COVID-19 PANDEMIC

RAEB'S Evidence Update

Highlights of health research synthesized by the Research, Analysis and Evaluation Branch

October 12, 2021

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RAEB's Rapid Responses for Ontario's Health Sector

Please contact *Evidence Synthesis Unit* for the full read of these rapid responses.

Long COVID Clinic Eligibility Criteria

Long COVID clinics were identified in Canada (British Columbia, Alberta, Manitoba, and Quebec) and the United Kingdom (UK).

- **Long COVID Clinics:** Most long COVID clinics include multi/interdisciplinary teams (i.e., primary care physicians, clinicians, and specialists [i.e., pharmacists, physiotherapists, pulmonary rehabilitation, respiratory nurses, speech and language therapists, dietitians, occupational therapists, and clinical psychologists]) that address persistent post-COVID-19 symptoms. In addition to this clinical service, long COVID clinics, in collaboration with other research organizations and institutions, provide evidence, research, and resources on long COVID.
- **Eligibility Criteria:** All identified jurisdictions require long COVID patients to be referred by a physician to a clinic based on one or more of the following eligibility criteria:
  - Clinical Diagnosis: Most jurisdictions require a patient to be diagnosed with COVID-19 and have documentation as proof of their diagnosis. Long COVID clinics in British Columbia and Quebec accept patients who do not have proof of their COVID-19 diagnosis (i.e., they were not tested for COVID-19) but have post-COVID-19 symptoms consistent with their suspected COVID-19 symptoms. Suspected COVID-19 diagnosis is confirmed through antibody testing. Furthermore, a post COVID clinic

in the UK suggests that their eligibility is based on a person's ongoing symptoms and impact on their life and is not based on the severity of the initial illness or on a positive test result.

- o Persistent Symptoms: Patients must experience persistent COVID-19 symptoms 12 weeks (British Columbia, Alberta) or 10 weeks (Manitoba) after their diagnosis; Quebec and the UK have unspecified post-diagnosis timeframes. Persistent symptoms include: shortness of breath, functional deterioration, fatigue, memory problems, mental health concerns, persistent cough, and muscle soreness.
- o Age: Alberta, Quebec, and the UK require long COVID patients to be 18 years of age or older.
- o Geographic Location: Quebec and the UK require long COVID patients to reside or be referred by a physician in a particular geographic location.

Research Evidence and Jurisdictional Experience

The research evidence profiled below was selected from highly esteemed academic journals and grey literature sources, based on date of publication and potential applicability or interest to the Ontario health sector.

Disease Management

Journal of Immunology: **SARS-CoV-2-reactive mucosal B cells in the upper respiratory tract of uninfected individuals**

October 4, 2021. This Canadian study reports the identification of SARS-CoV-2-reactive B cells in human tonsillar tissue obtained from children who were negative for COVID-19 prior to the pandemic and the generation of monoclonal antibodies recognizing the SARS-CoV-2 spike protein from these B cells. The study demonstrates pre-existing SARS-CoV-2-reactive antibodies in various B cell populations in the upper respiratory tract lymphoid tissue that may lead to the rapid engagement of the pathogen and contribute to prevent manifestations of symptomatic or severe disease. *Article*.

The Lancet: **Effectiveness of Pfizer vaccine up to six months in a large integrated health system (Kaiser Permanente) in the US**

October 4, 2021. This study of 3,436,957 individuals provides support for high effectiveness of the Pfizer vaccine against hospital admissions up until around six months after being fully vaccinated, even in the face of widespread dissemination of the delta variant. Reduction in vaccine effectiveness against SARS-CoV-2 infections over time is probably primarily due to waning immunity with time rather than the delta variant escaping vaccine protection. *Article*.

The Lancet: **Efficacy of COVID-19 vaccination on the symptoms of patients with long COVID in France**

September 29, 2021. This preprint study used data from the ComPaRe long COVID e-cohort to evaluate the effect of vaccination among patients with long COVID who still had persistent symptoms at baseline compared to unvaccinated controls. By 120 days, vaccination reduced the long COVID symptoms and doubled the rate of patients in complete remission. Vaccination also reduced both disease impact on patients' lives and the proportion of patients with an unacceptable symptom state. In the vaccination group, two (0.4%) patients reported serious adverse events leading to hospitalization. *Article*.

New England Journal of Medicine (NEJM): **Phase three safety and efficacy of AZD1222 (ChAdOx1 nCoV-19) COVID-19 vaccine**

September 29, 2021. In this randomized controlled study of the ChAdOx1 nCoV-19 (AstraZeneca) vaccine in over 32,000 participants from the United States, Chile, and Peru, the incidence of serious adverse effects was low (including no cases of vaccine-induced immune thrombotic thrombocytopenia). The overall vaccine efficacy was 74%, and 83.5% in participants 65 years of age or older. Efficacy was documented in a range of demographic subgroups. *Article*.

Health and Quality of Life Outcomes: **Design, validation, and implementation of the post-acute (long) COVID-19 quality of life (PAC-19QoL) instrument**

September 28, 2021. This study evaluated the use of a patient-centered instrument, the PAC-19QoL. Fifteen participants with long COVID agreed that 44 Quality of Life Indicators (QoLI) across four domains (i.e., psychological, physical, social, and work) were relevant for the assessment of their quality of life. The validation stage identified 35 of 44 QoLIs that differentiated between the 15 participants with long COVID-19 and 16 healthy people. Results suggest the PAC-19QoL instrument will enable an understanding of disease progression, on and off treatment, on the quality of life of patients with long COVID beyond simple symptomatology. *Article*.

BMJ Global Health: **Characterizing long COVID**

September 27, 2021. This systematic review of 39 studies found the nature of studies precludes a precise case definition or risk evaluation. The breadth of reported symptoms suggests a complex, heterogeneous condition affecting both those who were hospitalized and those managed in the community. Weakness, general malaise, fatigue, concentration impairment, and breathlessness were the most common symptoms reported. There is an urgent need for

prospective, robust, standardized, controlled studies into etiology, risk factors, and biomarkers to characterize long COVID in different at-risk populations and settings. *Article*.

Case Testing and Screening

Journal of the American Medical Association (JAMA): **Assessment of simulated surveillance testing and quarantine in a SARS-CoV-2-vaccinated population of students on a university campus**

October 1, 2021. This study examined a population of 5,000 simulated undergraduate students, across varying vaccine effectiveness rates of 50%, 75%, and 90%. The results suggest that surveillance testing and isolation of positive cases may continue to be important mitigation strategies on university campuses with a vaccinated student body with only modest erosion of vaccine effectiveness. Quarantining contacts offers limited added benefit over surveillance testing alone and may be effectively replaced by an increased testing frequency of reported contacts. *Article*.

Nature: **Mathematical modeling based on RT-qPCR analysis of SARS-CoV-2 in wastewater as a tool for epidemiology**

September 30, 2021. This study in Bratislava, Slovakia, based on wastewater monitoring from September 2020 until March 2021, observed high correlations between the number of viral particles in wastewater and the number of reported positive nasopharyngeal quantitative reverse transcription polymerase chain reaction (RT-qPCR) tests. The obtained results and subsequent mathematical modeling will serve as an early warning system for the occurrence of a local site of infection and predict the load on the health system up to two weeks in advance. *Article*.

Health Equity and Vulnerable Populations

Health Promotion International: **Pandemic-related racial discrimination and its health impact among non-Indigenous racially minoritized peoples in high-income contexts**

October 1, 2021. This systematic review found that racial discrimination is heightened during pandemic periods, due to the social association of specific racial groups with pandemic diseases. Fear-based responses to racially minoritized peoples during pandemic periods included verbal/physical abuse, hyper-surveillance, and avoidance, often occurring in public spaces, which had impacts on mental health and health care accessibility. Various coping strategies, including community support, avoidance, and problem solving, were documented in response to racial discrimination. Racism must be recognized as a public health issue, and efforts to address its increased impact in pandemic contexts should be considered. *Article*.

***JAMA*: COVID-19 vaccine decision-making factors in racial and ethnic minority communities in Los Angeles, California**

September 30, 2021. In this study, 70 participants from racial and ethnic minority communities described a complex vaccination decision-making process influenced by misinformation and politicization, deep apprehension related to historical inequity and mistreatment, access barriers related to social disadvantages, and a need for community engagement and trusted messengers. These findings suggest that COVID-19 vaccine equity will require multifaceted policies and programming that respect community concerns and the need for informed deliberation, investment in community-based engagement, improved accessibility and transparency of information, and reduced structural barriers in vaccination. *Article*.

Public Health Measures

***Nature*: Immune responses to two and three doses of the Pfizer vaccine in adults with solid tumors**

September 30, 2021. This study found that neutralizing antibodies were detected in 67% of patients undergoing active cytotoxic anti-cancer therapy (n = 53) after the first immunization, followed by a threefold increase after the second dose. At one week after a third immunization, 16 of 20 participants demonstrated a median threefold increase in antibody responses, but no improvement was observed in T-cell responses. Adverse events were mild. These results suggest that a third dose of the Pfizer vaccine is safe, improves immunity against SARS-CoV-2, and could be immunologically beneficial for patients with cancer on active chemotherapy. *Article*.

***Canadian Medical Association Journal (CMAJ)*: Closing Canada's COVID-19 vaccination gap**

September 27, 2021. This article suggests that vaccine mandates have proven to be the most effective strategy for increasing vaccination uptake, and Canadian provinces have seen modest success from offering financial incentives for getting vaccinated. Additional strategies include special access clinics for people with neurodevelopmental disorders, needle phobia, and anxiety in medical settings. Mobile teams bringing vaccines to the doorsteps of people living in low uptake neighbourhoods have also had success. *Article*.

Understanding the Disease

PLOS Medicine: **Incidence, co-occurrence, and evolution of long COVID features: A six-month retrospective cohort study of 273,618 COVID-19 survivors**

September 28, 2021. This study estimated the incidence and co-occurrence of nine core long COVID features. The incidence of each feature was: abnormal breathing (18.71% in the one- to 180-day period, 7.94% in the 90- to 180-day period); fatigue/malaise (12.82%, 5.87%); chest/throat pain (12.60%, 5.71%); headache (8.67%, 4.63%); other pain (11.60%, 7.19%); abdominal symptoms (15.58%, 8.29%); myalgia (3.24%, 1.54%); cognitive symptoms (7.88%, 3.95%); and anxiety/depression (22.82%, 15.49%). All nine features were more frequently reported after COVID-19 than after influenza and co-occurred more commonly. Significant differences in incidence and co-occurrence were associated with sex, age, and illness severity. *Article*.

Infection, Prevention and Control in Specific Settings

The Lancet: **Role of viral genomics in understanding COVID-19 outbreaks in long-term care facilities (LTCFs)**

September 27, 2021. This review of all genomic epidemiology studies on COVID-19 in LTCFs that had been published to date found that staff and residents were usually infected with identical, or near identical, SARS-CoV-2 genomes. Outbreaks usually involved one predominant cluster, and the same lineages persisted in LTCFs despite infection control measures. Outbreaks were most commonly due to single or few introductions followed by a spread rather than a series of seeding events from the community into LTCFs. The mortality rate among residents was high in all facilities, regardless of the lineage. When combined with local epidemiology, genomics allowed probable transmission sources to be better characterized. *Article*.

Trusted Resources

- The Evidence Synthesis Network (ESN) is a collaborative COVID-19 response initiative by Ontario's research and knowledge production community. The ESN website is a portal where research evidence requests can be made and includes previously completed ESN briefing notes.
- The Ontario COVID-19 Science Advisory Table is a group of scientific experts and health system leaders who evaluate and report on emerging evidence relevant to the COVID-19 pandemic, to inform Ontario's response to the pandemic.
- COVID-19 Evidence Network to support decision-making (COVID-END) in Canada:
  - COVID-END is a time-limited network that brings together more than 50 of the world's leading evidence-synthesis, technology-assessment, and guideline development groups to support decision-making. In addition to Living Evidence Profiles, COVID-END hosts an

inventory of best COVID-19 evidence syntheses from around the world. An up-to-date and comprehensive list of sources, organized by type of research evidence, is available on McMaster Health Forum's COVID-END website.

o The COVID-19 Evidence Spotlights from COVID-END provide updated information on COVID-19 responses with three types of products from COVID-END in Canada: 1) Canadian spotlights; 2) global spotlights; and 3) horizon scans. To receive an email containing hyperlinks to these products twice a month, subscribe here.

▪ In the second half of September, there were 12 newly added evidence syntheses. Two of these syntheses provide insight across two domains of the COVID-END taxonomy (public health measures and health system arrangements; and clinical management and health system arrangements) and the remaining focus on public health measures (n=5) and clinical management (n=5). Please visit Canadian Spotlight 9.2 to view the evidence, or browse past Canadian evidence spotlights. A complete list of the products is available here.

About RAEB

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