COVID-19 PANDEMIC – RAEB'S EVIDENCE UPDATE
Highlights of health research evidence synthesized by the Research, Analysis and Evaluation Branch (RAEB)
• June 28, 2021 •

FEATURED

ABOUT RAEB

Through research funding, brokering, translating, and sharing, we promote an enhanced evidence use capacity that supports all aspects of health policy, programming, and investment decision making. Services include:

- Literature reviews
- Jurisdictional scans
- Economic analysis
- Evaluation planning
- Research fund management
- Knowledge translation services

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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.

Effectiveness of Incentives to Promote COVID-19 Vaccine Uptake

- Incentives for COVID-19 Vaccines: Because incentive programs for COVID-19 vaccines have only recently been introduced, there is no direct evidence of their impact on vaccination rates. Mixed evidence was found from qualitative studies from the United States (US) examining the impact of financial incentives on willingness to be vaccinated among adults. One survey suggests that Israel's vaccination passport program may have led to an increase in willingness to be vaccinated.
  - Risks: Two articles raised concerns that financial incentives may either be ineffective at promoting, or may even discourage, COVID-19 vaccine uptake among individuals who have concerns about the safety of the vaccine.
  - Implementation: Vaccine lottery programs were launched in Alberta, Manitoba, and Nunavut; the evidence for whether lotteries are motivating Manitobans and Albertans to get vaccinated is mixed. In the US, 45 states, plus the District of Columbia, Puerto Rico, and the US Virgin Islands, have implemented COVID-19 vaccine lotteries. Preliminary outcomes of vaccine lottery programs in Ohio, California, and Oregon indicate a decrease in the number of vaccines administered following their launch. Across 10 international jurisdictions, prizes and awards are offered to encourage vaccination. Restrictions in access to public and private spaces (e.g., Israel, Saudi Arabia, United Arab Emirates) and disincentives in the form of fines (e.g., Indonesia) have also been implemented.
- Incentives for Other Vaccines: Evidence regarding the effectiveness of financial incentives in promoting uptake of other vaccines (e.g., influenza vaccine) was mixed, with eight systematic reviews finding some evidence that financial incentives (either alone or in combination with other interventions like outreach programs) increased vaccination uptake (three of which noted the need for further study), and three reviews finding no evidence of effectiveness. Two systematic reviews found that the use of non-financial rewards was associated with an increase in vaccination uptake.
- Incentives for Other Health-Related Behaviours: Evidence from systematic reviews of incentive programs designed to modify other health-related behaviours (e.g., prenatal care use, smoking cessation) was mixed.

EVIDENCE PRODUCTS PRODUCED WITH OUR PARTNERS

The COVID-19 Evidence Synthesis Network is comprised of groups specializing in evidence synthesis and knowledge translation. The group has committed to provide their expertise to provide high-quality, relevant, and timely synthesized research evidence about COVID-19 to inform decision makers as the pandemic continues. Please contact *Evidence Synthesis Unit* for the full read of these evidence products.

COVID-19-Related Hospital Funding

(Produced in collaboration with Ontario Health (Cancer Care Ontario))

Research and jurisdictional information was identified on the provision of COVID-19-related funding to hospitals and the health sector during (2020 to Spring 2021) and following (Summer 2021 to 2023) the pandemic:

- Limited evidence was identified about COVID-19-related hospital funding in the one to three-year period following the pandemic. One United States (US) study suggested that targeted financial support for hospitals could take several forms and should change over time to support surge versus ongoing operations as the pandemic evolves: 1) lump-sum payments to help hospitals prepare and respond to the surge in COVID-19 cases; 2) funds disbursed to offset hospitals' approximate losses due to reduced elective and outpatient revenue; and 3) targeted funding to further support individual hospitals, based on local assessments of the negative financial consequences of COVID-19.
- Information about health sector and hospital funding was identified in Canada, Australia, Finland, Germany, Sweden, the United Kingdom (UK), and the US. For example:
  - In the budget years 2021-22, most Canadian provinces are allocating funds to support health systems in ongoing COVID-19-related needs (e.g., vaccine roll-out, testing and screening, provision of personal protective equipment) and to recover from the COVID-19 pandemic.
  - Germany has implemented changes in the compensation payments for hospitals with intensive care capacities that postpone or cancel elective treatments to potentially treat COVID-19 patients (i.e., hospitals are eligible if they are in areas where less than 25% of free, operable intensive care beds are available and in which the seven-day cumulative incidence is above 70 cases per 100,000 residents).
  - In the US, the main sources of federal funds for hospitals include grants for covering lost revenue and unreimbursed costs associated with the pandemic, payment programs that help providers facing cash flow disruptions during an emergency (where about 80% in loans went to hospitals), and inpatient reimbursements for COVID-19 patients.
- Other types of funding for hospitals include: 1) funding to help hospitals manage backlogs in elective care (Sweden, UK); and 2) funding to establish dedicated clinics for patients experiencing long-term health impacts from COVID-19 (UK). A US study recommended that governments invest in expanding health system infrastructure and subsidizing payer coverage to deliver COVID-19 treatments or vaccines within the next 12 to 24 months to lower long-term costs.

RESEARCH EVIDENCE/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.

UNDERSTANDING THE DISEASE

- *Lancet:* Risk of hospitalization associated with infection with SARS-CoV-2 lineage B.1.1.7 in Denmark
  Jun 22, 2021. This study found that infection with SARS-CoV-2 lineage B.1.1.7 was associated with an increased risk of hospitalization compared with that of other lineages. The overall effect on hospitalizations in Denmark was lessened due to a strict lockdown, but these findings could support hospital preparedness and modelling of the projected impact of the epidemic in countries with uncontrolled spread of B.1.1.7. *Read*.
- *Nature:* SARS-CoV-2 viral load in nasopharyngeal swabs is not an independent predictor of unfavourable outcome
  Jun 21, 2021. This study assessed the ability of nasopharyngeal SARS-CoV-2 viral load at a patient's first hospital evaluation to predict unfavorable outcomes, drawing on data from adult patients (N=321) with confirmed COVID-19 through RT-PCR in nasopharyngeal swabs. The study found that nasopharyngeal SARS-CoV-2 viral load on admission is generally high in patients with COVID-19, regardless of illness severity, but it cannot be used as an independent predictor of unfavourable clinical outcome. *Read*.
- *NEJM:* Tofacitinib in patients hospitalized with COVID-19 pneumonia
  Jun 16, 2021. This study assessed the efficacy and safety of tofacitinib, a Janus kinase inhibitor (JAK), in patients (N=289) who were hospitalized with COVID-19. Patients were randomly assigned, at a median of 10 days after symptom onset, to receive tofacitinib or placebo. At 28 days, the risk of death or respiratory failure was lower in the tofacitinib group. These findings suggest that JAK inhibition represents an additional therapeutic option for treating COVID-19 pneumonia in patients who are not yet receiving invasive mechanical ventilation. *Read*.
- *JAMA:* Sperm parameters before and after COVID-19 mRNA vaccination
  Jun 17, 2021. This study assessed sperm parameters before and after COVID-19 mRNA vaccine (Moderna and Pfizer) administration among healthy men aged 18-50 years in Miami, Florida (N=45). The study found that there were no significant decreases in any sperm parameter after two doses of COVID-19 mRNA vaccine. The limitations of the study include the small number of men enrolled, limited generalizability beyond young, healthy men, short follow-up, and lack of a control group. *Read*.
- *PLOS One:* Reduced muscle mass as a predictor of intensive care unit (ICU) hospitalization in COVID-19 patients in Padova, Italy
  Jun 17, 2021. This study found that reduced muscle mass was a predictor of ICU admission in patients affected by COVID-19, as assessed with Computer Tomography (CT). The study suggested that radiologists should not only become aware of this finding, but should embed this information in their report to improve quality of care. *Read*.

RESEARCH EVIDENCE/JURISDICTIONAL EXPERIENCE cont'd

DISEASE MANAGEMENT

- *Lancet:* Effectiveness of BNT162b2 and ChAdOx1 nCoV-19 COVID-19 vaccination at preventing hospitalizations in people aged at least 80 years
  Jun 23, 2021. This study found that one dose of either the Pfizer or AstraZeneca vaccine resulted in substantial risk reductions of COVID-19-related hospitalization in people aged at least 80 years. *Read*.
- *Infection:* Micronutrient therapy and effective immune response for the management of COVID-19
  Jun 23, 2021. This review summarized evidence on micronutrient therapy of COVID-19 patients to provide insight into the role of essential vitamins/minerals in controlling the severity of the COVID-19 infection. Findings from the review indicate a bidirectional association between malnutrition and infection. Due to the range of favorable outcomes of micronutrient therapy, including safety and ease of use, the clinical applications of micronutrients as adjuvant therapies should be considered for COVID-19 patients. *Read*.
- *Cellular Immunology:* Antigen-specific adoptive immunotherapy for viral infections with a focus on COVID-19
  Jun 20, 2021. This review appraised the effects of viral-specific adoptive cell transfers (ACTs) in trials/studies as alternative treatments for SARS-CoV2 infection. The review identified that antigen-specific dendritic cell-based vaccines are of particular interest, as they are able to render the clearance of the virus and induce long-lived viral-specific immunity that may help fight against SARS-CoV2 infection. Seeing as these immunotherapies are still at the trial level, their safety and cost-effectiveness should be carefully evaluated. *Read*.
- *Complementary Therapies in Medicine:* Treatment of COVID-19 with traditional Chinese medicine
  Jun 19, 2021. This systematic review and meta-analysis evaluated the clinical efficacy of Lianhua Qinqwen capsules (LQ), a highly recommended compound widely used in clinical settings consisting of 13 traditional Chinese medicines, for the treatment of COVID-19. Compared with the control group, the LQ group showed a significant efficacy in improving clinical symptoms (e.g., fever, cough, fatigue), and in reducing the rate of clinical change to a severe or critical condition and fever time. Due to the limited quantity and quality of the included studies, further research is required with more and higher quality trials. *Read*.
- *Journal of Allergy and Clinical Immunology:* Risk of allergic reaction to SARS-CoV-2 vaccines
  Jun 18, 2021. This systematic review and meta-analysis, using an international consensus approach, found that the incidence of SARS-CoV-2 vaccine anaphylaxis is 7.91 cases/million (n=41,000,000 vaccinations; 26 studies, moderate certainty), the prevalence of polyethylene glycol (PEG) allergy is 103 cases/million (two studies, very low certainty), and the sensitivity for PEG skin testing is poor though specificity is high (15 studies, very low certainty). The review recommended vaccination over either no vaccination or performing SARS-CoV-2 vaccine/excipient screening allergy testing for individuals without history of a severe allergic reaction to the SARS-CoV-2 vaccine/excipient, and a shared decision-making paradigm in consultation with an allergy specialist for individuals with a history of a severe allergic reaction to the SARS-CoV-2 vaccine/excipient. *Read*.

RESEARCH EVIDENCE/JURISDICTIONAL EXPERIENCE cont'd

DISEASE MANAGEMENT

- *JAMA:* Incidence of SARS-CoV-2 infection in health care workers (HCWs) after a single dose of mRNA-1273 vaccine (Moderna)
  Jun 16, 2021. This study of HCWs (N=4,028) at Veteran Affairs Boston Healthcare System demonstrated an association between receipt of Moderna vaccine and a reduction in SARS-CoV-2 infection in HCWs beginning eight days after the first dose. These real-world findings reflect vaccination solely with Moderna and are consistent with aggregated data for BNT162b2 (Pfizer) and Moderna in HCWs. The first-dose risk reduction of 95% after day 14 highlights the potential for vaccination with mRNA-1273 to rapidly mitigate surges of vaccine-sensitive SARS-CoV-2 infection in HCWs. *Read*.

HEALTH EQUITY AND VULNERABLE POPULATIONS

- *JAMA Pediatrics:* Association between race and COVID-19 outcomes among 2.6 million children in England
  Jun 16, 2021. This study of 2,576,353 children (0-18 years of age) in England with COVID-19 disease found that children who were Black, Asian, or of mixed race had lower proportions of SARS-CoV-2 tests and had higher positive results and COVID-19 hospitalizations compared with White children. These results held after key demographic factors and selected comorbidities were accounted for. These findings suggest that race may play an important role in childhood COVID-19 outcomes, which reinforces the continued need for a race-tailored focus on health system performance and targeted public health interventions. *Read*.
- *Journal of Migration and Health:* SARS-CoV-2 among migrants and forcibly displaced populations
  Jun 16, 2021. This rapid systematic review found the incidence risk of SARS-CoV-2 of migrant populations varied from 0.12% to 2.08% in non-outbreak settings and from 5.64% to 21.15% in outbreak settings. Migrants showed a lower hospitalization rate compared to non-migrants. Negative impacts on mental health due to lockdown measures were found across the 13 studies. However, more robust and comparative study designs are needed. *Read*.

PUBLIC HEALTH MEASURES

- *PLOS One:* Analysis of the containment measures against the COVID-19 pandemic
  Jun 16, 2021. This study analyzed the impact of measures implemented against the pandemic by using a sample of more than 68 countries, including Canada. After controlling for daily COVID-19 tests, evidence suggests that school closures, shut-downs of non-essential business, mass gathering bans, travel restrictions in and out of risk areas, national border closures and/or complete entry bans, and nationwide curfews decreased the growth rate of the virus, and thus the peak of daily confirmed cases. Combinations of these measures decreased the daily growth rate at a level outweighing that of individual measures. *Read*.

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 produces Canadian and global spotlights and horizon scans on emerging issues, as well as hosting 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.
  - 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. COVID-19 responses can include the full spectrum of public health measures, clinical management, health system arrangements, and economic and social responses. In the first half of June, contributing Canadian evidence synthesis teams shared nine newly completed evidence syntheses and seven questions that they have newly taken on (see here). Three of these syntheses provides insight across all four domains of the COVID-END taxonomy (public health measures, clinical management, health system arrangements, and economic and social response) and one synthesis provides insight across two domains (public health measures and health system arrangements). The remaining focus on public health measures (n=4) and clinical management (n=1). The questions taken on focus on public health measures (n=6) and clinical management (n=1). To receive an email containing hyperlinks to these products twice a month, subscribe here.

* Figures in the header: Transmission electron microscope image shows SARS-CoV-2, the virus that causes COVID-19, isolated from a patient in the United States. Virus particles are emerging from the surface of cells cultured in the lab. The spikes on the outer edge of the virus particles give coronaviruses their name, crown-like. *National Institutes of Health's National Institute of Allergy and Infectious Diseases – Rocky Mountain Laboratories*