{4,8} The presence and extended duration of COVID-19 symptoms (e.g., shortness of breath) is associated with poor outcomes.^{7,8} However, the majority of pregnant women who test positive for SARS-CoV-2 on hospital admission have been found to be asymptomatic (40% to >80%).⁷⁻⁹

The indirect effects of the COVID-19 pandemic arise through several different mechanisms: 1) pandemic-related restrictive measures with respect to travel, social gatherings, stay-/work-from-home orders, and school closures; 2) extensive main-stream and social media coverage of crowded hospitals, illness and death; 3) economic consequences such as income loss, food and housing insecurity; and 4) restrictive measures with respect to health services including limited services offered, limited access to services, and changes in service delivery. Detrimental effects of these measures can be observed in population mental health, cardiovascular health, delayed surgeries, declines in child health, increases in all-cause mortality, etc.¹⁰⁻¹² In Canada, for instance, these effects included over 4000 excess deaths (unrelated to COVID-19) due to delayed care, a 70% increase in opioid-related deaths, 20%-35% lower levels of cancer screening (compared with pre-pandemic levels), high levels of anxiety (up to 21% in June 2021), and a 39% increase in food insecurity, among others.¹¹

We are now only beginning to unravel the depth of the consequences of the direct effects of COVID-19 pandemic and the indirect effects of restrictive pandemic measures. For example, we have only limited evidence on the wider effects of COVID-19 pandemic on reproductive health, including effects on fertility rates and the consequences of limited access to reproductive and maternity services with respect to adverse perinatal maternal outcomes.

Changes in the use of assisted reproduction

In the beginning of the pandemic, women may have chosen to postpone conception and childbirth due to pandemic-related uncertainty and financial instability, lack of support from family members due to travel restrictions, and anxiety about the unknown, potentially harmful effects of SARS-CoV-2 infection.¹³ In Canada, nearly 25% of 15 to 49 years old respondents of a large survey changed their childbearing plans because of the pandemic.¹³ In the USA, the general fertility rate declined in the first months of 2021,¹⁴ while in Finland and Denmark, the number of live births increased after an initial decline, which was attributed in part to generous financial assistance programs for families.¹⁴ Scientific and professional fertility societies (e.g., the Canadian Fertility and Andrology

Society and the American Society of Reproductive Medicine) issued guidelines early in the pandemic recommending suspension of new fertility treatments.¹⁵⁻¹⁶ A recent study of commercially insured US women showed more than an 80% decline in assisted reproductive technology (ART) procedures between March and April 2020.¹⁷ The sudden interruption of the reproductive services had a negative emotional impact on women who were planning or undergoing fertility treatment during the onset of the pandemic showed, predominantly on women of advanced age and those with diminished ovarian reserve, as shown by multiple studies from the USA, England, Germany, Italy, Denmark, Israel, India and China.¹⁸⁻²³ As a result of IVF clinic closures during the onset of the pandemic, a dramatic decline in the proportion of ART-conceived live births was observed approximately nine months later, in December 2020. In addition, a large decline in multiple births (i.e., twins, triplets, etc.) was observed during the same period (because IVF conception frequently results in twin birth). In the USA, for instance, the proportion of ART-conceived live births declined by 57% and the overall proportion of multiple births declined by 14% in December 2020.²⁴ Such 'delayed effects' of the pandemic are now being studied by using 'conception cohorts'.²⁵ Conception cohorts, which include all pregnancies conceived in any given calendar period, serve as the ideal population for assessing the effects of exposures during conception or at specific gestational ages. This is in contrast to 'birth cohorts' that we typically use to assess birth outcomes, which include all live births and stillbirths that occur in any given calendar period and were conceived during various calendar periods.²⁵

Adverse Perinatal Health Outcomes

Obstetric services were reduced after the onset of the pandemic to non-essential hospital admissions with a varying degree depending on the country/region.^{12,26-28} Maternity care provider visits were curtailed and in-person visits were mostly replaced by on-line visits or phone-call/telemedicine appointments.¹² However, such changes did not occur in all countries, for instance, these restrictive measures were not implemented during the first months of the pandemic in Sweden.²⁹ In parallel, iatrogenic (i.e., clinician-initiated) preterm delivery declined with fewer labor inductions and pre-labor cesarean deliveries in Canada in March-August 2020.³⁰ This phenomenon was also observed in Australia,³¹ but not in Sweden and the US.^{29,32} Such changes may have resulted in elevated rates of adverse pregnancy outcomes.³³⁻³⁵

One of the most intriguing findings in the early months of the COVID-19 pandemic was a decline in population rates of preterm birth (PTB) and low birth weight neonates;³⁶⁻³⁸ a study from Denmark showed a reduction in preterm infants <28 weeks' gestation,³⁶ a report from Ireland showed a reduction in low-birth-weight infants <1000 g and <1500 g,³⁷ and a study from the Netherlands reported declines in PTB at 32–36 weeks' gestation.³⁸ In Canada, preterm birth at <32 weeks gestation declined from 1.25%-1.18% in years 2015-2019 to 1.12% in 2020; this was mostly due to a decline in medical interventions (labor induction or cesarean delivery).³⁰ Such changes were not observed in the US (Figure 1).

Initial findings about lower rates of preterm birth early in the COVID-19 pandemic were viewed positively, as a possible consequence of stress reduction and lifestyle changes during the pandemic. However,

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this explanation conflicts with reported pandemic-related increases in anxiety and depression among pregnant women.^{9,11,12} A meta-analysis of 12 studies showed a 28% increase in pandemic-related stillbirth rates (with a 39% increase in high-income countries).⁹ In Canada, stillbirth rates remained relatively stable, except for the province of Ontario where a large spike in stillbirths occurred in April 2020.³⁰ The heterogeneity of available studies, inconsistent definitions, lack of information about medically indicated vs. spontaneous delivery, and various gaps in reporting of stillbirth, mean that the indirect effects of the COVID-19 pandemic on PTB and stillbirth remain unresolved.^{39,40} A systematic approach is needed for studying changes in spontaneous and medically-indicated PTB during the early and later pandemic periods (i.e., March–August 2020, September–December 2020, etc) and associated changes in stillbirth rates in different regions. Complex systems require complex approaches including multiple exposures that change simultaneously and various health outcomes that are correlated or occur on various causal pathways.

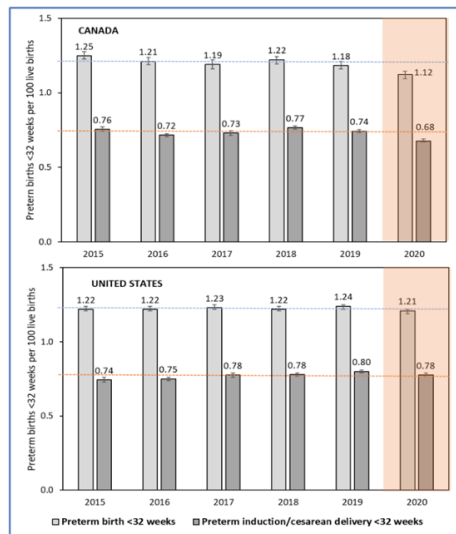


Figure 1: Rates of preterm birth and labour induction/Caesarean delivery at <32 weeks' gestation in Canada and the USA, 2015-2020

Adverse Maternal Health Outcomes

Adverse effects of SARS-CoV-2 on maternal health have been commonly reported. For instance, a large, international hospital-based study showed that pregnant women with a COVID-19 diagnosis were at two- to three-fold higher risk of severe pregnancy complications, including preeclampsia, eclampsia and Hemolysis, Elevated Liver enzymes and Low Platelets (HELLP) syndrome, ICU admission, referral to higher level of care, and infections requiring antibiotics.⁷ Maternal mortality in these women was 22-fold higher compared with pregnant women without a COVID-19 diagnosis.^{7,41} COVID-19-positive asymptomatic women had pregnancy outcomes similar to COVID-19-negative women, except for preeclampsia/eclampsia: asymptomatic COVID-19-positive women had a 1.6-fold higher adjusted risk, while symptomatic COVID-19-positive women had a 2-fold higher risk compared with COVID-19-negative women.⁷ Among women with a COVID-19 diagnosis, COVID-19 symptoms, including fever and shortness of breath, and

underlying chronic medical conditions increased the frequency of serious adverse maternal outcomes and death.^{7,42} Studies on the indirect effects of the COVID-19 pandemic on maternal health have focused mostly on maternal mental health; numerous studies have reported increased levels of anxiety and mental health conditions.^{9,12} Large increases in severe maternal morbidity and mortality unrelated to SARS-CoV-2 infection have not been observed to date.⁹ However, systematic investigations of the indirect effects of the COVID-19 pandemic on severe maternal morbidity and mortality are lacking. Large, multi-country population-based comparative studies are needed to evaluate the indirect effects of the COVID-19 pandemic on maternal health.

Indices Quantifying Socially Restrictive Pandemic Measures

The indirect effects of COVID-19 pandemic are difficult to measure because it is not easy to quantify the degree of pandemic-related restrictive measures. The COVID-19 pandemic has prompted a wide range of public health responses from public health agencies and governments globally to curb the spread of SARS-CoV-2 infection. Most pandemic-related response measures included restrictions with respect to travel, social gatherings, stay-/work-from-home orders for non-essential workers, cancellations of large gatherings and sports events, and school closures. Quantification of these complex measures is challenging. A summary indicator has been developed by the University of Oxford, as an index that quantifies pandemic-related restrictive measures.^{43,44} This composite stringency index (SI) integrates the rigor and scope of multiple containment and closure policies into a single numeric parameter in the 0–100 range. It consists of eight containment and closure policy indicators and one indicator of health system policies: 1) closures of schools and universities; 2) closures of workplaces; 3) cancellations of public events; 4) limitations on private gatherings; 5) closures of public transport; 6) orders to shelter-in-place; 7) restrictions on internal movement between cities/regions; 8) restrictions on international travel; and 9) presence of public information campaigns. The stringency index has been tracked over the course of the pandemic for various countries with the Oxford COVID-19 Government Response Tracker (OxCGRT) since January 2020 (Figure 2).⁴³

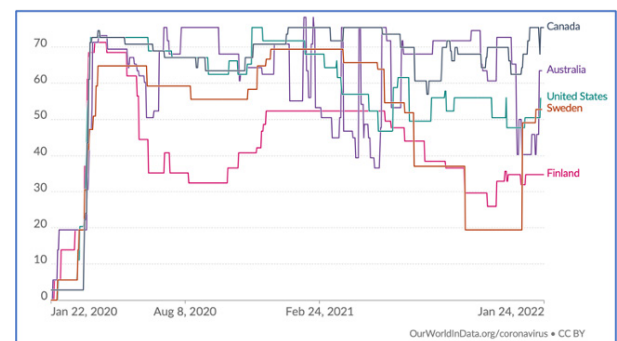


Figure 2: COVID-19 Stringency Index values in Australia, Canada, Finland, Sweden and the USA.

Specific OxCGRT data are available for a multitude of countries, as well as smaller geographical areas including, for instance, Canadian provinces⁴⁵ and individual states in the USA.⁴⁶ The SI has been designed for comparability across regions and over time,⁴⁴ and has been used widely by health care policy experts, data scientists, environmental and political scientists, and economists.^{9,47,48} Prior studies show that on

average, the SI correlates closely with distancing behaviors.⁴⁴ However, average behavioral responses and the actual compliance with these restrictions likely differ by states, geographic areas, and individuals.⁴⁹ It is apparent that a wide variation exists in pandemic-related response between countries, including the Nordic countries⁵⁰ that adopted somewhat less stringent measures in the first six months of the pandemic as compared, for instance, with Australia³¹ and Canada.⁴⁵

The SI has been used recently to compare health indicators such as COVID-19-related mortality and excess deaths; the report showed that among 9 high-income countries, Canada had the highest median SI and the lowest direct burden of infection despite very low baseline hospital and critical care capacity relative to other nations, and a relatively small population in relation to geographic size, creating logistical challenges for care delivery.⁵¹

Summary

The current literature indicates that although pregnant women are not at higher risk of SARS-CoV-2 infection, pregnancy is a risk factor for COVID-19-associated maternal morbidity and adverse perinatal and infant outcomes. Despite a large volume of scientific literature generated about COVID-19 effects on pregnancy and birth outcomes, a considerable knowledge gap exists regarding changes in pandemic-related maternity care and obstetric service restrictions and their short-term and long-term effects. In addition, little is known about how these effects vary among vulnerable groups of women and their infants including potential disparities in reproductive outcomes among women with low socio-economic status, women from rural areas, and those with underlying chronic conditions. For the years to come we will be studying these effects as SARS-CoV-2 and humans learn to co-exist.

Conflict of interest

The author has declared no conflict of interest.

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Addressing the needs of pregnant individuals during the COVID-19 pandemic

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Pandemics caused by emerging infections require the rapid generation of new data to inform the pandemic response and clinical care of affected individuals. This is true not only for the general population, but also for specific populations that may be differentially affected by the pathogen. One such population that has been the focus of our team's work since the outset of the COVID-19 pandemic, is pregnant individuals.

Pregnancy is a unique time with varied physiological changes and new considerations that affect the health of the pregnant individual. Importantly for the COVID-19 pandemic, pregnant individuals are more vulnerable to respiratory infections, more vulnerable to certain medical interventions to treat infection, and also have unique infection prevention and control needs during labour, delivery, and postpartum. These unique circumstances of pregnancy require the generation of data that are specific to the pregnant population in order to inform their clinical care and public health policies that impact them. Additionally, because the risk of certain adverse pregnancy outcomes may be elevated but still infrequent overall, it is important to have large cohorts of pregnant individuals in order to properly assess risks for this population. Finally, as prenatal care varies widely across the globe, data from pregnant cases in these varied settings are needed to understand effects and inform policy changes regionally.

In response to these needs, researchers and clinicians across Canada joined together to create a national surveillance program for SARS-CoV-2 affected pregnancies, known as CANCOVID-Preg.¹ The program was initiated in March 2020 and remains active to the present day. CANCOVID-Preg tracks not only the maternal course of infection and pregnancy outcomes, but also early infant outcomes. As a primary aim of this program is to inform public health policy and clinical care, findings have been reported on an ongoing basis throughout the pandemic to public health bodies, clinical societies, and the public (<https://ridprogram.med.ubc.ca/canccovid-preg/>). These reports have directly contributed to the prioritization of pregnant individuals for COVID-19 vaccination and national clinical care guidelines for pregnant individuals.²⁻⁴ To contribute to the global understanding of SARS-CoV-2 infection during pregnancy and better understand risks of rare outcomes, our team also contributes data to international collaborations.⁵

Findings from CANCOVID-Preg to date have shown several important aspects of SARS-CoV-2 infection during pregnancy.⁶ First, when compared to non-pregnant cases of SARS-CoV-2 infection, pregnant cases are more likely to require hospitalization for COVID-19 (RR 2.65 [95% CI: 2.41-2.88]) and admission to the intensive care unit (ICU; RR 5.46 [95% CI: 4.50-6.53]). A higher risk of hospitalization for COVID-19 and ICU admission was seen in those with older age,

higher body mass index, pre-existing conditions (hypertension, diabetes, and asthma), greater gestational age at diagnosis, and non-White race/ethnicity. Among hospitalized cases until October 2021, 100% of these cases were unvaccinated or not completely vaccinated (had not received at least 2 doses of a COVID-19 vaccine). Next, when compared to pregnant women without SARS-CoV-2 infection during pregnancy, pregnant cases experienced an increased risk of preterm birth (RR 1.63 [95% CI: 1.52-1.76]). Preterm birth is an important outcome that can result in lifelong sequelae for the infants affected. Another critical finding of this project to date has related to the racial/ethnic breakdown of individuals affected by SARS-CoV-2 during pregnancy. When compared to the racial/ethnic breakdown of reproductive age Canadian females (ages 15-45), we have seen a much higher representation of non-White individuals affected by SARS-CoV-2 during pregnancy. Races/ethnicities including Black, South Asian, and Other (including Indigenous) have been disproportionately affected by SARS-CoV-2 during pregnancy.

A second national project, known as COVERED, was also initiated to respond to the needs of pregnant women during the pandemic. COVERED is a COVID-19 vaccine registry for pregnant and lactating individuals (<https://covered.med.ubc.ca/>). This national, prospective, survey-based project welcomes individuals experiencing pregnancy during the pandemic to report their attitudes towards and experiences with COVID-19 vaccination, as well as their pregnancy and infant outcomes. This work was critically needed as pregnant individuals were not included in the initial COVID-19 vaccine trials and, therefore, vaccines were licensed and initially rolled out with insufficient data among the pregnant population. Participants in COVERED from across the country have contributed their own data to improve our understanding of COVID-19 vaccine reactogenicity, pregnancy and infant outcomes following vaccination, and attitudes towards vaccination. Data from this registry so far have reinforced that COVID-19 vaccination during pregnancy is safe. An immune sub-study from this project has collected biospecimens from a subset of pregnant participants including maternal blood, cord and infant blood, and breast milk. These specimens are being used to answer pertinent questions about trans-placental transfer of maternal antibodies to infants, taking into account timing of maternal vaccination, and the role of breast milk in infant antibody acquisition. This kind of information is critically important in informing vaccination policy and practice decisions for the pregnant population.

A national serosurveillance program completes our team's pandemic response projects to date. Routine blood screening for infectious diseases is performed as part of prenatal care in Canada with extremely high uptake of $\geq 95\%$. Therefore, these blood samples are highly representative of reproductive age females from all socioeconomic backgrounds and geographic areas of the country. These samples are frequently stored centrally for over one year. In addition, in jurisdictions that do not store these specimens, there are also routine prenatal genetic screening samples taken in most pregnancies, referred to as aneuploidy screening, that are usually stored for one year. The Canadian Population Serological Survey Utilizing Antenatal Serum Samples (The Antenatal Serostudies Project)

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is an initiative that performs SARS-CoV-2 antibody testing on the leftover serum from these prenatal samples throughout Canada (<https://ridprogram.med.ubc.ca/cancovid-preg-antenatal-serostudies/>). The low bias in collection of these samples sets this SARS-CoV-2 seroprevalence program apart from other similar projects in Canada. As the pandemic has progressed, we have been able to leverage these existing specimens to report on changing SARS-CoV-2 seroprevalence over time.⁷ Compared to SARS-CoV-2 PCR-positivity rates, we have seen that seropositivity rates were much higher, meaning that all provinces were significantly underreporting infections. Additionally, we detected seropositive individuals in all provinces prior to pandemic declaration, indicating wider early spread of the virus than previously thought. In some provinces, samples from early and late pregnancy are available, which has allowed for the detection of SARS-CoV-2 seroconversions during pregnancy.⁷ Additional analyses, post implementation of vaccination programs, have been able to differentiate vaccine-acquired versus infection-acquired immunity to continue to provide valuable information about protection and exposure of the Canadian population, through the Omicron wave and beyond.

There remains much work to do to continue to inform the public health response and clinical care of pregnant individuals as the pandemic continues. Adaptation of these projects has been key throughout the pandemic as vaccines have been introduced, new variants have emerged, and SARS-CoV-2 testing has become de-centralized such that public health bodies are no longer aware of every case detected. In the coming months, COVERED will provide analyses of various outcomes for pregnant and recently pregnant individuals receiving COVID-19 vaccines in Canada. CANCOVID-Preg will provide data on the impact of new variants and the outcomes related to new vaccine formulations that are being introduced in Fall 2022. Multiple analyses are also underway to provide a more detailed analysis of the severe cases of COVID-19 during pregnancy, the placental pathology associated in this cohort, and also more detailed infant outcomes. The antenatal serostudies project will continue to provide valuable data on protection and exposure of Canadians through assessment of both vaccine-acquired and infection-acquired immunity to SARS-CoV-2.

The CANCOVID-Preg surveillance program, COVERED vaccine registry, and the Antenatal Serostudies Project have been an important part of the pandemic response in Canada. We see the value in maintaining the national collaboration that has been established through these projects to respond to future pandemics and emerging infections in a rapid and less resource intensive way for future surveillance of pregnant populations.

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Conflict of interest

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The ongoing impact of the COVID-19 pandemic on people with chronic obstructive pulmonary disease: Lessons and opportunities

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The COVID-19 pandemic has wreaked havoc on the world, causing the death of over six million people worldwide to date. Now more than two years since it began, this global emergency is far from over and attention has now turned to how the world – and the most vulnerable members of our society – will have to live with this new disease. This commentary focuses on one such vulnerable population: people living with chronic obstructive pulmonary disease (COPD).

Back to basics: COPD 101

Over two million Canadians suffer from COPD,¹ which is the third leading cause of death worldwide.² The disease is characterized by irreversible airflow obstruction due to pathological changes in the airways (remodelling) and the surrounding alveolar tissue (emphysema). It is accompanied by symptoms including dyspnea, exercise limitation, chronic cough, and sputum production. Although COPD is causally associated with tobacco smoking, around one third of people with COPD have never smoked and biomass fuel smoke exposure, respiratory infections (e.g. tuberculosis), and abnormal lung development (e.g. premature birth) are recognized etiological factors. Current treatments for COPD may alleviate symptoms in some patients, but smoking cessation is the only intervention that has been definitively shown to alter the natural history of the disease.

In between periods of relative stability, people with COPD may experience sudden symptom flares known as acute exacerbations (AECOPD). Frequent exacerbations are associated with poorer quality of life,³ accelerated lung function decline,⁴⁻⁶ increased risk of death,⁷ and excess health care utilization.⁸ In Canada, AECOPD is second only to childbirth as the leading cause of hospitalization⁹ and is responsible for the majority of the direct healthcare costs associated with COPD, which was estimated to be \$1.5 billion in 2008.¹⁰ Because of its immense personal and societal burden, prevention of AECOPD is a major management goal for this patient population.¹¹

COPD as a risk factor for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection

The majority of AECOPDs are caused by respiratory viruses.¹² Furthermore, the COPD airways have poor innate antiviral responses.¹³ Together with the fact that COPD patients are an older population with multiple comorbidities, it was reasonable to assume that people with COPD would be a particularly vulnerable group at the emergence of the pandemic. However, this a priori assumption needed to be tested for this novel respiratory infection.

The first step was to understand whether people with COPD have greater susceptibility to SARS-CoV-2 infection. The availability of host cell surface molecules used as viral entry receptors and cofactors not only determines tissue tropism of the virus, but may also determine the organism's risk of developing disease after being exposed to the

virus. Differences in SARS-CoV-2 receptor expression in the airways and lungs may explain the epidemiological data suggesting that older patients with multiple comorbidities such as hypertension and diabetes were at higher risk of COVID-19.¹⁴ In the frantic early days of the pandemic, performing laboratory experiments on SARS-CoV-2 was extremely difficult and limited to a few highly specialized centres. An alternative approach was to interrogate existing data to predict how this novel virus would behave. With this in mind, our research group analyzed our lung gene expression data set – known as the Lung eQTL Study,¹⁵ containing the mRNA profiles of over 1,000 lung tissue samples – to determine the effects of various comorbidities and exposures on the expression of SARS-CoV-2-related genes. We found that mRNA for the primary SARS-CoV-2 entry receptor, angiotensin converting enzyme-2 (ACE2), was increased in the lungs of people with COPD and in current smokers.¹⁶ We also analysed airway epithelial cells collected by bronchoscopy and found that *ACE2* mRNA and ACE2 protein were increased in the small airways of people with COPD compared to controls.¹⁷ Subsequently, in vitro experiments using live virus confirmed that airway epithelial cells from COPD patients were more susceptible to SARS-CoV-2 infection, a phenomenon that appeared to be directly related to the amount of ACE2 expressed on cells.¹⁸ Together, these findings supported the notion that COPD patients are more vulnerable to contracting SARS-CoV-2 than people without COPD.

However, epidemiological support for an increased susceptibility to SARS-CoV-2 infection among COPD patients is lacking.¹⁹ This may be because cellular susceptibility explains only a fraction of an individual's risk of infection, the majority of which may be determined by likelihood of exposure. This in turn is a function of the prevalence of active cases in the community, and the behaviours of individuals that increase or decrease their exposure to such cases. It should also be noted that making inferences about individual susceptibility from observational data is difficult because it relies on adequate capturing and reporting of cases and their comorbidities. In summary, despite the cellular and molecular evidence supporting this theory, there is an absence of epidemiological evidence that COPD patients are at any greater risk of contracting SARS-CoV-2 than the general population.

COPD and clinical outcomes from COVID-19

More certain is our understanding that people with COPD are at risk of worse clinical outcomes after they contract SARS-CoV-2. Comparing the severity of COVID-19 across different studies is difficult since there is no universally adopted scale by which to grade the severity of disease. A useful, albeit imperfect, surrogate measure of severity is the need for hospital admission. In a systematic review including 698,000 patients from 16 countries, our research group found that people with COPD had more than four times the risk of COVID-19-related hospitalisation, and more than twice the risk of death from COVID-19, than people without COPD (Figure 1).²⁰ Intensive care unit (ICU) admission – another surrogate measure of disease severity – is less reliable since clinical decisions based on age and comorbidities will influence the likelihood of ICU admission. Nevertheless, we found

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that people with COPD were 35% more likely to be admitted to ICU for COVID-19 than those without COPD. Confounders such as age, sex, and comorbidities are highly likely to explain at least some of the increased risk of severe COVID-19 in COPD, but this is difficult to assess. We used meta-regression to explore the impact of age, and found that COPD has a greater relative influence on COVID-19 outcomes in younger patients (40–60 years) than in older patients.²⁰

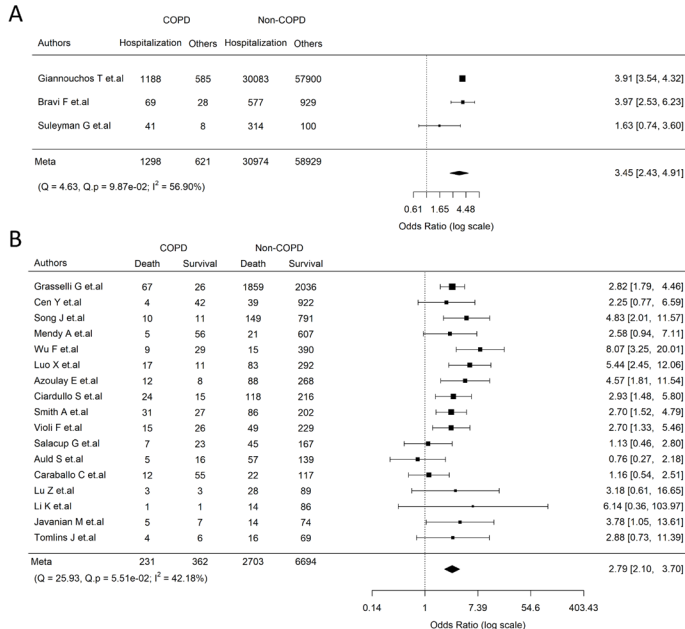


Figure 1: Increased risk of COVID-19-related hospitalization and death in COPD. Meta-analysis of published studies til August 2020. COVID-19 patients with COPD had four times the risk of hospitalisation and twice the risk of death compared to those without COPD. Full data published in Gerayeli et al¹⁹.

AECOPD during the pandemic

An interesting observation throughout the pandemic has been the apparent decline in the incidence of AECOPD. In a population-wide database from Denmark, there was a decrease in hospitalization for severe AECOPD (hazard ratio [HR] 0.34, 95% CI 0.33 to 0.36) and a reduction in all-cause mortality among COPD patients (HR 0.83, 0.76 to 0.90) compared to the pre-pandemic period.²¹ In Singapore – which endured strict, government-enforced lockdowns for an extended period – not only did the rate of hospital admissions for AECOPD halve during lockdown but there was also a sharp decline in the proportion of AECOPD cases testing positive for common respiratory viruses (10.5% during lockdown, compared to 48.8% pre-lockdown).²² This suggests that the reduction in AECOPD may be explained, in part, by the impact of public health measures on the exposure of COPD patients to other viruses likely to cause AECOPD. Indeed, surveillance programs have reported a decrease in the prevalence of these viruses in the community during the pandemic.²³

However, there are some major caveats to this interpretation. For example, the rate of unreported mild AECOPDs during the pandemic is not known. There are also several reports of COPD patients avoiding seeking health care during an exacerbation out of fear.²⁴ It is therefore possible that there has been a ‘hidden pandemic’ of undiagnosed and untreated AECOPD during this period. Nevertheless, the reduction in AECOPD is likely a reflection of changing behaviour among COPD

patients who, through careful attention to public health messaging or even fear and anxiety, have been strict adherents to social distancing and hygiene measures.²⁵ There are also some qualitative data suggesting adherence to prescribed treatments has also increased during this period.²⁶

To put these observations into perspective, let us consider the totality of public health measures during the COVID-19 pandemic period as an ‘intervention’ for reducing AECOPD among all COPD patients. A meta-analysis of nine studies published in the first year of the pandemic, when measures were most strict, found a relative risk reduction in severe AECOPD of 50%.²⁷ This exceeds even the most optimistic estimates for our currently available COPD drug treatments (Figure 2).^{28–31} Another way of quantifying the effects of an intervention is the number needed to treat (NNT), which is calculated as the inverse of the absolute risk reduction (1/ARR). The study from Denmark described earlier reported a 17% ARR in severe AECOPD,²¹ which translates to a NNT of five: that is, only five COPD patients need to be ‘treated’ with COVID-19 public health measures to prevent one severe AECOPD. (For context, any new drug that achieved such an effective and efficient reduction in AECOPD would be a game changer!). The purpose of this exercise is not to make light of the enormous personal and societal costs of the COVID-19 public health measures, but rather to illustrate how far we have to go to make meaningful progress in the

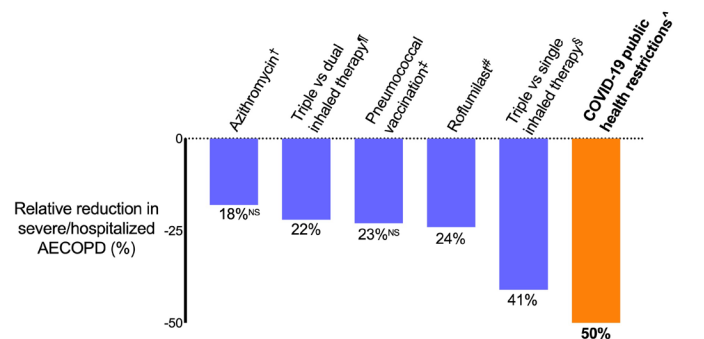


Figure 2: Effects of various interventions on acute exacerbations of COPD (AECOPD). If combined COVID-19 public health measures are considered an intervention for the prevention of severe AECOPD, the effect is greater than that of all currently available treatments. †Long-term low-dose azithromycin therapy compared to placebo (randomized controlled trial, RCT).²⁹ ‡Triple inhaled therapy with inhaled corticosteroid (ICS), long-acting beta-agonist (LABA) and long-acting muscarinic antagonist (LAMA) versus dual LABA/LAMA therapy (meta-analysis).²⁸ #Roflumilast versus placebo (RCT).³¹ §Triple ICS/LABA/LAMA inhaled therapy versus single LABA or LAMA therapy (meta-analysis).²⁸ *Public health measures including general public health messaging, closures, and stay-at-home orders during the COVID-19 pandemic (meta-analysis).²⁷ NS, not statistically significant.

COPD and COVID-19: lessons that must be learned

Albert Einstein is quoted as saying: “In the midst of every crisis, lies great opportunity”. If there is any silver lining to be found in the COVID-19 crisis for people with COPD it is that the medical community has heightened awareness of the vulnerability of this population. Understanding the greater risk of poor outcomes from COVID-19 gives us an opportunity to prioritize people with COPD for anti-viral treatments and vaccines. We also have opportunities to protect them during their interactions with the health care system using technology,

for example with telehealth consultations and remote pulmonary rehabilitation services.³² By better understanding the reduction in AECOPD observed during the pandemic we have an opportunity to craft new preventative measures for people with COPD. For example, the selective implementation of measures such as hand hygiene and mask wearing may prove to be low risk, low cost, but effective means of reducing the rate of AECOPD. If this is a once in a generation health crisis, it is also a once in a generation opportunity to learn from the recent past and ultimately improve outcomes for people living with COPD.

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Conflict of interest

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The role of cadavers and virtual reality in laparoscopic training

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Abstract

Laparoscopic surgery, which is minimally invasive surgery using small incisions and a camera, has been demonstrated as a lower risk alternative for many procedures. However, complications still arise. Limited technical training is a large contributor to laparoscopic complications. Maximizing surgical training that can occur outside of the operating theatre is paramount now more than ever given the current corona virus disease 2019 (COVID-19) pandemic restrictions. Virtual reality, a form of electronically simulated training, and cadavers can help fulfill this need. Virtual reality and cadavers offer unique training benefits. Virtual reality may be most useful for basic laparoscopic skills and for novice trainees who have had limited laparoscopic exposure. Both fresh frozen and Thiel cadavers (cadavers preserved with low formaldehyde embalming technique) offer a more realistic laparoscopic surgical training experience compared to virtual reality and should be directed towards more advanced trainees. The purpose of this review is to discuss the use of virtual reality and cadavers for laparoscopic surgery training.

Introduction

Patients are electing for laparoscopic surgery more frequently due to the faster recovery compared to open procedures, which can be attributed to its less invasive approach with small incisions and a camera.^{1,2} Although laparoscopic surgery has been demonstrated as a lower risk alternative for a variety of open surgeries, such as bariatric surgery,³ resection of gynecologic malignancies,⁴ and distal pancreatectomy,⁵ complications such as bleeding, hernias, and damage to neighboring structures can still arise.³⁻⁵ The majority of laparoscopic complications are a consequence of inadequate training, rather than the surgical technique,² as laparoscopic procedures are advanced and require extensive training for proficiency.⁶ Further, many of the skills from open surgical procedures do not transfer to laparoscopic skills.⁷ Both residents and surgeons perceive the need for more laparoscopic training.⁸

As new laparoscopic equipment and techniques emerge, many physicians do not feel there is enough time or support for them to learn and integrate the new procedure into their practice.⁹ Residency programs have policies restricting work hours,¹⁰⁻¹³ resulting in decreased training time. Even when residents have the opportunity to work on advanced laparoscopic cases, patient safety limits the amount of procedural work they can perform.^{14,15} These issues have been amplified by the corona virus disease 2019 (COVID-19) pandemic as there has been decreased elective operative time and mandates to isolate and stay home.¹⁶ Therefore, maximizing surgical training that can occur outside of the operating theatre is paramount now more than ever;¹⁷ virtual reality (electronically simulated three dimensional training) and cadavers are helpful for fulfilling this need.

Laparoscopic training can be done using virtual reality (VR) or cadavers.¹⁸⁻²⁰ Fresh frozen cadavers (FFCs) and Thiel cadavers (TCs; cadavers preserved with low formaldehyde) have proved useful for laparoscopic training.^{13,21} The purpose of this review is to discuss the use of VR and cadavers for laparoscopic surgery training. This review has collated nine systematic reviews, three randomized trials and multiple other articles from the past decade.

Virtual Reality

VR simulators are effective in training laparoscopic tasks such as knot tying and suturing.¹⁸⁻²⁰ As demonstrated by a prospective randomized study, the more challenging the VR training, the more trainees will see

improvement in their skills.² Residents who receive simulator training can acquire competence in surgical techniques more rapidly than those only trained in the operating room.^{10,23,24} A randomized controlled trial showed trainees who received VR training were faster and had fewer knot tying errors.²⁰ The external validity of this trial is limited, as it only demonstrated that individuals who practice knot tying with VR have faster VR knot tying times compared to controls with no training. A recent systematic review concluded that VR has the most utility for improving the steep laparoscopic surgery learning curve when used to teach trainees with no laparoscopic experience such as medical students and novice residents.²⁵

There is evidence that tasks trained on VR or in skills labs are transferrable to the operating room.²⁶⁻²⁸ In a randomized double-blinded study of 16 surgery residents, VR trained individuals demonstrated fewer operative errors and a 26% faster gallbladder dissection time when performing a laparoscopic cholecystectomy compared to controls who received standard training that did not include VR.²⁹ In a systematic review of 10 randomized controlled trials and one comparative study, Sturm and colleagues found that skills acquired through simulation could reduce operative time, performance errors and need for surgeon takeover in actual laparoscopic cholecystectomy and colonoscopy procedures.²⁶ Performance errors scores were reduced from a baseline of 6.8 to 3 after VR training.²⁶ Furthermore, VR trained individuals did not require any surgeon takeover, while 6 of 8 non-VR trained individuals did.²⁶ Despite these findings, the transferability of skills from training sessions to the operating room is still debated.²⁵ If further studies show that VR training is an accurate measure of intraoperative skills, VR could be used to assess laparoscopic skills before trainees operate on patients. Although the initial cost of VR equipment is variable and can be expensive,³⁰ once purchased it can be used numerous times by multiple trainees. This advantage contrasts with cadavers which are a limited resource with finite utility.

Fresh Frozen Cadavers

Formalin preserved cadavers are excellent for teaching anatomy amongst medical students, but the concentration of formaldehyde compromises tissue consistency which is of greater concern for surgical training than learning anatomy.³¹ FFCs have been suggested as surgical training models.^{21,32} Compared to formalin preserved cadavers, FFCs have an easier preservation process since they are simply washed with antiseptic soap and then frozen -20°C.²¹ The lack of formalin in FFCs allows the abdominal wall to expand freely, which is an important feature for laparoscopic training.²¹ The ease of preservation and life-like features make FFCs a desirable laparoscopic training tool.

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FFCs have been received as a better training tool than VR amongst trainees of all levels who used both modalities.³³ However, this conclusion is based on subjective experiences, as learners were asked to fill out questionnaires on the quality of training after VR and cadaver sessions.³³ The perceived higher quality training with cadavers may be due to other variables such as the tutors, tools used to practice procedures, or the novelty of operating on a cadaver, rather than characteristics specific to the FFCs.

A major reason why FFC's were considered superior to VR was the presence of tactile feedback which is difficult to replicate with VR.³³ However, in a study comparing VR and computer enhanced training devices, Kanumuri et al. found that haptic feedback, which is an electronically generated output such as a vibration, did not result in superior training.¹⁸ This finding could be attributed to the fact that the computer-simulated haptic feedback was not realistic enough to impact training. Alternatively, despite its perceived importance for surgical training among trainees, haptic feedback may not be important for training.

Training with FFCs can bring novices to a safe skill level, defined as no intraoperative complications when performing a task, within 8-10 repetitions; this was applicable to nondominant to dominant hand transfer, simulated appendectomy, and intracorporeal and extracorporeal knot tying.³³ The utility of FFCs is most apparent when training complex laparoscopic procedures such as kidney,³⁴ prostate and bladder surgery.³⁵ Due to the high cost of cadavers, it is suggested that multiple uses of cadavers are coordinated between different specialties.^{34,36} Although FFCs are clearly a valuable teaching resource, they are costly, require storage space, take time to thaw, and would rely on body donations.

Thiel Cadavers

Thiel's embalming technique uses low concentrations of formaldehyde and results in long lasting preservation that does not compromise tissue flexibility or coloration of the cadaver.^{13,37} Unlike FFCs, cooling and thawing is not necessary, and the cadavers appear more lifelike.^{13,37} In addition to preservation of lifelike features, TCs are a valuable resource for dissections, laparoscopic training and surgical training.² Specifically, TCs have proven excellent models for teaching laparoscopic bariatric, colon and hernia procedures because the peritoneal cavity can be inflated, lungs can be ventilated, and the articular joints remain moveable.^{2, 38} In a qualitative study where surgeons performed radical nephrectomies, TCs were perceived as more lifelike with regards to their tissue planes, colouration and tactile feedback compared to FFCs.³⁹

TCs offer similar and perhaps elevated training benefits compared to FFCs,³⁹ but they have a more demanding preservation process requiring the injection of two solutions followed by immersing the cadaver in an additional solution for at least two months.⁴⁰ TCs are more expensive and are a limited resource that would require a facility, storage space, and a trained embalmer.² With cost-benefit ratios in mind,² the best use of TCs would be at large academic centers where all parts of the cadaver can be used by surgical trainees from a variety of disciplines. In summary VR, FFCs and TCs offer unique strengths and weaknesses for laparoscopic surgery training (table 1).

	Virtual Reality	Fresh Frozen Cadavers	Thiel Cadavers
Strengths	<ul style="list-style-type: none"> Helpful for practicing basic skills (i.e. knot tying) Can be reset and used multiple times 	<ul style="list-style-type: none"> Lifelike features and anatomy Simple preservation process 	<ul style="list-style-type: none"> Life like features and anatomy Ready to use (no thaw time) Better than FFCs for tissue planes, colouration and tactile feedback
Weaknesses	<ul style="list-style-type: none"> Less effective for practicing complex skills and full surgical procedures 	<ul style="list-style-type: none"> Takes time to thaw before use Requires storage space Requires body donations 	<ul style="list-style-type: none"> Complex embalming method More expensive than FFCs Requires storage space Requires body donations

Table 1: Strengths and weaknesses of Virtual Reality, Fresh Frozen cadavers (FFCs), and Thiel cadavers for laparoscopic surgery training

Discussion

Residents and surgeons can benefit from more laparoscopic training based on self-reported measures as well as expert opinions.^{8,10,14} For this reason, determining how to combine the different training methods in order to achieve the best quality laparoscopic training is a worthwhile endeavor. Based on the review and synthesis of available evidence, there may be a benefit to using VR simulators initially followed by cadavers.

A stepwise curriculum based on scientific methodology for VR laparoscopic cholecystectomy has been suggested,⁴¹ but more work on designing and evaluating a VR curriculum is needed. It is possible for VR to train basic laparoscopic skills such as suturing and knot tying, but synthesizing these skills to safely execute a surgery must also be practiced.^{18-20,33} VR training has diminishing returns; when the procedure being taught becomes more complex VR becomes less effective.³³ For this reason, VR would be most useful amongst junior trainees learning basic laparoscopic skills, whereas cadavers are best suited for senior residents who are learning more complex skills and full procedures.^{33,42}

Fully utilizing training resources for surgery that are available outside of the clinical setting is of great relevance during the current COVID-19 pandemic.¹⁶ Laparoscopic surgery is aerosol generating and may theoretically be associated with increased transmission of COVID-19.⁴³ However, there has been no conclusive evidence that COVID-19 can be transmitted through laparoscopic surgery.^{43,44} Though there is debate regarding the safety of laparoscopic surgery during COVID-19,⁴³ and various recommendations have been made to increase safety,⁴⁵ limited elective training time remains a barrier to high volume laparoscopic training in residency.¹⁶ Virtual reality and cadaver training offers a viable adjunct to current surgical residency training.^{18-20, 31-33, 37, 38}

Notably, cadaver training with supervision can allow trainees to obtain similar clinical results as experts.⁴⁶ When comparing TCs versus FFCs both provide life-like features and flexible tissues for excellent laparoscopic training. Therefore, analysis of cost, resources, space, and embalmer training specific to the center would be the most useful factors to consider when choosing which preservation technique to use.⁴⁷

Limitations of this review include the heterogeneity of the trainees consisting of both medical students and residents from a variety of institutions, the fact this review was not performed in a systematic nature but is rather a narrative synthesis, and the lack of discussion regarding animal models for training which would contribute valuable discussion.

Conclusion

Virtual reality and cadavers provide quality training for laparoscopic surgery and can enhance patient safety. A curriculum that starts with VR followed by cadaver sessions could maximize the benefits of both modalities and provide residents and practicing surgeons with laparoscopic skills that transfer to the operative setting, improve outcomes, and ensure patient safety.³³ Additional studies that specifically evaluate VR training followed by cadaver training are needed to substantiate this claim.

Conflict of interest

The authors have declared no conflict of interest.

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Clinical anatomy of the sternalis muscle: A case report

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Abstract

We present a case report of the incidental finding of the sternalis muscle during a student dissection project on thoracic anatomy at The University of British Columbia (UBC). The muscle occurred in an 85-year-old female donor, whose cause of death was unrelated to the chest wall or thoracic cavity. The donor's musculoskeletal system was normal. The sternalis muscle is an unusual finding in anatomical studies, having a prevalence at autopsy of between 0.5 -23.5% (average 7.8%), and in-vivo of between 6.2 – 6.8%. We estimate the prevalence of the muscle in our study as 1.4%. It is important for healthcare workers to be aware of the sternalis muscle because of its significance as an unexpected finding during surgery or mammogram screening. A heightened index of suspicion for the occurrence of this muscle will prevent misdiagnoses and unusual tests, along with the attendant emotional or financial cost for patients presenting with this normal anatomical variation.

Introduction

The sternalis muscle is an uncommon anatomical variant found in the anterior chest wall. It runs subcutaneously along the sternum, anterior to the pectoralis major muscle, with fibres running parallel to the sternum and perpendicular to the pectoralis major¹. For a muscle to be classified as the sternalis muscle, it must be located between the superficial fascia of the anterior thoracic region and the pectoral fascia; must originate from the sternum or infraclavicular region; insertion must be on the lower ribs, costal cartilages, aponeurosis of the external oblique abdominis muscle, or the sheath of the rectus abdominis; and innervation must be by the anterior thoracic and/or intercostal nerves². The function of the sternalis is undetermined, however, it may play a role in the movement of the shoulder joint or elevation of the lower chest wall¹.

The nerve and blood supply of the sternalis muscle is variable. Original cadaveric observation pointed towards innervation by the medial or lateral pectoral nerves^{3,4}. Another possibility is intercostal innervation, as anterior intercostal nerve branches have been observed protruding through or medial to the muscle belly³. Blood supply is primarily by perforating branches of the internal thoracic artery, with additional supply from the pectoral branch of the thoracoacromial artery⁴.

Despite early (16th century) studies, the origin of the sternalis muscle is still unknown⁵. Common hypotheses suggest it arises from thoracic muscles including the panniculus carnosus, sternocleidomastoid, rectus abdominis and the pectoralis major⁴. The hypothesis attributing origin to the panniculus carnosus is no longer supported and the relationship of the sternalis muscle to the sternocleidomastoid was determined to be incidental⁴.

Possible innervation by the intercostal nerves supports origin from the rectus abdominis, but it is difficult to determine if the muscle is directly innervated by or simply in close proximity to the nerves⁵. It was also thought that the sternalis muscle could be an upward extension of the rectus abdominis, yet, fiber orientation of the sternalis is not consistent with the transverse fibers of the rectus abdominis, and is instead associated with the aponeurosis of the external obliques⁶.

The hypothesis regarding pectoralis major origin was initially disregarded. However, it is now thought that sternalis is a result of a portion of the pectoralis major being displaced and rotated during development⁷. The strongest evidence for a pectoralis major origin is based on innervation. In a systematic review of 375 studies, 51.9% found sternalis innervation was the pectoral nerve and 43.1%, the intercostal nerves⁴. However, the observed intercostal innervation may be inaccurate, resulting in the pectoral nerve comprising the majority of sternalis innervation.

Prevalence rates of the sternalis muscle in the literature, range from 0.5 – 23.5%, with an average of 7.8%³ - figures mostly derived from autopsy or cadaveric dissection. With in vivo studies made possible by multi-detector computed tomography (MDCT), cited sternalis prevalence rates are 6.2% and 6.8% in Korean and Chinese populations respectively^{1,8}. While these numbers are comparable to the cited average of 7.8%, higher rates have been reported in Asian populations (11.8%) and lower rates in European populations (4.4%)⁴. There is minimal to no difference in prevalence rates between sexes⁴. At UBC's Southern Medical Program, this is the first case of the sternalis muscle being observed out of approximately 70 retrospective dissections - a prevalence of about 1.4%.

Given its significant variation in presentation, numerous systems have been created to classify the sternalis muscle (Table 1). The earliest system proposed grouped the muscle based on the morphology of the muscle bellies. With time and the advent of MDCT, more detailed classification systems have emerged^{2,8,9}. The classification system that is now vastly used to classify the sternalis muscle is the one proposed by Ge et al.,⁸ which is based on MDCT findings.

Case Report

The present case is an 85-year-old female cadaveric donor whose cause of death was reported as advanced dementia. The donor was dissected as part of a FLEX (flexible learning) research project at the Southern Medical Program, a distributed campus of the Faculty of Medicine, UBC. According to available donor information, there was no history of any musculoskeletal abnormalities of the thorax or elsewhere in the body. The dissection was performed under the Human Donor Program of UBC and classified as Research Ethics Boards (REB) exempt. The cadaver was preserved and dissected using standard methods^{10,11}. Reflection of the thoracic superficial fascia revealed a bilateral muscle lying longitudinally above the plane of the pectoralis fascia and muscle (Figure 1). The muscle was oriented parallel and superficial to the sternum and medial and superficial to the pectoralis major. Its fibers ran perpendicular to those of the pectoralis major, but the muscle also consisted of a small number of fibers oriented parallel to, and continuous

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with the right pectoralis

Author	Year	Classification	Sub-classification
Jewel, et al.	2001	Type I: unilateral sternalis muscle	I1: simple unilateral belly I2: 2 or more unilateral bellies I3: muscle belly crossing the midline I4: unilateral belly passing into another muscle or into well-defined muscle bundles of this muscle: preclavicularis medialis, sternocleidomastoideus, pectoralis major
		Type II: bilateral sternalis muscle	II1: 2 simple symmetric muscle bellies II2: 2 simple asymmetric muscle bellies II3: 2 bellies connected with the pectoralis major on the ipsilateral side II4: 2 muscle bellies – one simple unilateral and the other connected with both right and left pectoralis major muscles
Raikos, et al.	2011	Unilateral sternalis muscle	A: single muscle belly B: sternomastalis muscle C: 2 or more muscle bellies D: muscle belly crossing the midline E: bicipital sternalis muscle crossing the midline F: muscle belly passing into a well-defined muscle or into a fasciculus of this muscle
Ge, et al.	2014	Type I: simple sternalis (single head and belly)	IA: muscle located in the same hemi-thorax IB: the superior end connects with the fusion of two sternocleidomastoids at the midline
		Type II: double/multi-headed sternalis	IC: the superior end crosses the midline and connects with the contralateral sternocleidomastoid or infraclavicular region IIA: muscle located in the same hemi-thorax IIB: at least one of the heads connect with the fusion of two sternocleidomastoids at the midline, the remaining heads are in the same hemi-thorax IIC: at least one of the heads crosses the midline to the contralateral sternocleidomastoid or infraclavicular region
		Type III: double/multi-bellied sternalis	IIIA: muscle located in the same hemi-thorax IIIB: at least one of the bellies connect with the fusion of two sternocleidomastoids at the midline, the remaining bellies are in the same hemi-thorax IIIC: at least one of the bellies crosses the midline to the contralateral sternocleidomastoid or infraclavicular region

Table 1: Summary of the various classification systems used to describe

the sternalis muscle.

major (Figure 1). Continuous tendinous attachments to the ipsilateral sternocleidomastoid muscle as well as the rectus abdominis sheath was observed bilaterally.

Based on the classification system proposed by Ge et al.,⁸ the right and left muscle would both be considered Type IB (Figure 1). The tendon of origin of the right sternalis appears slightly separated, but this is likely an artefact of dissection, not the presence of an additional muscle belly.

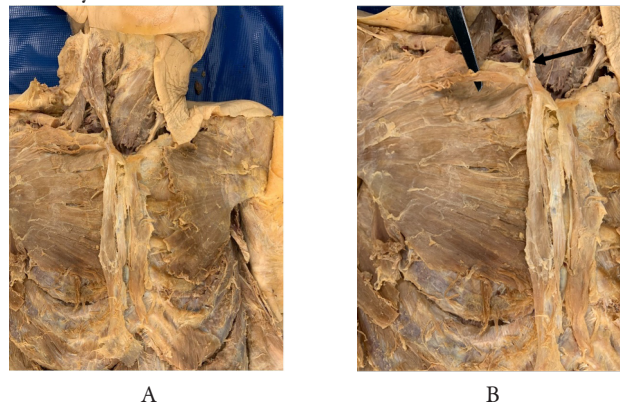


Figure 1: Superior view of the lower neck and thorax showing the right and left sternalis muscle, A – panoramic view and B – close up view.

Both superficial and deep fascia have been removed to expose the muscles. In B, note the right sternalis muscle fibers running perpendicular to, but continuous with clavicular fibres of the pectoralis major on the right side (raised by the tip of scissors). The sternalis was also continuous with the tendon of the sternocleidomastoid muscle on the right side (arrow).

Discussion

A lack of awareness of the sternalis muscle among physicians may create various clinical implications related to surgery, radiology, and oncology. It was found that only 3.8% of surgical residents were able to identify the muscle on CT or anatomical figure¹². Its unknown status and orientation of fibers could make its presence confusing if found incidentally during surgery. This in turn may lead to patients being under anesthesia for longer than expected and could alter the procedural plan¹³.

The pectoralis major is commonly used during skin sparing mastectomies to create a subpectoral pocket to house the breast implant. In the presence of sternalis, the pectoralis major may be laterally displaced leading to the possibility of poor aesthetic outcome of the implant¹⁴. This is especially a concern if the muscle is present unilaterally. Additionally, the subpectoral pocket may be too small, resulting in incomplete coverage of the implant leading to visible chest deformities.

Despite these disadvantages, the sternalis can have a surgical advantage, provided the surgeon is aware of its existence. Ishii et al.,¹⁵ describe a case in which the sternalis was sutured to the pectoralis major to prevent collapse of adipose tissue when inserting a tissue expander. Creating a submuscular pocket allows the implant to be placed in the appropriate position remediating the issue of asymmetry and/or visible deformity. In cases where a partial rib resection is required, a contour deformity might occur, which the sternalis muscle could be used as a muscle flap to fill¹⁶.

Radiologically, the sternalis muscle presents the most significance when performing mammography, as deep tissue adjacent to the chest wall is imaged, specifically on the craniocaudal view. This view extends

along the chest near the sternum, and in the presence of sternalis can reveal irregular structures which can initially be misidentified as masses¹⁷. Thus, recognition of the sternalis minimizes patient recall, follow-up exams, and unnecessary biopsies¹⁷. Diagnosis of the sternalis muscle can be made on physical examination by its location, configuration and lack of corresponding abnormality on ultrasound¹⁷. Opacities that are small, asymmetric and located at the medial posterior edge of a craniocaudal mammogram view are suggestive of the sternalis muscle and no further investigations are indicated.

Although uncommon, there has been one reported case of the sternalis muscle causing long-term pain and soft tissue swelling in the parasternal region. Sonography and MRI confirmed the presence of the sternalis muscle, with sonopalpation confirming it was the origin of pain¹⁸. It is thought that pain may have been due either to muscular imbalance, as significant hypoplasia of the right pectoral muscle was observed, or compression of either the lateral pectoral nerve or intercostal nerves¹⁸. Thus, patients presenting with long-term parasternal pain and soft tissue swelling should be investigated for the presence of a sternalis muscle.

Conclusions

Although there was no mention of muscle superficial to the sternum in textbooks that were consulted, anatomists are generally familiar with the sternalis muscle. Unfortunately, most physicians and medical students are unaware of its existence. By raising awareness of the sternalis muscle, its presence and significance will be recognized more readily in clinical contexts. This enhanced awareness should prove advantageous in surgical reconstructions following mastectomies, and preventing mammographic misdiagnoses, prolonged surgical time, and unnecessary testing, with the attendant emotional and financial cost to patients.

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Conflict of interest

The author has no conflict of interest to declare.

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Impact of the COVID-19 pandemic on the eye health of populations of low socioeconomic-status:

The need for diabetic retinopathy screening and access to spectacles

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Abstract

Canadian eye-care services were less used during the COVID-19 pandemic compared to prior rates. This could have long term economic and healthcare outcomes, especially for populations of low socioeconomic status. For individuals without pre-existing eye conditions, disruptions to access to screening for diabetic retinopathy and access to spectacle correction of refractive error can lead to declined eye health and functional vision impairment. Understanding the specific barriers exacerbated by the pandemic can reveal opportunities for improvement.

Introduction

The COVID-19 (Coronavirus disease 2019) pandemic drastically limited access to healthcare services, including the reduced utilization of eye-related care. In Canada, an estimated 143,000 necessary eye surgeries were missed or delayed in 2020.¹ Considering the healthcare costs, productivity losses, and cost from reduced wellbeing, there is a projected \$1.3 billion cost attributed to the underutilization of eye health services in 2020 that will be seen for Canada in 2021-2023.¹ Factors contributing to this underutilization include cancelled or restricted elective surgery times, closure or limited access to outpatient clinics, and COVID-19 related obstacles leading to patients' declined care of eye health.¹

It is well established that vulnerable populations of low socioeconomic status (SES) disproportionately bear the brunt of both COVID-19 infection outcomes and collateral loss from the strategies employed to limit the pandemic.² The article will explore how the COVID-19 pandemic has impacted the eye health of urban populations with low SES. The focus will be on two of the largest areas of care needs for those without known eye conditions: diabetic retinopathy screening and accessing correction using spectacles.

Screening for Diabetic Retinopathy

Diabetic retinopathy is the leading cause of blindness and visual impairment in the Canadian working-age population.^{3,4} A comprehensive review of existing studies for at-risk populations have identified Indigenous Canadians to have increased proportion of developing diabetic retinopathy,⁵ where urban/suburban residents experience higher rates than non-urban indigenous residents.⁶ It is recommended for people with diabetes to undergo an asymptomatic eye-disease screening examination performed by an optometrist or ophthalmologist every year,³ which is important to prevent vision loss and progression of proliferative retinopathy.⁷ Currently, there is no published Canadian data on the extent of reduction of retinopathy screening examinations during the pandemic. However, a study commissioned by the Canadian Council of the Blind utilized data from the United Kingdom's pandemic outcomes to extrapolate that in Canada, there was an estimated 11,575 missed referrals for diabetic retinopathy screening, leading to around an additional 199 people likely to have developed vision loss.¹

For diabetic retinopathy and its screening, populations with low SES face barriers that increase the likelihood of both needing care and missing care. Seminal studies have found that patients with diabetes in lower socioeconomic positions, as gauged by household income, employment status, and living in underprivileged areas of urban settings, are associated with an increased risk of retinopathy.^{8,9} In Canada prior to the pandemic, diabetic patients with lower income were found to have a 40% decrease in odds (odds ratio 0.60) of utilizing eye screening services for retinopathy.¹⁰ Canadian patients with diabetes had identified that uncertainty around costs associated with eye examinations, difficulty negotiating time-off, knowledge gaps, and shifting life priorities such as finances all contributed towards barriers to attending diabetic retinopathy screening.¹¹ For Canadians who are homeless, a study showed that only 14% of the population surveyed had seen an optometrist/ophthalmologist in the past year, compared to the 41% rate of the general Canadian population.¹²

These factors of homelessness and barriers to accessing screening were exacerbated during the pandemic.¹ Stakeholders for the Canadian Council of the Blind reported pandemic-related delays in governmental mobility assistance services that would contribute to missed eye examinations.^{1,13} People of low SES were disproportionately impacted by the pandemic, including through job insecurity due to holding uncredentialed positions that were more vulnerable to unemployment, reduced access to alternative housing (e.g. shelters), and lack of healthcare infrastructure in communities of low SES.² Of the over 11,000 estimated missed referrals for retinopathy screening in Canada, diabetic patients with low SES face more barriers that increase their likelihood of missing their retinopathy screening, thus incurring the resulting vision/health consequences of untreated disease progression.¹

Access to Spectacles

Spectacles (i.e. glasses or contact lenses to correct refractive error) are deemed Priority Assistive Products and categorized by the World Health Organization as "an absolute necessity to maintain or improve an individual's functioning."¹³ Canada ratified the mandate of the United Nations Convention on the Rights of Persons with Disabilities to ensure access at an affordable cost for all individuals.¹⁴ In British Columbia, adults can receive glasses coverage either from Indigenous Services Canada (every 2 years) or BC Employment and Assistance (every 3 years).^{15,16} If glasses undergo breakage or loss before the allotted time period, replacement is only considered under exceptional circumstances requiring submission of incident, insurance, medical or police reports, and will not be considered for causes of misuse or carelessness.^{15,16}

Faced with high demands of acquiring coverage, populations of low

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SES forgo the use of glasses or overwear contact lenses. In a study prior to the pandemic, Canadian people that were homeless only reported a 29.5% portion of having refractive glasses in their possession out of those who required them, and 70.0% of all participants surveyed expressed dissatisfaction with their current vision.¹² Uncorrected refractive error was the largest contributor to functional visual impairment in this population.^{12,17} To avoid the risk of breaking or losing glasses, especially in inner-city environments with challenges in maintaining possessions,¹⁷ it can seem more prudent to wear contact lenses, such as wearing the same disposable contact lenses for periods of months. However, overwearing contact lenses is a major risk factor for keratitis, which is a corneal infection leading to ulceration and blindness.¹⁸ Case reports have documented how non-compliant contact lens overwearing compounded with difficulties navigating homelessness and comorbid substance use can precipitate complicated and vision threatening presentations of eye infection.^{19,20,21}

The pandemic, being a time of devastating financial strain and restricted access to glasses/contact lenses distributors, had further limited access to reliable vision aids. A survey of working professionals with dry-eye and vision strain in Canada, USA, and UK reported that of those requiring prescription eye devices, 23% of participants had lost access during the COVID-19 pandemic.²² It is reasonable to surmise that people with low SES who are homeless, unemployed and/or under increased financial strain would likely have experienced an equal or higher proportion than the 23% found in this study, given the increased obstacles faced by these populations.² As well, the limited availability of optometry and ophthalmology appointments would have further delayed care for those who developed eye infections from contact overuse, leading to poorer care outcomes.¹

Conclusion

Reduced access to diabetic retinopathy screening and vision aids presents as two major sources of declined vision and eye health in individuals of low SES. The stress of the COVID-19 pandemic on our public health systems revealed and further widened the existing gaps of inequitable delivery of care for this vulnerable population, leading to anticipated poorer eye health outcomes and resulting economic costs in the future. Targeting advocacy strategies and community outreach initiatives to address these issues is a promising opportunity to improve visual functioning and eye health, during both pandemic and post-pandemic times.

Conflict of interest

The author has no conflict of interest to declare

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Is a cure for type 1 diabetes on the horizon?

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Abstract

Type 1 diabetes (T1D) is a chronic autoimmune condition characterized by the progressive destruction of β -cells that produce insulin. Although insulin injections are lifesaving, many patients struggle with hypoglycemia unawareness or extreme glycemic lability, leading to significant morbidity and mortality associated with the challenges and flaws in attempting to regulate insulin through a syringe. Cell replacement therapies, which are aimed at replacing β -cells that are lost in T1D, show great promise achieving insulin-independence and allow for the tighter regulation of insulin secretion in vivo, but many hurdles must be addressed before this treatment modality can be feasible at the clinical level. This commentary discusses these challenges, and highlights current efforts aimed at solving them.

Introduction

Type 1 diabetes (T1D) is an autoimmune condition characterized by the progressive destruction of insulin-secreting β -cells, leading to insulin deficiency and hyperglycemia.¹⁻⁴ Though insulin injections have been life saving for almost 100 years, patients struggle with tremendous morbidity and mortality as insulin injections cannot mimic the regulated secretion of endogenous insulin by the pancreas. Currently, the only experimental cell replacement therapy available to patients with T1D is pancreatic islet transplantation, where pancreatic islets from living donors are transplanted into individuals with T1D. Although islet transplantation has shown great promise as a potential cure for those with T1D, this therapy is limited by the need for lifelong immunosuppression, paucity of islet donors, and primary graft failure.⁵ Human embryonic stem cells (hESCs) hold great promise as a potentially unlimited source of β -cells for transplant due to their ability to self-renew and their potential to differentiate into different cell types⁶, but many hurdles must be addressed before stem cell-based therapies can be clinically feasible for diabetic patients. These hurdles range from difficulties in generating mature and functional insulin-secreting β -cells with high enough yield and efficiency, and issues with immune rejection of implanted hESC-derived β -cells.⁵ This commentary aims to provide a brief overview of current research efforts aimed at solving these issues.

Difficulties In Generating Mature And Functional Insulin Secreting Cells

The differentiation of insulin-secreting β -cells from hESCs in vitro is a complex multistage protocol and involves the consecutive regulation of various signalling pathways involved in pancreatic organogenesis.⁵ Once differentiated, cells are examined for the expression of key human β cell maturity markers such MAFA, PDX1, NKX6.1, NKX2.2, INS, IAPP, PCSK1 and UCN3, and for the presence of glucose-stimulated insulin secretion (GSIS).⁷⁻¹⁰ Although there has been a considerable push to successfully generate insulin-secreting β -cells derived from hESCs over the past two decades, questions still remain about (1) the maturity of these hESC-derived β -cells and their ability to adequately respond to glucose stimuli, and (2) the differentiation efficiency of current protocols aimed at producing insulin-secreting cells.⁵ For example, early efforts by D'Amour and colleagues to generate β -cells resulted in polyhormonal cells that failed to respond to glucose and maintain the expression of key β -cell maturity markers such as PDX1 and NKX6.1,

with the average percentage of insulin-positive cells being 7.3%.¹¹ Since then, significant advancements have been made in efficiently generating monohormonal cells that are transcriptionally similar to mature β -cells, glucose-responsive and capable of regulating blood glucose in mice weeks after transplantation. However, these β -cells are still functionally immature, secrete low levels of insulin in response to glucose stimulation, lack dynamic insulin secretion, and still exhibit a lower expression of key β -cell transcription factors such as MAFA and UCN3 relative to mature human β -cells.^{12,13} Despite these drawbacks, recent publications with refined protocols have reported hESC-derived β -cells with improved differentiation efficiency (up to 90%), higher GSIS, dynamic insulin secretion, and fast in vivo glucose regulation upon transplantation.¹⁴⁻¹⁸ With further advancements in our understanding of β -cell development, and further refinements to differentiation protocols to increase efficiency and scalability, we may be very close to seeing a robust stem cell product for T1D in the near future.

Immune Rejection Of Transplanted Cells

The autoimmune pathogenesis of T1D presents a hurdle to the widespread clinical use of stem-cell based therapies. In those with T1D, β -cell destruction occurs when autoreactive T-lymphocytes recognize β -cell antigens such as insulin and glutamic acid decarboxylase 65 (GAD65).^{19,20} Therefore, the presence of autoreactive T-lymphocytes presents a significant challenge, as the introduction of hESC derived β -cells can induce a primed immunological attack against transplanted cells resulting in graft failure and rejection.^{21,22} One specific way researchers are tackling this issue is through the use of a semipermeable encapsulation device that acts as physical barrier between transplanted hESC derived β -cells and the recipient's immune system, which improves safety and reduces the need for immunosuppression.²³ The key aim of macroencapsulation is to create an environment that allows for the normal secretion of insulin in response to changes in glycemia and the free exchange of nutrients and wastes, while still maintaining graft survival by sequestering these cells from the host's immune system.²³ However, studies suggest that macroencapsulation prevents the normal maturation and function of hESC-derived β -cells in vivo, likely because current macroencapsulation techniques trigger inflammation and allow the build-up of islet amyloid polypeptide (IAPP) aggregates known as amyloid fibrils, which are cytotoxic to implanted cells and limit nutrient and oxygen delivery.^{24,25} One way this is being addressed is through the implementation of a next-generation macroencapsulation device that allows for substantial graft revascularization, which could prevent the aggregation of IAPP by reducing the time it takes for secreted IAPP to diffuse from β -cells in to the circulation.²⁵ However, facilitating revascularization through this macroencapsulation device will inevitably allow the access of immune cells to the site of engraftment, which

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would require consistent immunosuppression to limit alloimmune, and possibly autoimmune, reactions to implanted cells.²⁶ Fortunately, advances in genome editing could provide an opportunity to manipulate hESCs prior to differentiation and transplantation, by making certain genetic changes that enhance the survival of transplanted hESC derived β -cells in vivo. Right here at the University of British Columbia (UBC), researchers are looking at whether or not β -cell expression of a potent chemokine known CCL22 could improve graft outcomes, as it can attract immune-suppressive regulatory T-cells to the site of transplantation and can downregulate the local immune response.²⁵ Such genetic changes, if successful, could obviate the need for encapsulation, or improve graft survival and function within macroencapsulation devices, leading to a more robust stem cell product with widespread clinical adaptation.

Conclusion

Although considerable advancements have been made in generating more robust and functional hESC-derived β -cells over the past 2 decades, many hurdles, including our incomplete understanding of β -cell development and the risk of graft rejection still stand in the way before type 1 diabetics can actually benefit from this treatment modality. Nonetheless, diabetes researchers around the world are all working together to find solutions to these challenges. With promising results recently being reported in a phase 1/2 trial testing hESC-derived β -cells²⁶, we might be looking at a future where insulin injections are a thing of the past.

Conflict of interest

The author has no conflicts of interest to declare.

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Starting medical school during the COVID-19 pandemic: A UBC perspective

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Abstract

The medical class of 2024 started medical school in unprecedented times due to the COVID-19 pandemic. Innovative solutions were required from the faculty to support the shift to online learning with tools such as Zoom™. Due to the unprecedented times, students found themselves amassing their medical education from the comfort, or discomfort, of their homes. Students more than ever had to be resilient in a time of uncertainty and social isolation. The ripple effects have the potential to change medical education forever and give students the flexibility to support their own learning styles.

Introduction

Medical school acceptance is often described as the best day of a student's life - an experience that only gets better on the first day of school when students meet their new classmates, sit in new lecture halls, and envision their next four years of medical school. This picture looked different for the medical classes of 2024 who started school online during the coronavirus disease 2019 (COVID-19) pandemic. As students eagerly awaited their first day, the faculty was working tirelessly to not only manage current medical students entering clerkship, beginning electives and residency, but also to re-model medical education for a global pandemic. In this article we aim to share a perspective about the medical school experience during COVID-19.

Starting Medical School During COVID-19

The University of British Columbia (UBC) houses Canada's first distributed MD Undergraduate Program (MDUP).¹ Historically all students spend their first semester at the UBC Vancouver campus, before heading to their respective sites in Kelowna, Prince George, Victoria or remaining in Vancouver.² COVID-19 changed everything, with the introduction of restrictions on gathering sizes and mask mandates to reduce virus transmissibility. With a summer to prepare for COVID-19, the Class of 2024 became the first class to start at their distributed sites, beginning their medical education virtually. The learning environment for the Class of 2024 was limited to the Zoom™ classroom for their first year.

Zoom™ presented a learning curve for faculty and students alike. In their office, faculty would now record lectures in advance or provide live lectures to an audience devoid of real-time feedback/response. Students were limited to their households for eight or more hours of online school each day. The isolation caused by COVID-19 required resiliency from the Class of 2024.

Furthermore, cadaveric dissection was halted. The faculty quickly adapted, building a virtual anatomy laboratory experience where students interact with 3D models of specimens through a web interface.³ Laboratory handouts with images of cadaveric specimens were assembled in place of hands-on cadaver learning.

The Benefits of Online School

Despite challenges transitioning to online studies, students and faculty alike learned a substantial amount throughout the year. Many students displayed considerable resiliency, which will be discussed further

in a subsequent section. Additionally, students even found some advantages of online delivery. The flexibility within students' schedules and the significant reduction of time spent commuting gave them the opportunity to optimize their schedules. Many students used this extra time and flexibility to engage in extracurricular activities like medical interest groups, recreational sports teams, or for self-care. Additionally, students could attend conferences and interest group events online, allowing for networking with residents and attendings from any location.

In fall of 2021 the Classes of 2024 and 2025 commenced in a hybrid learning model. In this model, cadaveric dissection resumed in-person along with collaborative small-group sessions, while lectures remained available over Zoom™ or for viewing in a lecture hall. Retaining the Zoom™ links for lectures provided students with flexibility within their schedules. We believe that the hybrid model allows students to adapt their learning to match their individual learning styles.

The Downsides of Online School

Although there have been benefits to COVID-19-adapted medical education, there are also shortcomings to being a medical student in a pandemic – the most obvious being the lack of real patient contact. Family Practice placements were intended to enable real patient experience and practice skills learned in clinical sessions, but the variability in these sessions was vast and many students engaged predominantly in virtual patient visits. With the return to direct patient clinical experiences, students will need to maximize opportunities to hone their acquisition of patient interaction and physical exam skills over their remaining years of the program.

With the implementation of online school, students were no longer able to experience cadaveric dissections as part of their anatomy curriculum. Cadaveric dissection alongside pro-section examination has substantial evidence for effectively teaching medical students anatomy.⁴ Although the virtual anatomy laboratory produced was impressive, the experience of observing real-life anatomical specimens is unparalleled when compared to specimens viewed on a screen. From our perspective, having now experienced both online and in-person anatomy, activities such as determining where a structure lies in relation to other landmarks and being able to rotate specimens have facilitated better learning in our anatomy laboratories.

For the 2020-2021 school year, shadowing was halted; therefore, the opportunity to explore different specialties was diminished. Exams also shifted online, with Objective Structured Clinical Exams (OSCEs) taking place over Zoom™. Instead of performing physical exam maneuvers, students verbally explained them while an examiner listened. Limitations on school activities coupled with public health restrictions made meeting classmates and building connections and friendships more difficult. In our experience, students at the distributed sites had an

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easier time connecting due to the size of their classes.

Resiliency and New Skills Going Forward

Although medical students are generally studious and dedicated individuals, pandemic-era students faced circumstances necessitating greater self-motivation. Students were forced to be resilient and form positive coping skills against burnout.⁵ In contrast, students in preclinical years have been found to adopt more negative coping skills than students in clinical years.⁶ Resiliency and skills such as grounding, problem solving, and adaptability are known to be important to the mental health and career longevity of practicing physicians.⁷⁻⁹ Although our classmates faced an arduous first year, we hope that they will benefit from the skills gained during this time.

Conclusion

Starting medical school during a pandemic was no small feat. Many changes were made to how the MDUP was delivered during this time; classes started at the distributed sites, Zoom™ was the main platform for lecture delivery, and students found themselves at home for most of their days. This new model came with advantages and disadvantages. Some valued innovations will likely change medical education permanently. Perhaps, UBC will continue to utilize Zoom™ for lectures and have students start at their sites. Overall, the medical students in this class faced challenges unlike any class before them. Thankfully, the Class of 2024 can always feel proud that they successfully navigated their medical education amidst a global pandemic.

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Conflict of interest

The authors have no conflicts of interest to declare.

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A biopsychosocial approach to the effects of COVID-19 on palliative care

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Abstract

The COVID-19 pandemic created unusual barriers to care for patients suffering from life-limiting illnesses. Consequences of COVID-19 such as biological symptom burden, social isolation, and psychological grief led to adverse experiences for patients, families, and providers. Palliative care medicine focuses on holistic care and relief of suffering, being a key pillar for the management of COVID-19. However, the pandemic emphasized how these services are currently undersupported. Strategies for improvement may include training for non-palliative providers, increased telemedicine services, and earlier intervention for COVID-19-exacerbated mental illnesses. Palliative care must become a shared responsibility, rather than one managed by a specialized group.

Introduction

The field of palliative care medicine considers the whole patient - the biological, psychological, and social aspects.^{1,2} Palliative care aims to address not just symptoms, but also quality of life, support systems and goals of care of the patients.^{1,2} Palliative care as a specialty started with a focus on patients at the very end of life.¹ There has since been an increase in advocacy for moving palliative care upstream to patients with longer prognosis, due to more evidence that the early introduction of a palliative approach to care can decrease health care spending, improve quality of life, and prolong patient survival.^{3,4}

With its holistic focus on maximizing comfort and relieving suffering [Figure 1], palliative care services were a key pillar in the management of the coronavirus disease 2019 (COVID-19) pandemic.⁵⁻⁷ The global devastation of the pandemic is reflected by the staggering six million mortalities as of May 2022.⁸ Along with this large-scale loss of life, the pandemic has created unusual challenges for the care of patients with life-limiting illnesses. Restrictions on hospital visitation hindered the communication with loved ones that patients so desperately needed in periods of suffering.⁵ Decisions surrounding end-of-life and goals of care, typically made by patients in careful collaboration with family members and health care providers, were often forced by circumstance

to occur with an unfitting urgency.^{5,9}

The COVID-19 pandemic has emphasized the importance of palliative care and its underserved potential within our health care system. In this article, we will discuss the impacts of COVID-19 on the delivery of palliative care and suggest possible future solutions.

What are the implications of COVID-19 on palliative care?

Among all fields of medicine, palliative care stands out as a champion in the prioritization of holistic patient health and the consideration of a biopsychosocial approach to care [Figure 2].^{1,10,11} The COVID-19 pandemic has taken a toll on all of these aspects, with both short-term and long-term effects.^{5,6}

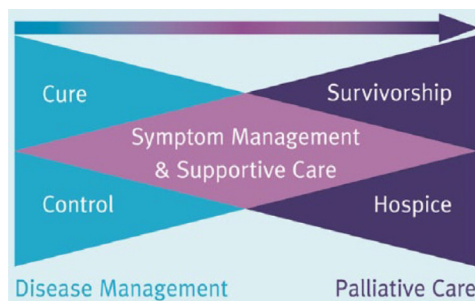


Figure 1: The bow-tie model of palliative care. The two overlapping triangles represent the interconnecting principles of disease management and palliative care. The process gradually switches in focus over time, where survivorship is a possible outcome. Hawley P. Barriers to access to palliative care. *Palliat care* 2017; 10: 1178224216688887.

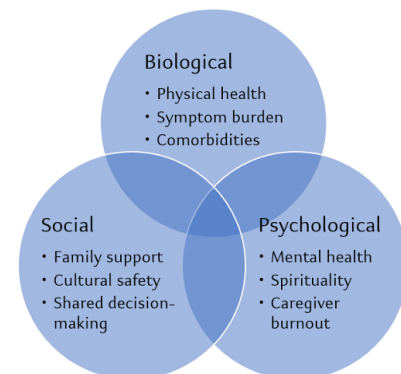


Figure 2: The biopsychosocial model of care. Represented as a Venn diagram showing the intersection between different aspects of health, the biopsychosocial approach holistically considers the interdisciplinary factors in a patient's life to provide full care.

Biologically, the symptom burden of COVID-19 is vast, including features such as breathlessness, arthralgias, and chest pain; these concerns all may require a palliative approach to care with a focus on symptom management.⁵ Similarly, the post-infectious phenomenon of COVID-19 (colloquially known as “long COVID”) can persist for months after infection, with patients who are older and have multiple comorbidities being at higher risk.^{12,13} Considering the significant number of patients suffering from symptom issues and the broad scope of their medical needs, simply having more funding for specialist palliative care providers will likely be insufficient - there is an urgent need to expand primary palliative care training for all care providers from physicians to allied health workers.^{14,15}

Socially, the isolation in health care settings due to public health measures caused significant burden. Many patients feared going to a hospital or hospice, increasing the number of home deaths that

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happened without adequate supports.^{16,17} Patients in hospital were often unable to access their physicians as readily as before, leading to delayed diagnoses and late presentations in crisis.⁵ The emotional difficulty for patients and their families was immense, especially for those who died in institutions without the presence of their loved ones.⁶ Notably, patients with COVID-19 from marginalized populations (e.g. those with mental health illnesses, substance use disorders, homelessness) became even further isolated from accessing adequate health care.^{18,19}

Psychologically, the negative impacts of the pandemic extended to both patients and providers alike. Patients with COVID-19 often experience anxiety, agitation, and depression.^{20,21} The families of deceased patients with COVID-19 are at higher risk for developing mental health conditions such as complicated grief and post-traumatic stress disorder, compared to those who are non-bereaved.²² As a result, more robust psychological and bereavement supports are needed to prepare for the expected, ongoing increase in the prevalence of mental illness and trauma.^{22,23}

Furthermore, the unique levels of exposure to suffering and death during the pandemic has been a considerable burden among clinicians. Under strained conditions while caring for COVID-19 patients, health care providers were forced to make life-changing decisions such as allocation of scarce resources.²⁴ This can cause them to experience a huge magnitude of moral injury - “the psychological, social and spiritual impact of events involving betrayal or transgression of one’s own deeply held moral beliefs and values occurring in high stakes situations.”²⁴ The effects can cause destructive emotions such as guilt, remorse, extreme negative self-attributions, lack of self-forgiveness, self-punishment, and a loss of identity/role.²⁴ Limitations on peer support among providers for knowledge sharing and emotional debrief may further contribute to burnout and fatigue.^{25,26}

What are possible solutions?

Given the multidimensional nature of palliative care, a multifaceted approach will be required for improving its integration into patient health. Solutions should be aimed at each of the biological, social, and psychological aspects of care. Respectively, interventions may include: 1) promotion of COVID-19 palliative care education for non-palliative specialists, 2) increased uptake and variety of telemedicine options, and 3) strategies to address the long-term effects of grief and moral injury amongst patients and health care providers.

Given its prevalence, variable course, and potential for morbidity, COVID-19 must be recognized as a critical diagnosis requiring symptom relief as a mainstay of management - not only from palliative specialists, but from all providers.^{14,15,27} Goals of care must be constantly revisited in partnership with patients and their families, but a lack of guidance in these discussions for COVID-19 was identified as a barrier among providers.²⁸ Increased education and promotion of palliative training targeted towards non-palliative specialists can facilitate a more widespread delivery of these services. The practice of palliative medicine must become a shared responsibility, rather than one managed by a specialized group.^{14,15} Efforts to put this into place have begun - many algorithms and quick-access COVID-19 resources for symptom management and advanced care planning have been created.^{29,30} There must be ongoing promotion and visibility of these resources to support their integration into care.

To mitigate challenges of social isolation, the innovation and influx of telemedicine may be an important support measure.³¹ Implementation of telehealth systems during the pandemic has been received favourably in

many health care settings, including on palliative services.^{32,33} However, while uptake of technology such as video-conference tablets increased significantly during the COVID-19 period, further work can be done to include this as a standard of care and to expand its scope. For example, virtual support groups targeting family members of COVID-19 patients could help support mental health, grief and bereavement, beyond being used for patients to communicate with loved ones.³¹

Finally, the psychological long-term effects of the pandemic may be addressed through provider training to recognize COVID-19 experiences as a risk factor for several health conditions.^{20,23} With projected increases of illnesses such as prolonged grief disorder and post-traumatic stress disorder, especially among those who experienced an unexpected loss or death due to COVID-19, early identification and support (e.g. bereavement resources for families) will be paramount for recovery.^{22,23,34} Similarly, workplaces must promote organizational-level supports to address the deep-rooted impacts of moral injury among health care providers.^{24,35,36} Among many possibilities, these may include creating updated decision-making guidelines to remove the ethical responsibility from direct providers, proactively offering spaces for dialogue of distress and self-forgiveness, as well as opportunities to access compassion-based therapies and psychoeducation.²⁴

Conclusion

In our current culture of health care, it is easy to measure the impact of global crises solely in terms of the objective epidemiological statistics. However, the COVID-19 pandemic has shown the need to focus on the holistic experiences of patients, families, and providers. All patients should have access to a palliative approach to care, and the delivery of these services should be incorporated in every physician’s practice. Among providers, palliative medicine must become a shared responsibility and field of practice. Altogether, the lessons learned during the COVID-19 pandemic along with the identified need for increasing palliative care training and measures will serve to better prepare our health care system in responding to future crises.

Conflict of interest

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Science communication in the age of misinformation: Lessons from a data science podcast

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Abstract

Throughout the COVID-19 pandemic, there has been a proliferation of misinformation and fake news on topics ranging from treatment choices for COVID-19 to public health and policy. More than ever, scientists and doctors are needed to combat this new infodemic. Therein, the authors discuss their approach to science communication in an age of misinformation through examples from their data literacy podcast, *The Secret Life of Numbers*. Science communication is an essential component of research, so much so that our responsibility as scientists and medical professionals is not complete until findings are effectively communicated.

Our new “-demic”

While “pandemic” has become part of our everyday vernacular, a new “-demic” has been on the rise: an infodemic. The World Health Organization (WHO) defines infodemic as “too much information including false or misleading information in digital and physical environments during a disease outbreak”.¹ An overabundance of information, particularly misinformation, can have dire consequences, including sowing distrust of mainstream science and public health. Indeed, during the COVID-19 pandemic, we have entered a new era of fake news and alternative facts. Some notable highlights include controversy between Joe Rogan and Spotify regarding false health claims on his podcast *The Joe Rogan Experience*, the craze surrounding ivermectin as a miracle drug for COVID-19, and when Donald Trump recommended injecting disinfectant as a means of treating COVID-19 infections.²⁻⁴

A key antidote to the misinformation crisis is providing easily accessible, high-quality, digestible information to the public. When science becomes political, and public health becomes polarizing, we

need experts on the front line reaching out to the masses. In many ways, doctors and scientists have already answered this call by sharing their expertise in bite-sized posts on TikTok and other social media platforms.^{5,6} By increasing public understanding of how research is conducted and providing distilled synopses of relevant research at an accessible level, we can improve scientific literacy and critical reasoning. Science communication is an umbrella term for both the public dissemination of science by experts and a dialogue between the public and experts.⁷ A key aim of science communication is to translate scientific findings and principles to make them more readable and relatable to the public. It is with this hope that we launched our science communication podcast focused on data literacy, *The Secret Life of Numbers*.⁸

The Process of *The Secret Life of Numbers*

Our goal at *The Secret Life of Numbers* is to encourage data literacy. With our combined knowledge in biochemistry, medicine, and data science, we explain the mathematics and equations that shape everyday numbers. The podcast was developed during the early days of the COVID-19 pandemic as we realized that not everyone understood the numbers

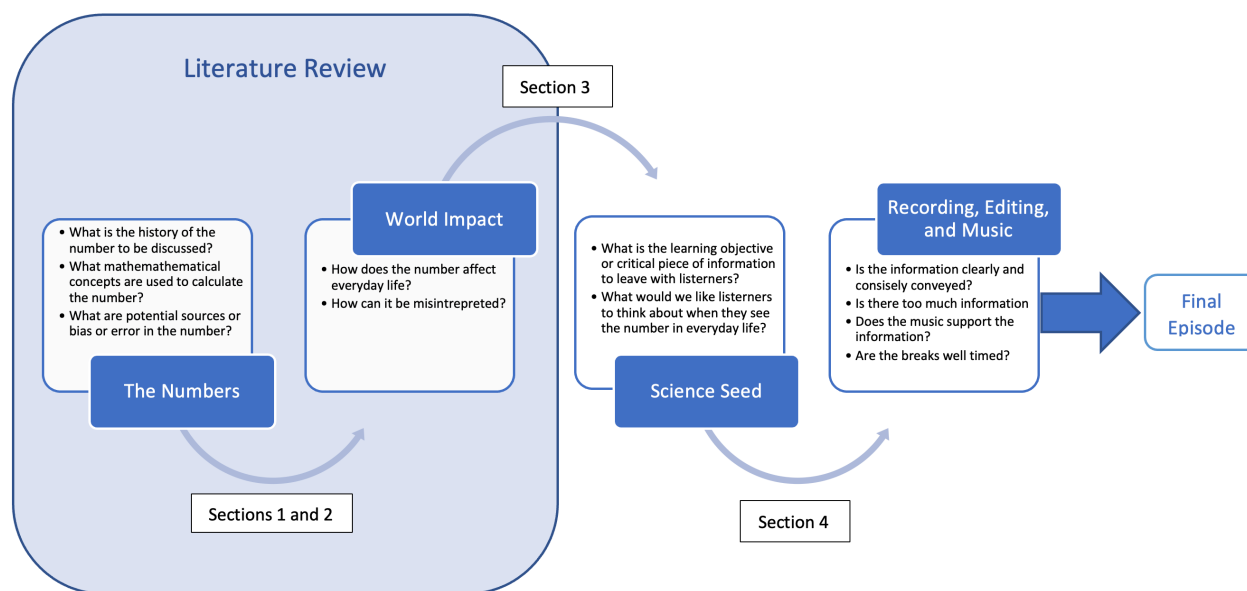


Figure 1. Flow chart of the process of creating an episode of *The Secret Life of Numbers* podcast.

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we were hearing about the pandemic. More broadly, we realized how little we question the numbers we hear daily. From our own intellectual curiosity, and our desire to share our knowledge, we began the podcast.

Creating an episode of *The Secret Life of Numbers* follows a distinct process led by our guiding principles and the questions we strive to answer for our audience. We have four sections to an episode which are illustrated in Figure 1: an introduction to the number, an explanation of its origin and any underlying statistics, a discussion about how the number and adjacent scientific concepts fit into a larger worldview, and a takeaway message in our “Science Seed” segment. For example, our first episode is about whether antibacterial towelettes really kill 99.9% of germs. After introducing the topic, we explain the regulations and tests that are conducted by scientists and outlined by organizations such as the International Organization for Standardization (ISO). In the case of antibacterial wipes, carrier testing is used. This testing involves a carrier such as a glass slide being treated with the wipe and exposed to specific strains of bacteria at measured concentrations. After an incubation period in the bacterial solution, the carrier is then tested using cell culture methods to see if the wipe was truly able to kill the bacteria it was exposed to.⁹ But there’s a catch: does this really mean that 99.9% of all germs were killed? If so, how does this apply to you?

These questions lead us to the next part of an episode, where we explain the impact that these numbers have on our everyday lives. For example, while hand sanitizers are effective at killing the bacteria on which they are tested, they do not remove dirt and debris.¹⁰ It is for this reason that handwashing is often recommended, if possible, in place of hand sanitizer.¹⁰ Here we arrive at the “Science Seed” segment which challenges listeners to think critically about the numbers that they encounter in their everyday life by providing a bite-sized scientific or statistical principle. In this episode, the “Science Seed” is the difference between efficacy, the performance of an intervention under ideal conditions (i.e. a laboratory setting), and effectiveness, the performance of an intervention under “real world” conditions. In the case of over-the-counter hand sanitizer and towelette wipes, unless used as directed, they will not be as efficacious as initially measured in the lab setting. Our final step is editing and post-production where we listen for clarity and concision in our content and finalize the episode with music breaks to create a seamless listening experience.

As of October 2022, *The Secret Life of Numbers* has released three full seasons with 30 full episodes. We have grown the podcast to have listeners in 40 countries around the world and counting. Season 4 of the podcast is set to be released early 2023.

Fighting the Infodemic

As scientists, we see it as part of our role to foster data literacy and encourage the public to think critically about the media and information that they consume. Now, during this time of what seems like infinite data and information, those that can explain it are needed more than ever. As Mark Walport, the former Chief Scientific Advisor to the United Kingdom Government, once said “Science is not finished until it’s communicated.”¹¹ Indeed, our responsibility as scientists and medical experts is not completed until it has been translated to the public. We hope that by sharing our approach to science communication in a podcasting medium, we will inspire other scientists, medical students, and doctors to fight the infodemic.

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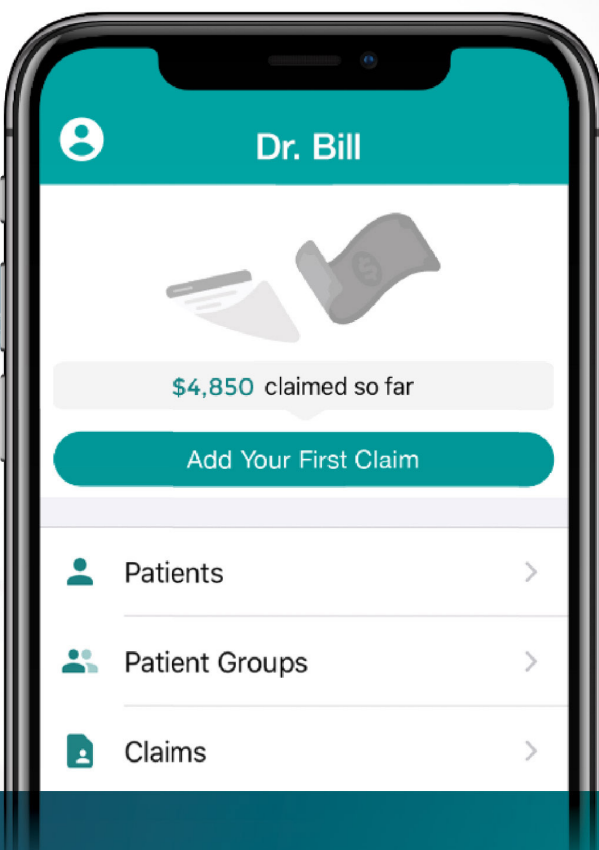
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