Chapter

Implications of COVID-19 on Public Policy, Supply Chain Disruptions, and Monitoring Methods

Timothy J. Tse, Farley Chicilo, Jeffrey Popiel and Martin J.T. Reaney

Abstract

Transmission of the severe acute respiratory syndrome coronavirus 2, referred to as COVID-19, has persisted beyond 2020 and led to a global pandemic with far reaching consequences. Many changes in public policy and health measures were developed and implemented with the intention of slowing the spread of the novel virus. Disruptions from the global pandemic created major supply chain consequences due to stockpiling of essential goods (alcohol-based hand sanitizers and surface disinfectants), impacts on trade routes, and limitations on modes of transportation due to border closures. Rapid increase in the use of hand sanitizers and surface disinfectants significantly affected the production capacity of high-quality ethanol (e.g., USP and FCC grade) resulting in regulatory changes in countries facing shortages. Prompt enactment of government policies allowed for use of alcohol with higher impurities to offset heightened demand and increase commercial availability. Changes in monitoring methods were also observed, where many agencies began to track viral shedding through municipal wastewater. In this chapter, we will discuss the impacts of COVID-19 on public policies and health measures, economics as it relates to supply chain disruptions, and the implementation of novel monitoring methods to survey the spread of COVID-19.

Keywords: COVID-19, public policy, monitoring methods, hand sanitizer, surface disinfectant, pandemic

1. Introduction

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; aka. COVID-19) has led to unprecedented global responses in the attempt to limit and slow propagation of the virus. These responses included the shutdown of major manufacturing plants [1], limitations on social gatherings, travel and transportation restrictions, enacting state of emergencies, and public health measures (e.g., social distancing, use of face coverings and hygienic practices, closures of non-essential businesses and schools, and vaccine mandates) [2]. Even with the development and implementation of safe and effective vaccines, and continued efforts to prevent transmission among the public, COVID-19 has persisted in spreading globally, and new more virulent variants have evolved.

The enactment of public policy restrictions, including social distancing, travel restrictions, access to testing, and contact tracing initiatives decreased COVID-19 infection, morbidity, and mortality rates [3, 4]. Such policies and tools were especially effective in slowing transmission and reducing the strain on healthcare facilities that have been stretched beyond their typical operating capacity [5]. Many governments implemented a variety of technologies, incentives, and practices to track infection, promote vaccination, and enforce restrictions [6]. Biomolecular approaches (e.g., nucleic acid amplification tests) were also implemented to help provide quantitative numbers to investigate spread and infection rates. Altogether, these technologies were implemented to slow the spread of infection and provide strategic advice for informing public health policies.

Unfortunately, economic recovery from the COVID-19 pandemic has been slow, primarily due to supply chain disruptions that have led to low inventories, employment layoffs, and reductions in industrial production and services [1]. Furthermore, as restrictions began to ease, formerly constrained demand for consumer goods surged beyond manufacturing capacity. With diminished inventory and a weakened shipping industry, recovery was slow, and meeting consumer demand became challenging [7]. The demand for antiseptics and medical supplies increased significantly while supply chain constraints intensified. Faced with shortages governments and municipalities implemented impromptu solutions for increasing regional production of much needed hand sanitizers [8]. One effective response was the introduction of legislation that allowed the use of lower-grades of ethanol (often technical-grade ethanol) in the formulation of disinfectant and sanitizing products [8–10].

As the COVID-19 pandemic waned and vaccination limited the severity of viral infection, many governments removed restrictions and opted for more permissive policies that allowed citizens to live with a higher risk of contracting the virus. Health policies designed to reduce transmission among the public were mitigated or ceased altogether. With the implementation of gradual re-opening measures in many countries, policies defining travel restrictions, social distancing, facial coverings, etc. were removed through the 2nd, 3rd, and 4th quarters of 2021, and first quarter of 2022 [2]. Direct monitoring methods for COVID-19 (e.g., contact tracing and biomolecular tests) were also removed during the relaxation of restrictions. For example, Germany ceased free covid testing in August of 2021 with the acknowledgement that testing was both expensive and specifically benefitted the unvaccinated [11]. Currently, many monitoring methods have now targeted wastewater-based epidemiology (WBE) studies to survey the spread of infection in different communities [12–18]. Although these methods can provide early detection [19–22], interpretation of data can be limited in scope when compared with testing of populations, as is discussed below.

Finally, with continued policy changes, the economic recovery due to the COVID-19 pandemic has been slow. GDP dropped sharply across the globe at the start of the pandemic but rebounded somewhat shortly after. Global GDP at the end of 2020 was only a few percentage points less year-over-year than at the end of 2021 [23]. Worldwide merchandise trade decreased significantly, while trade of medical goods increased. Nearly all industries managed to recover by the end of 2021, with transportation & warehousing, tourism, and live entertainment-based industries having yet to return to pre-pandemic levels [24, 25]. Late pandemic supply chain disruptions have shown that pre-pandemic conditions have not returned [26, 27]. With continued risk of future supply-chain catastrophes, some in business are moving to models that develop localized value chains. The purpose of this book chapter is to discuss and review the impacts of COVID-19 on public policy, health measures, economic disruptions, and the importance of surveillance methods for the early detection of infections.

2. Economic disruptions and supply chain shortages, including ethanol-based products

The economic contraction that occurred during the COVID-19 pandemic affected global markets in 2020, 2021, and into 2022. Prominent among economic challenges were supply chain disruptions, which broadly impacted the delivery of goods and services. For example, manufacturers, builders, and retailers had reduced or delayed access to input materials, building materials, and stock items [9, 26]. Sales sharply decreased as pandemic-related restrictions were introduced in March 2020 which led to an excess of inventory. In some cases, this inventory was written off or liquidated. In later stages of the pandemic in 2021–2022, economic recovery placed additional stress on markets. Manufacturing industries halted or reduced output, canceled orders, and reduced reorders which led to manufacturing that was retooled or refocused to provide goods that were in high demand [26].

Among supply shortages, much of the world's consumers and businesses had challenges acquiring antiseptics such as rubbing alcohol, hand sanitizer, antiseptic wipes, and surface disinfectants at the beginning of the pandemic, which was exacerbated by consumer hoarding [9]. Due to the circumstances of limited world-wide supply of United States Pharmacopeia (USP) or Food-Chemicals Codex (FCC) grade ethanol, Canada modified acceptance criteria to include ethanol that was produced by alternative methods with specific label and usage requirements [28]. Health Canada expedited processing of Site Licenses and Product Licenses for hand sanitizer manufacturing and sales and waived the need for a review of good manufacturing practices (GMP) for new manufacturers, requiring only a signed declaration instead of the usual full GMP documentation [29]. Hand sanitizer supply expanded quickly with the new regulations, and shortages were rapidly addressed. Unfortunately, many producers failed to meet quality standards for ethanol as defined by new regulations [9]. In addition to supporting production of hand sanitizer, Health Canada expedited applications for Drug Identification Numbers (DIN) allowing the sale of surface disinfectants [30].

Worldwide lockdowns contributed to production and acquisition challenges by exacerbating industry down-time and supply-chain shortages, leading to cascading delays [26]. For many businesses the early response to Covid was a strategic long-term decrease in production achieved by layoffs, and a reduction of parts and other inputs (e.g., semiconductors for automakers) [26]. The shipping industry followed this pattern by reducing schedules.

After lockdown restrictions began to ease there was an unanticipated surge of product orders, combined with reduced capacity, making responding to new demand difficult [1]. Many laid off workers decided not to return to their positions through resignation, and retirement. These social factors lead to a labour shortage [31, 32]. In Canada the unemployment rate increased to 9.5%. This represents the loss of almost one million jobs in 2021 [23]. In the United States of America (U.S.A.) record numbers of resignations occurred in 2021, with 4.4 million workers resigning [33]. Employee resignations occurred for multiple reasons: while some workers planned to avoid potential workplace COVID-19 infection (Delta and Omicron variants), others were faced with lifestyle choices related to the epidemic and other pandemic-related stresses, such as reduced availability of childcare and elder care services [33]. Indeed, a large cohort of "baby boomers" simply chose to retire. Continuing resignations required extra resources used in hiring, onboarding and offboarding, thereby decreasing the efficiency of businesses and further contributing to industrial disruptions [33]. The job market became increasingly competitive with a new human resource focus on retention strategies [33].

Any business with a complex supply chain was susceptible to production backlogs, which resulted in backorders of inputs and delayed product shipments [23]. Freight costs more than doubled by the end of 2020, with smaller businesses being impacted more significantly, receiving lower priorities due to lower volume orders and higher shipping rates than larger companies with long-term contracts [34]. Tourism-based industries, such as hotels, restaurants, the arts and entertainment, recreation, and travel, diminished quickly when stay-at-home measures were put in place to limit COVID-19 transmission [23]. Once public health measures were lifted, there was a record number of job openings in 2021 due to the quick rise in job availability from impacted industries returning to regular business operations [23]. Through 2021, tourism-based industries exhibited the slowest recovery since the beginning of the pandemic, with transportation and warehousing as the next slowest, showing 16% below pre-pandemic GDP levels in Canada from February 2020 to January 2022, whereas most other industries achieved full GDP recovery [24].

To add to the economic challenges caused by the pandemic, the state of Texas had temperatures dip below freezing with snowfall in late February 2021 [35]. Chemical and petrochemical supply chains were heavily affected, as Texas is the nation's leading producer, and this extraordinary weather system caused major disruptions across the state [35]. Manufacturing facilities in these industries took months to recover [35] and as a result, industries involving plastics, packaging, fertilizers, pesticides, synthetic fibers, cleaners, lubricants, paint, and many more were affected by reduced supply in a market that was already suffering from supply backlogs [35].

In the U.S.A., high demand for import shipments quickly created a shortage of drayage vehicles and drivers while freight value moved by all transport vehicles fell 9.1 percent year over year from 2019 to 2020 [26, 34]. Although this year-over-year decrease is significant, it does not show the extreme swing of GDP in the first three quarters of 2020 as compared between **Figures 1** and **2**. Exports from Canada to the U.S.A. decreased by 70 billion dollars (16%) and imports by 43 billion dollars (11%) [23]. By the end of 2020 the U.S.A. and Canadian economies saw an overall contraction, despite significant recovery in the third quarter, owing to significantly decreased trade between U.S.A. and Canada [23, 25].

Worldwide merchandise trade decreased by 7% in 2020 [38], while the trade of medical goods increased, as demand for PPE (personal protective equipment) and other medical items (ventilators, AEDs, various consumables, drugs) escalated [39]. The first lockdown (and economic contraction) started in China, with lockdowns occurring months before those enacted elsewhere in the world [2]. This afforded China the ability to experience an economic expansion in the 2nd quarter of 2020, as seen in **Figure 2**.

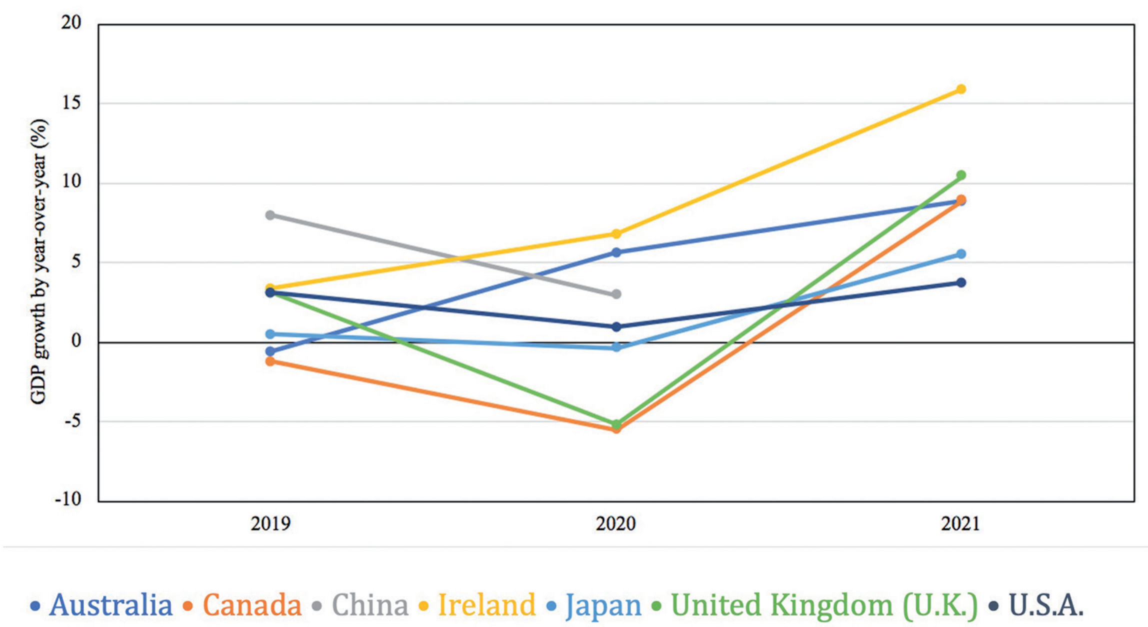

Figure 1.
GDP growth expressed in % change year-over-year. Reconstructed from [36].

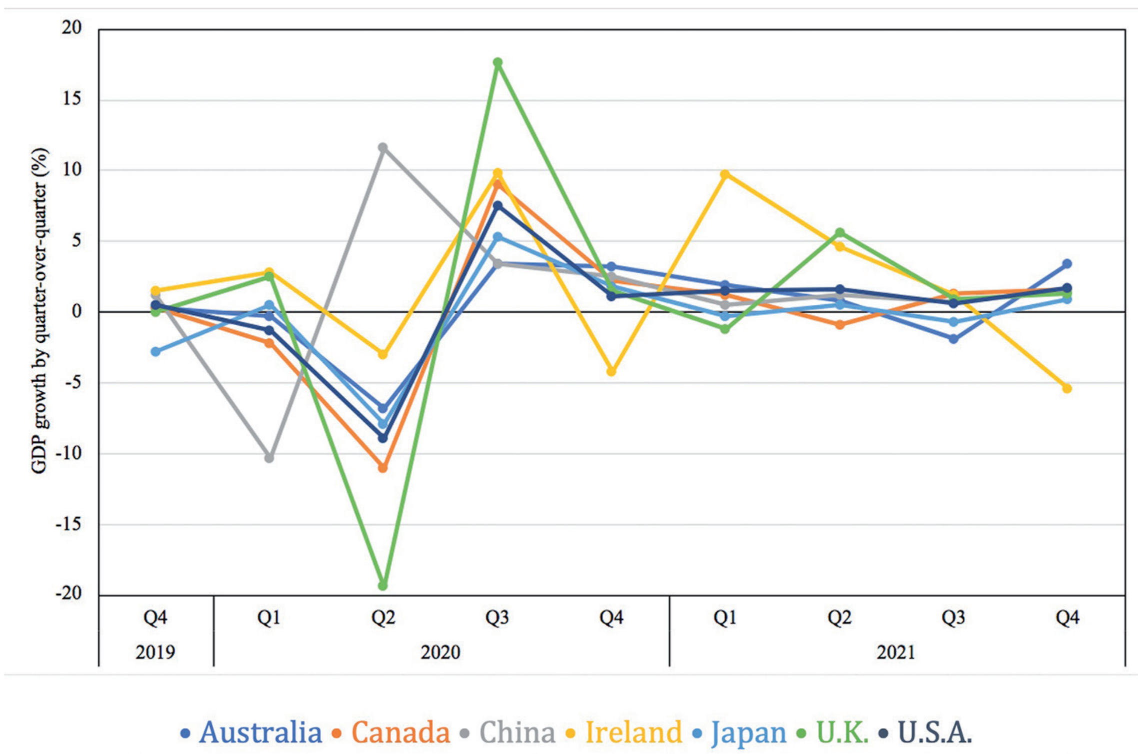

Figure 2.
GDP growth expressed in % change quarter-over-quarter. Reconstructed from [37].

Despite the short-term risks of using a lean, or 'just-in-time' approach to doing business, economists see value in maintaining its use [40]. It is possible that the economy may have maintained stability for a longer period if it had used more supply reserves, but the supply required to outlast the continued demand would have been insurmountable in many cases, as any physical product requires a reliable influx of materials to match output; a larger stock merely acts as a longer-lasting buffer to ease supply shock.

Economists have been analyzing and formulating potential solutions to avoid economic contractions like those experienced in 2020 [41]. It has been speculated that putting less reliance on international supply chains and focusing on more local value chains might increase economic loss and create more vulnerabilities in domestic economies [39]. Each country has their own specialized industries and products and continued association to these markets allows for optimal economic gains. In contrast, this interconnectivity also increases the potential negative impacts resulting from global supply chain issues, suggesting a need for more economic self-sufficiency [27]. Relying on a globalized economy may show some benefit, but only in the long-term, and such reliance leaves industries in a vulnerable position in the case of worldwide or specific supplier-affecting disruptions, especially for businesses with complex supply chains.

3. Public healthcare policies

The onset of the COVID-19 pandemic in early 2020 forced governments across the globe to act quickly to reshape public health policy. A major effort to alleviate the stress on health care was described as a "flatten the curve" strategy, but ultimately this approach recognized that the spread of the virus could be slowed but not stopped [42]. Indeed, the spread of the virus continued throughout 2021, and into 2022. In response, governments, health care agencies, and private industries have continued to enact public health measures to mitigate the spread of the virus and its effects. Public health measures have included mandating behavioral practices (social distancing, limited gathering sizes, etc.) [43], use of hygienic products (hand sanitizers, masking) [9], travel restrictions [44], and modifications to the delivery of health care services (online doctors' visits, postponement of elective surgery) [45]. Rates of COVID-associated morbidity and mortality are proportional to the amount of circulating COVID-19 virus within a population, and as of May 2022, total COVID-19 associated deaths are estimated to be more than 6.27 million [46]. This staggering loss of human life highlights the necessity of effective public health policy to minimize infection. Multiple peaks of global COVID-19 deaths were observed from 2022 to 2022. Such waves were often preceded by lower case numbers which, in turn, can cause complacency among the public. However, the emergence of increasingly

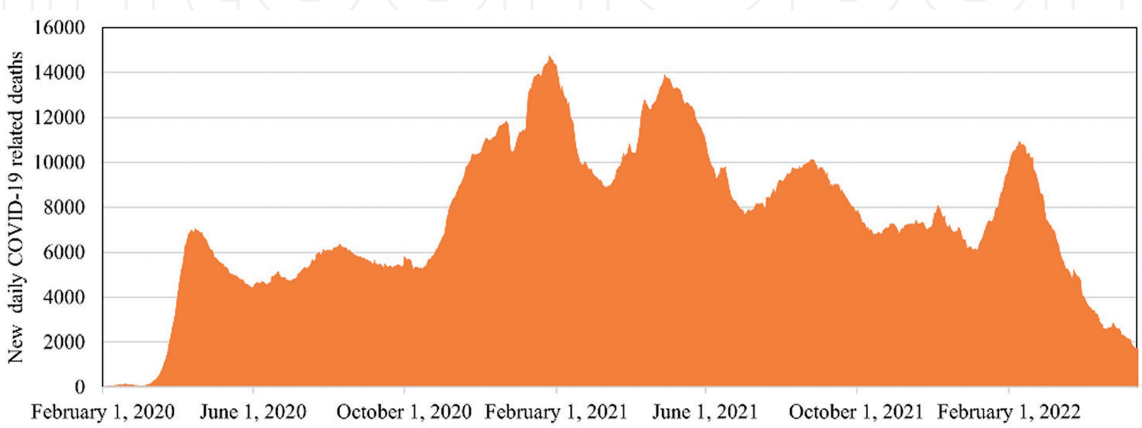

Figure 3.
Global figures of new deaths from February 1, 2020, to may 15, 2022. New COVID-19 deaths reported show patterns of repeated waves of outbreaks across the world as the pandemic progressed. Reconstructed from [46].

contagious strains of COVID-19, such as the Delta and Omicron variants, make the pandemic likely to continue into the foreseeable future (**Figure 3**).

The COVID-19 pandemic has had devastating and lasting effects on the health care system. The resulting increase in hospitalization rates and diminished resources available to treat patients has added significant burden to an already strained system. Policies designed to increase available ventilators [47], intensive care unit (ICU) beds [48], access to COVID-19 testing kits, and vaccination have been important tools that governments have enacted to fight the ongoing pandemic and minimize loss of life. Unfortunately, policies cannot address the immediate need for additional health care workers as it takes many years of training and specialization to care for patients, especially those in critical care settings [49].

To combat avoidable and unnecessary hospitalizations, well-enforced behavioral policies, such as social distancing and face masks, are often quickly enacted, as they do not overly disrupt economic and social systems and have demonstrated effectiveness in reducing transmission [50]. Reducing viral transmission via face-to-face interactions leads to an overall decrease in hospitalization rates. Most critically, this reduction extends to those who are at the highest risk for COVID-associated morbidity and mortality, such as individuals with underlying health care issues and patients over the age of 65 [51]. Public policy involving social distancing has taken various forms, ranging from severe restrictions on personal movement, to limited or no restrictions at all. Importantly, travel restrictions and encouragement of virtual or teleworking, helps limit travel and public contact, something that many in the workforce were able to do effectively during the COVID-19 pandemic [51–53]. Teleworking practices have the added benefit of reducing non-essential travel both internationally and domestically, which delays transmission of the virus. Indeed, there is strong evidence that restrictions on international travel from countries with high infection rates helps in slowing the spread of COVID-19 [44]. To eliminate avoidable public transmission, China imposed drastic lockdowns as outbreaks emerged throughout the country, including restricting travel from other nations, and between regions [54]. Chinese restrictions extended to include the separation of family members in the case of diagnosed infections. India suffered devastating infection rates during April and May of 2021 and imposed district specific restrictions during the second wave of infections to help mitigate the spread through densely populated regions [55]. In the United States and Canada, restrictions and guidelines varied significantly from region to region, owing to local policies, population density, and infection rates. Evidence in the United States suggests that stricter enforcement of public policy measures is likely linked to lower infection rates [56], while sudden, removal of restrictions has led to additional outbreaks [55, 57, 58]. Many governments chose to enact "phases" of restrictions, which lead to gradual policy changes intended to ease the stress on both public and private health care systems by controlling the total number of cases.

Hygienic methods such as hand washing, use of sanitizers, and implementation of personal protective equipment (PPE) have also been shown to be effective at reducing transmission of the COVID-19 virus. Although hand washing is a highly effective practice, the use of hand sanitizers was found to be substantially more convenient than hand washing. The resulting high demand for alcohol-based sanitizers, as well as other essential supplies, led to global shortages [9, 59]. The consequences of these shortages are still being studied, but food and supply scarcities are likely to cause an increase in prices, which disproportionately affect those with lower socioeconomic status [60]. To try and combat shortages, governments have encouraged sourcing from local suppliers while trying to minimize disruptions to essential imports. Even so, supply chain issues can be particularly challenging in rural populations where food security is already an issue [61].

Large, population-scale testing was implemented as a major intervention strategy to manage COVID-19 infections across the world as community infections increased. Improved access to testing allows for earlier identification of infections, encouraging individuals to self-quarantine and slow the spread of COVID-19. However, difficulties in acquiring testing methods, and significant delays in obtaining results, were frequent criticisms of large-scale testing efforts [62]. If wait times for testing are exceedingly long, individuals are less likely to test. Likewise, the longer the wait between preforming a test and obtaining the results, the less likely an individual will isolate, particularly if they are asymptomatic [63]. Mass testing can be costly, and so testing of health-care workers, symptomatic individuals, and those who are at risk of serious health complications are prioritized. Further exacerbating testing issues was a shortage of reagents, which caused supply chain issues and contributed to the wide disparities of testing rates between countries [64, 65]. A proposed solution to reduce the use of testing supplies is the pooling of samples, allowing for multiple individuals to be tested simultaneously by combining samples and testing with a single reaction. If the result from the pooled samples is negative, then all subsequent individuals are considered negative. However, if a positive result is observed, then individuals are tested separately, reducing the strain on the testing process. Remarkably, Chinese authorities in the city of Qingdao were able to test over seven million people over the course of three days using the method of pooling samples [66]. While the pooling method has demonstrated efficiency, there are limitations to the technique, including the need for relatively low positivity rates, longer reporting delays [63], and a reduction in test sensitivity [67]. Another frequently used method to determine community positivity rates is the testing of wastewater, which can predict general infection rates and is discussed in greater detail below.

Restrictions stemming from public policies can have far reaching impacts, and so constraints and policy changes must be carefully considered to prevent unnecessary disruptions to the economy, crucial supply chains, and earnings by those who are disproportionately affected by the pandemic [68]. Throughout the COVID-19 pandemic, health care experts have advocated for the enactment and enforcement of public health policies, imposing restrictions on social distancing, face coverings in public settings (especially where social distancing may not be possible), respiratory hygiene, and, where necessary, lockdowns [69]. There is evidence that demographic factors such as race, gender, and socioeconomic conditions play a role in transmission, contraction, and overall mortality rates and so not all measures are equally effective [51, 70, 71]. Critically, stay at home orders have adverse effects on supply chain issues, employment, and mental health [72, 73]. Research has shown that the practice of social distancing has caused negative impacts on isolation [74], family stresses [75], domestic violence [76], consumption of alcohol [77], and mental health [78], and so preventative and behavioral policies should be considered before major shutdowns of schools, businesses, and strict stay at home orders are enforced. Many factors play a role in COVID-19 related infections, and government policies should be careful to consider the effectiveness, financial costs, and negative outcomes associated with the policy enforcement. The development and distribution of safe and effective vaccines has helped to reduce the number of deaths and the pressures on hospital systems [79], however higher vaccination rates are concentrated in higher income countries, and vaccination hesitancy, along with the emergence of new more virulent COVID-19 variants, can slow development of broad spread immunity [80]. The consequence of the continued spread of the virus indicates that the COVID-19 pandemic is likely far from over, and public policies will serve as an effective tool in reducing transmission in the future.

4. Infection tracking and surveillance

A variety of technologies have emerged to alleviate the temporal and social restrictions brought on by the COVID-19 pandemic. These include the use of artificial intelligence (medical tracking), social media platforms (creating awareness of infections and providing real-time updates), virtual and augmented reality communications, blockchain (integration of point-of-care diagnostics for self-testing), additive manufacturing (production of personal protective equipment), 5G cellular technology and smart applications (remote monitoring of COVID-19), geographical information systems (spatial tracking of COVID-19), and autonomous robots (use of drones for disinfection) [6]. These valuable technologies provided critical information regarding COVID-19 and offered alternative communication means for health-related and employment-related meetings.

To manage the spread of COVID-19, other unprecedented techniques were adopted including contact tracing and the use of digital technologies [3, 4] as well as initiatives to provide early detection, monitoring efforts, and surveillance technologies. These technologies were introduced to slow and contain the spread of COVID-19 and provide advisory bodies important details in making informed public health strategies to combat the virus.

Contact tracing involves the identification of individuals who have come into close contact with an infected person, testing them, and, in case of an infection, tracing their own contacts to reduce the spread of an infection throughout a population [81]. Unfortunately, traditional manual contact tracing is labor-intensive, time-consuming, and may not be adequate in monitoring for COVID-19 in real time, especially in the instance of high infection rates [82]. Consequently, the development of digital tracking apps, including contact tracing apps (CTAs), have garnered attention in early detection by combining proximity tracing and contact tracing [3]. These novels CTAs, such as Canada's COVID Alert app [83], rely on self-reporting from infected individuals, as well as the implementation of Bluetooth connectivity to measure and record the spatial proximity between users, and alert nearby persons if they are within proximity to an infected individual [3]. Unfortunately, these applications are technologically limited as they can raise privacy concerns and older smartphones may not be compatible. Digital applications such as CTAs can also exacerbate inequities, such as age and income discrepancies in accessing smartphones, which can ultimately lead to a decline in CTAs effectiveness in preventing the spread of COVID-19 [3]. Another unforeseen occurrence resulting from the use of CTAs comes from a significant increase in the volume of people who receive notifications after being in close proximity of a COVID-19 positive individual. A dramatic surge of notifications was observed by contact tracing apps in the UK in July 2021, where the total number of individuals notified increased by nearly 50% in a single week. This surge in CTA alerts resulted in what was coined the "pingdemic" and required those affected to self-isolate for 10 days [84]. This caused significant consequences for many industries, including manufacturing and hospitality, as hundreds of thousands of individuals were required to stay home, leading to the shutdown of several production lines [84].

With the gradual lifting of social and travel restrictions, and the reopening of borders, access to PCR testing for COVID-19 has subsided and measuring an accurate clinical picture of the spread of the virus has become increasingly more difficult [85]. This has, however, paved the way for wastewater testing to play an increasingly critical role in monitoring for COVID-19 transmission within communities [85]. Currently, there are 5 genes that have routinely been used to screen for the presence of COVID-19. These include the ORF1ab, E-, N-, S-, and the RNA dependent RNA polymerase (RdRp) genes [86–88], encoding for numerous structural and non-structural proteins. Specifically, the RdRp gene is essential for the replication and transcription of the virus, and is encoded by the open reading frame, ORF1ab gene. In addition, ORF1ab is the largest gene that encodes for several nonstructural proteins [89]. Meanwhile, The E-, N-, and S- genes encode for structural proteins including, envelope proteins, nucleocapsid proteins, and spike proteins, respectively [90–92].

Recently, WBE studies have been employed to monitor the spread of COVID-19. Wastewater infrastructure is an important component of early warning systems to detect disease, due to increased water usage for hygienic purposes (hand washing, disinfection, cleaning, etc.) [19]. As COVID-19 and viral RNA are shed in bodily excreta (saliva, feces, sputum) of infected individuals [93], detection in wastewater [94] can provide early warnings and infer trends for authorities to make informed decisions on public policies and restrictions [19–22].

WBE studies [16, 17] have been used in several countries including Italy, Netherlands, Portugal, Spain, Australia, China, France, Israel, United States, Turkey, and Canada [12–15]. These studies typically involve the extraction of viral RNA material and amplifying the nucleic acid to detect the presence of COVID-19 (i.e., Nucleic acid amplification tests; NAATs, quantitative polymerase chain reaction; qPCR, reverse transcriptase PCR; RT-PCR, etc.) [95], and are important in evaluating the spread, genetic diversity, and geographic distribution of the virus [94, 96]. WBE modeling can be used to provide an estimate on the number of infected individuals in a population based on: (1) concentration of COVID-19 RNA at the inlet of the wastewater treatment plant, (2) volumetric flow rate of the wastewater treatment plant, (3) fecal load, (4) RNA shedding in the stool, and (5) RNA losses in the sewer pipe [97]. For the sensitive detection of viruses in wastewater, samples are often concentrated before quantification [98, 99]. For the surveillance of COVID-19, wastewater samples are often concentrated using centrifugation [100], filtration [101–105], polyethylene glycol precipitation [103, 106, 107], or aluminum flocculation [108, 109]. Unfortunately, RNA extraction efficiency can vary due to co-concentration of organic compounds (e.g., humic substances) [12]. Recent studies of COVID-19 in wastewater have also observed viral recoveries between 3 and 50% [12], although calibration against RNA losses in the wastewater can provide improved accuracy [97]. Nonetheless, these techniques have demonstrated reliability in identifying the true magnitude of infection within a population [97] and have been widely used to monitor for early detection of novel viral pathogens [110–113], including enterovirus, adenoviruses, hepatitis viruses, and more recently COVID-19. As WBE assesses changes in SAR-CoV-2 titres, these studies collectively include asymptomatic individuals, as well as those exhibiting very mild symptoms. Unfortunately, translation of COVID-19 titres in wastewater to actual individual numbers is extremely difficult. Therefore, these analyses are typically used to infer the spread of COVID-19 within a community and monitor for the emergence of related variants.

While PCR tests performed on wastewater samples are identical to those performed at COVID-19 clinics, the N- and E-genes are more commonly targeted as they are more well-preserved in wastewater [85]. However, there are challenges with wastewater testing, including variability of the data produced by each sample which can produce a significant margin of error [85]. Furthermore, the operations and designs among different wastewater treatment facilities can result in varying dilutions of the tested samples, thus affecting signals of COVID-19 in the wastewater [114, 115]. For example, in some facilities, rainfall may combine with wastewater, resulting in the dilution of COVID-19. Additionally, residential, and industrial water uses can affect COVID-19 signals in municipal wastewater. Therefore, comparing COVID-19 levels between different communities, cities, health regions, etc. is very difficult and wastewater analyses for COVID-19 should be primarily used to establish trends in COVID-19 prevalence, rather than determining an absolute concentration or comparing to active cases in the community; active cases may not include asymptomatic individuals, whereas wastewater analyses will.

Altogether, wastewater surveillance of COVID-19 provides a powerful tool in evaluating incidences of disease at the community level. However, WBE studies also need to be integrated into other public health studies, such as randomized testing of individuals. Current data on COVID-19 and other viruses suggest that WBE epidemiology is a viable option in assessing and mitigating viral outbreaks [12–17]. The widely used q(RT)-PCR approach enables rapid and strain level RNA/DNA quantification, however, the primers and probes should be chosen carefully, depending on sequence preservation [90–92]. Finally, targeted, and untargeted sequencing of viruses in wastewater has the potential to track the spread of specific sequence variants and identify mutations that could affect detection in clinical settings [12] and provide early detection for emergence of novel strains.

5. Conclusion

The COVID-19 virus has continued to adapt and persist beyond 2020 and will likely continue in some form for years to come. Learning from the continued spread of this deadly virus is critical, and responses by governments to the global spread of COVID-19 has continuously adapted to new challenges and developing information. The consequences of the pandemic cannot be underestimated and has caused serious impacts on the global economy and healthcare capacity, as well as the physical and mental health of the public. COVID-19 associated morbidity and mortalities continue to climb across the world, even with the distribution of effective vaccines. Indeed, as travel restrictions are slowly lifted across the globe, the implementation of public health policies and expanding access to tracking the spread of the virus are powerful tools for minimizing unnecessary hospitalizations.

The world economy has suffered because of the pandemic, but only in part, as many countries enacted polices to prevent total recession, and some economies have even exhibited financial benefit. Specialized industries have yet to recover fully in 2022, and some businesses have been disproportionately impacted, owing to the challenges of public restrictions throughout 2020 and 2021. As major public restrictions begin to relax, many unrecovered industries can be expected to see continued economic improvements.

Having established efficient ways of tracking the COVID-19 virus through technological and biomolecular methods (e.g., nucleic acid amplification tests and WBE studies), governments around the world will be better prepared in surveying for future diseases of concern. Furthermore, with economists working on restructuring modern practices in supply-chain management, the world economies will be better prepared in the coming years to avoid similar challenges that are still prevalent two years into the pandemic.

Acknowledgements

This work was supported by the Saskatchewan Agricultural Development Fund (20190155, 20190154, 20180281, 20180248, 20180255, 20170133); National Sciences and Engineering Research Council of Canada Discovery Grant (RGPIN-2018-06631); and Mitacs (IT19122, IT16156).

Conflict of interest

Dr. Martin J. T. Reaney is the founder of, and has an equity interest in, Prairie Tide Diversified Inc. (PTD, Saskatoon, SK, Canada: previous company name is Prairie Tide Chemicals Inc.).

Author details

Timothy J. Tse*, Farley Chicilo*, Jeffrey Popiel* and Martin J.T. Reaney*
University of Saskatchewan, Saskatoon, Canada

*Address all correspondence to: timothy.tse@usask.ca; fhc246@mail.usask.ca; jeffrey.popiel@usask.ca and martin.reaney@usask.ca

References

[1] Loss Prevention Magazine. The Global Supply Chain Crisis: What Happened and When Will it End? [Internet]. 2022. Available from: https://losspreventionmedia.com/the-global-supply-chain-crisis/?msclkid=bf2bd13dc4c311ec9f713df83beb1b9f [Accessed: May 21, 2022]

[2] Hale T, Angrist N, Goldszmidt R, Kira B, Petherick A, Phillips T, et al. A global panel database of pandemic policies (Oxford COVID-19 government response tracker). Nature Human Behaviour. 2021;**5**:529-538. DOI: 10.1038/s41562-021-01079-8

[3] Klar R, Lanzerath D. The ethics of COVID-19 tracking apps – Challenges and voluntariness. Research Ethics. 2020;**16**: 1-9. DOI: 10.1177/1747016120943622

[4] Kondylakis H, Katehakis DG, Kouroubali A, Logothetidis F, Triantafyllidis A, Kalamaras I, et al. COVID-19 mobile apps: A systematic review of the literature. Journal of Medical Internet Research. 2020;**22**:e23170. DOI: 10.2196/23170

[5] Tangcharoensathien V, Bassett MT, Meng Q, Mills A. Are overwhelmed health systems an inevitable consequence of covid-19? Experiences from China, Thailand, and New York state. BMJ. 2021;**372**:n83. DOI: 10.1136/bmj.n83

[6] Mbunge E, Akinnuwesi B, Fashoto SG, Metfula AS, Mashwama P. A critical review of emerging technologies for tackling COVID-19 pandemic. Human Behavior and Emerging Technologies. 2021;**3**:25-39. DOI: 10.1002/hbe2.237

[7] Bartik A, Bertrand M, Cullen Z, Glaeser E, Luca M, Stanton C. The impact of COVID-19 on small business outcomes and expectations. Proceedings of the National Academy of Sciences. 2020;**117**:17656-17666. DOI: 10.1073/pnas.2006991117

[8] Tse TJ, Purdy SK, Shen J, Nelson FB, Mustafa R, Wiens DJ, et al. Toxicology of alcohol-based hand rubs formulated with technical-grade ethanol. Toxicology Reports. 2021;**8**:785-792. DOI: 10.1016/j.toxrep.2021.03.034

[9] Mustafa R, Purdy SK, Nelson FB, Tse TJ, Wiens DJ, Shen J, et al. Canadian policy changes for alcohol-based hand rubs during the COVID-19 pandemic and unintended risks. World med. Health Policy. 2021:1-13. DOI: 10.1002/wmh3.463

[10] Tse TJ, Nelson FB, Reaney MJT. Analyses of commercially available alcohol-based hand rubs formulated with compliant and non-compliant ethanol. International Journal of Environment Research. 2021;**18**:3766. DOI: 10.3390/ijerph18073766

[11] Reuters. Germany to Stop Free COVID-19 Tests – Report [Internet]. 2021. Available from: https://www.reuters.com/business/healthcare-pharmaceuticals/germany-stop-free-covid-19-tests-report-2021-08-09/ [Accessed: June 6, 2022]

[12] Farkas K, Hillary LS, Malham SK, McDonald JE, Jones DL. Wastewater and public health: The potential of wastewater surveillance for monitoring COVID-19. Current Opinion in Environmental Science & Health. 2020;**17**:14-20. DOI: 10.1016/j.coesh.2020.06.001

[13] Kirby AE, Walters MS, Jennings WC, Fugitt R, LaCross N, Mattioli M, et al.

Using wastewater surveillance data to support the COVID-19 response – United States, 2020-2021. MMWR. 2021;**70**:1242-1244. DOI: 10.15585/mmwr.mm7036a2

[14] Global Institute of Water Security. COVID-19 Early Indicators [Internet]. 2022. Available from https://water.usask.ca/covid-19/ [Accessed: April 8, 2022]

[15] Monteiro S, Rente D, Cunha MV, Gomes MC, Marques TA, Lourenço AB, et al. A wastewater-based epidemiology tool for COVID-19 surveillance in Portugal. Science of the Total Environment. 2022;**804**:150264. DOI: 10.1016/j.scitotenv.2021.150264

[16] Larsen DA, Wigginton KR. Tracking COVID-19 with wastewater. Nature Biotechnology. 2020;**38**:1151-1153. DOI: 10.1038/s41587-020-0690-1

[17] Rooney CM, Moura IB, Wilcox MH. Tracking COVID-19 via sewage. Current Opinion in Gastroenterology. 2021;**37**:4-8. DOI: 10.1097/MOG.0000000000000692

[18] Nghiem LD, Morgan B, Donner E, Short MD. The COVID-19 pandemic: Considerations for the waste and wastewater services sector. CSCEE. 2020;**1**:100006. DOI: 10.1016/j.cscee.2020.100006

[19] Berglund EZ, Thelemaque N, Spearing L, Faust KM, Kaminsky J, Sela L, et al. Water and wastewater systems and utilities: Challenges and opportunities during the COVID-19 pandemic. Journal of Water Resources Planning and Management. 2021;**147**:02521001

[20] Aguiar-Oliveira MDL, Campos AR, Matos A, Rigotto C, Sotero-Martins A, Teixeira PFP, et al. Wastewater-based epidemiology (WBE) and viral detection in polluted surface water: A valuable tool for COVID-19 surveillance – A brief review. International Journal of Environmental Research and Public Health. 2020;**17**:9251. DOI: 10.3390/ijerph17249251

[21] Ahmed W, Tscharke B, Bertsch PM, Bibby K, Bivins A, Choi P, et al. SARS-CoV-2 RNA monitoring in wastewater as a potential early warning system for COVID-19 transmission in the community: A temporal case study. Science of the Total Environment. 2021;**761**:14426. DOI: 10.1016/j.scitotenv.2020144216

[22] Gonzalez R, Curtis K, Bivins A, Bibby K, Weir MH, Yetka K, et al. COVID-19 surveillance in southeastern Virginia using wastewater-based epidemiology. Water Research. 2020;**186**:116296. DOI: 10.1016/j.watres.2020.116296

[23] Government of Canada. State of Trade 2021 – A Closer Look at Foreign Direct Investment (FDI) [Internet]. 2021. Available from: https://www.international.gc.ca/transparency-transparence/state-trade-commerce-international/2021.aspx [Accessed: May 21, 2022]

[24] Statistics Canada. Gross Domestic Product (GDP) at Basic Prices, by Industry, Monthly (x 1,000,000). 2022. Available from: https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=3610043401 [Accessed: June 3, 2022]

[25] Bureau of Economic Analysis. Gross Domestic Product (Third Estimate), Corporate Profits, and GDP by Industry, Fourth Quarter and Year 2021 [Internet]. 2022. Available from: https://www.bea.gov/sites/default/files/2022-03/gdp4q21_3rd.pdf [Accessed: May 26, 2022]

[26] The White House. Why the Pandemic Has Disrupted Supply Chains

[Internet]. 2021. Available from: https://www.whitehouse.gov/cea/written-materials/2021/06/17/why-the-pandemic-has-disrupted-supply-chains/ [Accessed: May 21, 2022]

[27] Seric A, Görg H, Liu W, Windisch M. Risk, Resilience, and Recalibration in Global Value Chains [Internet]. 2021. Available from: https://voxeu.org/article/risk-resilience-and-recalibration-global-value-chains [Accessed: June 3, 2022]

[28] Government of Canada. Technical-Grade Ethanol for use in hand Sanitizers and Hard-Surface Disinfectants: Notice to industry [Internet]. 2020. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/natural-non-prescription/legislation-guidelines/covid19-technical-grade-ethanol-hand-sanitizer.html [Accessed: May 21, 2022]

[29] Government of Canada. Licensing Approach to Produce and Distribute alcohol-Based Hand Sanitizers: Guidance Document [Internet] 2020. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/covid-19-expediated-licensing-alcohol-hand-sanitizer.html [Accessed: May 21, 2022]

[30] Government of Canada. Expedited Access to Disinfectants, Hand Sanitizers and Personal Protective Equipment to Help Limit the Spread of COVID-19, as well as Swabs for Testing [Internet]. 2020. Available from: https://recalls-rappels.canada.ca/en/alert-recall/expedited-access-disinfectants-hand-sanitizers-and-personal-protective-equipment-help?msclkid=c2996cb7c4e311ec8a800161041e8606 [Accessed: May 21, 2022]

[31] International Labour Organization. Impact of the COVID-19 Crisis on Loss of Jobs and Hours Among Domestic Workers [Internet]. 2020. Available from: https://www.ilo.org/wcmsp5/groups/public/---ed_protect/---protrav/---travail/documents/publication/wcms_747961.pdf [Accessed: May 21, 2022]

[32] Ragan. Research: Key Factors Fueling 'The Great Resignation' [Internet]. 2021. Available from: https://www.ragan.com/research-key-factors-fueling-the-great-resignation/?msclkid=eb8c5cf5c4c911ec8da582649fb9537d [Accessed: May 21, 2022]

[33] Tessema M, Tesfom G, Faircloth M, Tesfagiorgis M, Teckle P. The "great resignation": Causes, consequences, and creative HR management strategies. Journal of Human Resource Sustainability Studies. 2022;**10**:161-178. DOI: 10.4236/jhrss.2022.101011

[34] United States International Trade Commission. The Impact of the COVID-19 Pandemic on Freight Transportation Services and U.S. Merchandise Imports [Internet]. 2020. Available from: https://www.usitc.gov/research_and_analysis/tradeshifts/2020/special_topic.html [Accessed: May 21, 2022]

[35] Supply Chains. Chemical Manufacturing Supply Chain [Internet]. 2021. Available from: https://comptroller.texas.gov/economy/economic-data/supply-chain/2021/chem.php [Accessed: May 21, 2022]

[36] OECD. Gross Domestic Product (GDP) (indicator) [Internet]. 2022. Available from: https://www.oecd-ilibrary.org/economics/gross-domestic-product-gdp/indicator/english_dc2f7aec-en [Accessed: June 6, 2022]

[37] OECD. Quarterly GDP (indicator) [Internet]. 2022. Available from: https://www.oecd-ilibrary.org/economics/quarterly-gdp/indicator/english_b86d1fc8-en [Accessed: June 3, 2022]

[38] Liu X, Ornelas E, Shi H. The 2020 Trade Impact of the COVID-19 Pandemic [Internet]. 2021. Available from: https://voxeu.org/article/2020-trade-impact-covid-19-pandemic [Accessed June 3, 2022]

[39] Arriola C, Kowalski P, van Tongeren F. Localising Value Chains in the post-COVID World Would add to the Economic Losses and Make Domestic Economies more Vulnerable [Internet]. 2020. Available from: https://voxeu.org/article/localising-value-chains-after-covid-would-add-economic-losses-and-make-domestic-economies-more-vulnerable [Accessed: June 3, 2022]

[40] Pisch F. Just-in-time Supply Chains after the COVID-19 Crisis. [Internet]. 2020. Available from: https://voxeu.org/article/just-time-supply-chains-after-covid-19-crisis [Accessed: June 3, 2022]

[41] Magableh GM. Supply chains and the COVID-19 pandemic: A comprehensive framework. European Management Review. 2021;**18**:363-382. DOI: 10.1111/emre.12449

[42] Thunström L, Newbold S, Finnoff D, Ashworth M, Shogren J. The benefits and costs of using social distancing to flatten the curve for COVID-19. Journal of Benefit-Cost Analysis. 2020;**11**:179-195. DOI: 10.1017/bca.2020.12

[43] Chan EYY, Huang Z, Lo ESK, Hung KKC, Wong ELY, Wong SYS. Sociodemographic predictors of health risk perception, attitude and behavior practices associated with health-emergency disaster risk Management for Biological Hazards: The case of COVID-19 pandemic in Hong Kong, SAR China. International Journal of Environmental Research and Public Health. 2020;**17**:3869. DOI: 10.3390/ijerph17113869

[44] Wells CR, Sah P, Moghadas SM, Pandey A, Shoukat A, Wang Y, et al. Impact of international travel and border control measures on the global spread of the novel 2019 coronavirus outbreak. Proceedings of the National Academy of Sciences. 2020;**117**:7504-7509. DOI: 10.1073/pnas.2002616117

[45] Mann DM, Chen J, Chunara R, Testa PA, Nov O. COVID-19 transforms health care through telemedicine: Evidence from the field. Journal of the American Medical Informatics Association. 2020;**27**:1132-1135. DOI: 10.1093/jamia/ocaa072

[46] Ritchie H, Mathieu E, Rodés-Guirao L, Appel C, Giattino C, Ortiz-Ospina E, Joe Hasell, Macdonald B, Beltekian D, and Roser M. Coronavirus Pandemic (COVID-19) [Internet]. 2020. Available from: https://ourworldindata.org/coronavirus [Accessed: May 15, 2022]

[47] Iyengar K, Bahl S, Vaishya R, Vaish A. Challenges and solutions in meeting up the urgent requirement of ventilators for COVID-19 patients. Diabetes and Metabolic Syndrome: Clinical Research and Reviews. 2020;**14**:499-450. DOI: 10.1016/j.dsx.2020.04.048

[48] Tyrrell CSB, Mytton OT, Gentry SV, Thomas-Meyer M, Allen JLY, Narula AA, et al. Managing intensive care admissions when there are not enough beds during the COVID-19 pandemic: A system review. Thorax. 2021;**76**:302-312. DOI: 10.1136/thoraxjnl-2020-215518

[49] Rasmussen S, Sperling P, Poulsen MS, Emmersen J, Andersen S. Medical students for health-care staff shortages during the COVID-19 pandemic. The Lancet. 2020;**395**:79-80. DOI: 10.1016/S0140-6736(20)30923-5

[50] Mulugeta T, Tadesse E, Shegute T, Desta T. COVID-19: Socio-economic

impacts and challenges in the working group. Heliyon. 2021;**7**:e07307. DOI: 10.1016/j.heliyon.2021.e07307

[51] Bick A, Blandin A, Mertens K. Work from home after the Covid-19 Outbreak [Internet]. 2021. Available from: https://www.dallasfed.org/-/media/documents/research/papers/2020/wp2017r1.pdf [Accessed: June 3, 2022]

[52] Shortall R, Mouter N, Van Wee B. COVID-19 and transport. A review of factors of relevance to the design of measures and their effects worldwide. European Journal of Transport and Infrastructure Research. 2022, 2020;**22**:118-130. DOI: 10.18757/ejtir.2022.22.1.5597

[53] Haider M, Anwar AI. The prevalence of telework under Covid-19 in Canada. Information Technology and People. 2022. DOI: 10.1108/ITP-08-2021-0585

[54] Prem K, Liu Y, Russell TW, Kucharski AJ, Eggo RM, Davies N, et al. The effect of control strategies to reduce social mixing on outcomes of the COVID-19 epidemic in Wuhan, China: A modelling study. The Lancet Public Health. 2020;**5**:261-270. DOI: 10.1016/S2468-2667(20)30073-6

[55] Gupta N, Rana S, Panda S, Bhargava B. Use of COVID-19 test positivity rate, epidemiological, and clinical tools for guiding targeted public health interventions. Frontiers in Public Health. 2022;**10**:821611-821611. DOI: 10.3389/fpubh.2022.821611

[56] Mahmoudi J, Xiong C. How social distancing, mobility, and preventive policies affect COVID-19 outcomes: Big data-driven evidence from the District of Columbia-Maryland-Virginia (DMV) megaregion. PLoS One. 2022;**17**:e0263820. DOI: 10.1371/journal.pone.0263820

[57] Huntley K, Wahood W, Mintz J, Raine S, Hardigan P, Haffizulla F. Associations of stay-at-home order enforcement with COVID-19 population outcomes: An interstate statistical analysis. American Journal of Epidemiology. 2022;**91**:561-569. DOI: 10.1093/aje/kwab267

[58] Burki T. Lifting of COVID-19 restrictions in the UK and the Delta variant. The Lancet Respiratory Medicine. 2021;**9**:e85. DOI: 10.1016/S2213-2600(21)00328-3

[59] Andal V, Lakshmipathy R, Jose D. Effect of sanitizer on obliteration of SARS –CoV2/COVID 19: A mini review. Materials Today: Proceedings. 2022;**55**:264-266. DOI: 10.1016/j.matpr.2021.07.026

[60] Government of Canada. (2020a). Hard-Surface Disinfectants and Hand Sanitizers (COVID-19): Disinfectants and Hand Sanitizers Accepted under COVID-19 Interim Measure [Internet]. 2021. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/disinfectants/covid-19/products-accepted-under-interim-measure.html [Accessed: May 26, 2022]

[61] International Food & Agricultural Trade Policy Council. Agricultural Export Restrictions: Welfare Implications and Trade Disciplines [Internet]. 2009. Available from: https://www.researchgate.net/profile/Siddhartha-Mitra-5/publication/331478130_Agricultural_Export_Restrictions_Welfare_Implications_and_Trade_Disciplines/links/5c7bb80692851c69504f933d/Agricultural-Export-Restrictions-Welfare-Implications-and-Trade-Disciplines.pdf [Accessed: June 6, 2022]

[62] Strickland J, Reed D, Hursh S, Schwartz L, Foster R, Gelino B. Johnson, M behavioral economic methods to

inform infectious disease response: Prevention, testing, and vaccination in the COVID-19 pandemic. PLoS One. 2022;**17**:e0258828. DOI: 10.1371/journal.pone.0258828

[63] Mercer T, Salit M. Testing at scale during the COVID-19 pandemic. Nature Reviews. Genetics. 2021;**22**:415-426. DOI: 10.1038/s41576-021-00360-w

[64] Guan D, Wang D, Hallegatte S, Davis S, Huo J, Li S, et al. Global supply-chain effects of COVID-19 control measures. Nature Human Behaviour. 2020;**4**:577-587. DOI: 10.1038/s41562-020-0896-8

[65] Songok E. A locally sustainable approach to COVID-19 testing in Africa. The Lancet Microbe. 2020;**1**:e197. DOI: 10.1016/S2666-5247(20)30118-X

[66] Xing Y, Wong G, Ni W, Hu X, Xing Q. Rapid response to an outbreak in Qingdao, China. The New England Journal of Medicine. 2020;**383**:e129. DOI: 10.1056/NEJMc2032361

[67] Bateman AC, Mueller S, Guenther K, Shult P. Assessing the dilution effect of specimen pooling on the sensitivity of SARS-CoV-2 PCR tests. Journal of Medical Virology. 2020;**93**:1568-1572. DOI: 10.1002/jmv.26519

[68] Linkov I, Keenan JM, Trump BD, editors. COVID-19: Systemic Risk and Resilience. 1st ed. Cham: Springer; 2021. pp. 1-9. DOI: 10.1007/978-3-030-71587-8

[69] Garg S, Kim L, Whitaker M, O'Halloran A, Cummings C, Holstein R, et al. Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed coronavirus disease 2019 — Covid-net, 14 states, march 1-30, 2020. MMWR. 2020;**69**:458-464. DOI: 10.15585/mmwr.mm6915e3

[70] Hooper MW, Na'poles AM, Pe'rez-Stable EJ. COVID-19 and racial/ethnic disparities. Journal of the American Medical Association. 2020;**323**:2466-2467. DOI: 10.1001/jama.2020.8598

[71] Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, et al. Gender differences in patients with COVID-19: Focus on severity and mortality. Frontiers in Public Health. 2020;**8**:152. DOI: 10.3389/fpubh.2020.00152

[72] Brodeur A, Gray D, Islam A, Bhuiyan S. A literature review of the economics of COVID-19. Journal of Economic Surveys. 2021;**35**:1007-1044. DOI: 10.1111/joes.12423

[73] Belot M, Choi S, Tripodi E, Broek-Altenburg E, Jamison J, Papageorge N. Unequal consequences of Covid 19: Representative evidence from six countries. Review of Economics of the Household. 2021;**19**:769-783. DOI: 10.1007/s11150-021-09560-z

[74] Maxwell H. COVID-19: A lonely pandemic. Cities & Health. 2020;**5**:S80-S82. DOI: 10.1080/23748834.2020.1788770

[75] Kalluri N, Kelly C, Garg A. Child care during the COVID-19 pandemic: A bad situation made worse. Pediatric. 2021;**147**:1. DOI: 10.1542/peds.2020-041525

[76] Piquero A, Jennings W, Jemison E, Kaukinen C, Knaul F. Domestic violence during the COVID-19 pandemic - evidence from a systematic review and meta-analysis. Journal of Criminal Justice. 2021;**74**:101806. DOI: 10.1016/j.jcrimjus.2021.101806

[77] Colbert S, Wilkinson C, Thornton L, Richmond R. COVID-19 and alcohol in Australia: Industry changes and public

health impacts. Drug and Alcohol Review. 2020;**39**:435-440. DOI: 10.1111/dar.13092

[78] Kola L, Kohrt B, Hanlon C, Naslund J, Sikander S, Balaji M, et al. COVID-19 mental health impact and responses in low-income and middle-income countries: Reimagining global mental health. Lancet Psychiatry. 2021;**8**:535-550. DOI: 10.1016/s2215-0366(21)00025-0

[79] Ciotti M, Ciccozzi M, Pieri M, Bernardini S. The COVID-19 pandemic: Viral variants and vaccine efficacy. Critical Reviews in Clinical Laboratory Sciences. 2022;**59**:66-75. DOI: 10.1080/10408363.2021.1979462

[80] Sallam M. COVID-19 vaccine hesitancy worldwide: A concise systematic review of vaccine acceptance rates. Vaccine. 2021;**9**:160. DOI: 10.3390/vaccines9020160

[81] Williams SN, Armitage CJ, Tampe T, Dienes K. Public attitudes towards COVID-19 contact tracing apps: A UK-based focus group study. Health Expectations. 2021;**24**:377-385. DOI: 10.1111/hex.13179

[82] Ferretti L, Wymant C, Kendall M, Zhao L, Nurtay A, Abeler-Dörner L, et al. Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing. Science. 2020;**368**:eabb6936. DOI: 10.1126/science.abb6936

[83] Government of Canada. Download COVID Alert Today. [Internet]. 2021. Available from https://www.canada.ca/en/public-health/services/diseases/coronavirus-disease-covid-19/covid-alert.html [Accessed: April 10, 2022]

[84] Rimmer A. Sixty seconds on . . . The pingdemic. BMJ. 2021;**374**:n1822. DOI: 10.1136/bmj.n1822

[85] CTV News. Wastewater Now 'One of Our Only Reliable Tools' to Detect COVID-19 Prevalence. [Internet]. 2022. Available from: https://www.ctvnews.ca/health/coronavirus/wastewater-now-one-of-our-only-reliable-tools-to-detect-covid-19-prevalence-1.5862546 [Accessed: April 16, 2022]

[86] Rangaiah A, Shankar SM, Basawarajappa SG, Shah PA, Chandrashekar A, Munegowda A, et al. Detection of SARS-CoV-2 in clinical samples: Target-specific analysis of qualitative reverse transcription-polymerase chain reaction (RT-PCR) diagnostic kits. IJID Regions. 2021;**1**:163-169. DOI: 10.1016/j.ijregi.2021.11.004

[87] Agrawal S, Orschler L, Lackner S. Long-term monitoring in SARS-CoV-2 RNA in wastewater of the Frankfurt metropolitan of area in southern Germany. Scientific Reports. 2021;**11**:5372. DOI: 10.1038/s41598-021-84914-2

[88] van Kasteren PB, van der Veer B, van den Brink S, Wijsman L, de Jonge J, van den Brandt A, et al. Comparison of seven commercial RT-PCR diagnostic kits for COVID-19. Journal of Clinical Virology. 2020;**128**:104412. DOI: 10.1016/j.jcv.2020.104412

[89] National Center for Biotechnology Information (NCBI). ORF1ab polyprotein [Severe acute respiratory syndrome coronavirus 2] [Internet]. 2022. Available from: https://www.ncbi.nlm.nih.gov/gene/43740578 [Accessed: April 18, 2022]

[90] Kirtipal N, Bharadwaj S, Kang SG. From SARS to SARS-COV-2, insights on structure, pathogenicity and immunity aspects of pandemic human coronaviruses. Infection, Genetics and Evolution. 2020;**85**:104502. DOI: 10.1016/j.meegid.2020.104502

[91] Barreto HG, de Pàdua Milagres FA, de Araújo GC, Daúde MM, Benedito VA. Diagnosing the novel SARS-CoV-2 by quantitative RT-PCR: Variations and opportunities. Journal of Molecular Medicine. 2020;**98**:1727-1736. DOI: 10.1007/s00109-020-01992-x

[92] Lu X, Wang L, Sakthivel SK, Whitaker B, Murray J, Kamili S, et al. US CDC real-time reverse transcription PCR panel for detection of severe acute respiratory syndrome coronavirus 2. Emerging Infectious Diseases. 2020;**26**:1654-1665. DOI: 10.3201/eid2608.201246

[93] Daughton C. The international imperative to rapidly and inexpensively monitor community-wide COVID-19 infection status and trends. Science of the Total Environment. 2020;**726**:138149. DOI: 10.1016/j.scitotenv.2020.138149

[94] Sinclair RG, Choi CY, Riley MR, Gerba CP. Pathogen surveillance through monitoring of sewer systems. Advances in Applied Microbiology. 2008;**65**:249-269. DOI: 10.1016/S0065-2164(08)00609-6

[95] Centers for Disease Control and Prevention. Nucleic Acid Amplification Tests (NAATs). [Internet]. 2022. Available from: https://www.cdc.gov/coronavirus/2019-ncov/lab/naats.html#:~:text=The_NAAT_procedure_works_by,sensitive_for_diagnosing_COVID_19 [Accessed: April 8, 2022]

[96] Ghernaout D, Ghernaout B. Controlling COVID-19 pandemic through wastewater monitoring. OALib Journal. 2020;**7**:e6411. DOI: 10.4236/oalib.1106411

[97] Saththasivam J, El-Malah SS, Gomez TA, Jabbar KA, Remanan R, Krishnankutty AK, et al. COVID-19 (SARS-CoV-2) outbreak monitoring using wastewater-based epidemiology in Qatar. Science of the Total Environment. 2021;**774**:145608. DOI: 10.1016/j.scitotenv.2021.145608

[98] Haramoto E, Kitajima M, Hata A, Torrey JR, Masago Y, Sano D, et al. A review on recent progress in the detection methods and prevalence of human enteric viruses in water. Water Research. 2018;**135**:168-186. DOI: 10.1016/j.watres.2018.02.004

[99] Bofill-Mas S, Rusiñol M. Recent trends on methods for the concentration of viruses from water samples. Current Opinion in Environmental Science Health. 2020;**16**:7-13. DOI: 10.1016/j.coesh.2020.01.006

[100] Wurtzer S, Marechal V, Mouchel JM, Maday Y, Teyssou R, Richard E, et al. Evaluation of lockdown effect on SARS-CoV-2 dynamics through viral genome quantification in waste water, greater Paris, France, 5 march to 23 April 2020. Euro Surveillance. 2020;**25**:2000776. DOI: 10.2807/1560-7917.ES.2020.25.50.2000776

[101] Ahmed W, Angel N, Edson J, Bibby K, Bivins A, O'Brien JW, et al. First confirmed detection of SARS-CoV-2 in untreated wastewater in Australia: A proof of concept for the wastewater surveillance of COVID-19 in the community. Science of the Total Environment. 2020;**728**:138764. DOI: 10.1016/j.scitotenv.2020.138764

[102] Medema G, Heijnen L, Elsinga G, Italiaander R, Brouwer A. Presence of SARS-Coronavirus-2 RNA in sewage and correlation with reported COVID-19 prevalnce in the early stage of the epidemic in the Netherlands. Environmental Science & Technology Letters. 2020;**7**:511-516. DOI: 10.1021/acs.estlett.0c00357

[103] Bar-Or I, Yaniv K, Shagan M, Ozer E, Weil M, Indenbaum V, et al. Regressing SARS-CoV-2 sewage measurements onto COVID-19 burden in the population:

A proof-of-concept for quantitative environmental surveillance. Frontiers in Public Health. 2021;**9**:561710. DOI: 10.3389/fpubh.2021.561710

[104] Nemudri A, Nemudraia A, Wiegand T, Surya K, Buyukyoruk M, Cicha C, et al. Temporal detection and phylogenetic assessment of SARS-CoV-2 in municipal wastewater. Cell Reports. 2020;**1**:100098. DOI: 10.1016/j.xcrm.2020.100098

[105] Balboa S, Mauricio-Iglesias M, Rodríguez S, Martínez-Lamas L, Vasallo FJ, Regueiro B, et al. The fate of SARS-CoV-2 in WWTPS points out the sludge line as a suitable spot for detection of COVID-19. Science of the Total Environment. 2021;**772**:145268. DOI: 10.1016/j.scitotenv.2021.145268

[106] Wu F, Zhang J, Xiao A, Gu X, Lee WL, Armas F, et al. SARS-CoV-2 titers in wastewater are higher than expected from clinically confirmed cases. mSystems. 2020;**5**:e00614-e00620. DOI: 10.1128/msystems.00614-20

[107] Zhang D, Ling H, Huang X, Li J, Li W, Yi C, et al. Potential spreading risks and disinfection challenges of medical wastewater by the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Science of the Total Environment. 2020;**741**:140445. DOI: 10.1016/j.scitotenv.2020.140445

[108] Randazzo W, Cuevas-Ferrando E, Sanjuán R, Domingo-Calap P, Sánchez G. Metropolitan wastewater analysis for COVID-19 epidemiological survey. International Journal of Hygiene and Environmental Health. 2020;**230**:113621. DOI: 10.1016/j.ijheh.2020.113621

[109] Randazzo W, Truchado P, Cuevas-Ferrando E, Simón P, Allende A, Sánchez G. SARS-CoV-2 RNA in wastewater anticipated COVID-19 occurrence in a low prevalence area. Water Research. 2020;**181**:115942. DOI: 10.1016/j.watres.2020.115942

[110] Bisseux M, Didier D, Audrey M, Christine A, Hélène PL, Jean-Luc B, et al. Monitoring of enterovirus diversity in wastewater by ultra-deep sequencing: An effective complementary tool for clinical enterovirus surveillance. Water Research. 2020;**169**:115246. DOI: 10.1016/j.watres.2019.115246

[111] Lun JH, Crosbie ND, White PA. Genetic diversity and quantification of human mastadenoviruses in wastewater from Sydney and Melbourne, Australia. Science of the Total Environment. 2019;**675**:305-312. DOI: 10.1016/j.scitotenv.2019.04.162

[112] Bibby K, Crank K, Greaves J, Li X, Wu Z, Hamza IA, et al. Metagenomics and the development of viral water quality tools. npj Clean Water. 2019;**2**:1-13. DOI: 10.1038/s41545-019-0032-3

[113] Miura T, Lhomme S, Le Saux JC, Le Mehaute P, Guillois Y, Couturier E, et al. Detection of hepatitis E virus in sewage after an outbreak on a French island. Food Environment Virology. 2016;**8**:194-199. DOI: 10.1007/s12560-016-9241-9

[114] Hata A, Katayama H, Kojima K, Sano S, Kasuga I, Kitajima M, et al. Effects of rainfall events on the occurrence and detection efficiency of viruses in river water impacted by combined sewer overflows. Science of the Total Environment. 2014;**268-269**:757-763. DOI: 10.1016/j.scitotenv.2013.08.093

[115] Bogler A, Packman A, Furman A, Gross A, Kushmaro A, Ronen A, et al. Rethinking wastewater risks and monitoring in light of the COVID-19 pandemic. Nature Sustainability. 2020;**3**:981-990. DOI: 10.1038/s41893-020-00605-2