ACOG | Clinical
The American College of Obstetricians and Gynecologists

Vaccinating Pregnant and Lactating Patients Against COVID-19

Practice Advisory | December 2020

By reading this page you agree to ACOG's Terms and Conditions. Read terms

Published December 13, 2020

This Practice Advisory was developed by the American College of Obstetricians and Gynecologists' Immunization, Infectious Disease, and Public Health Preparedness Expert Work Group in collaboration with Laura E. Riley, MD; Richard Beigi, MD; Denise J. Jamieson, MD, MPH; Brenna L. Hughes, MD, MSc; Geeta Swamy, MD; Linda O'Neal Eckert, MD; Cynthia Gyamfi-Bannerman, MD, MSc; and Mark Turrentine, MD.

Summary of Key Information and Recommendations

COVID-19 vaccine development and regulatory approval are rapidly progressing. Thus, information and recommendations will evolve as more data are collected about these vaccines and their use in specific populations. This Practice Advisory is intended to be an overview of currently available COVID-19 vaccines and guidance for their use in pregnant and lactating patients.

- On December 11, 2020, the U.S. Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the Pfizer-BioNtech mRNA vaccine (BNT162b2) for use in individuals age 16 years and older as a 2-dose regimen given 3

weeks apart. This vaccine has shown to be 95% effective at preventing COVID-19 illness after the second dose.

- On December 12, 2020, after an explicit, evidence-based review of all available data, the Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for use of the Pfizer-BioNTech COVID-19 vaccine in persons aged ≥16 years for the prevention of COVID-19 illness.
- ACOG recommends that COVID-19 vaccines should not be withheld from pregnant individuals who meet criteria for vaccination based on ACIP-recommended priority groups.
- COVID-19 vaccines should be offered to lactating individuals similar to non-lactating individuals when they meet criteria for receipt of the vaccine based on prioritization groups outlined by the ACIP.
- Individuals considering a COVID-19 vaccine should have access to available information about the safety and efficacy of the vaccine, including information about data that are not available. A conversation between the patient and their clinical team may assist with decisions regarding the use of vaccines approved under EUA for the prevention of COVID-19 by pregnant patients. Important considerations include:
    - the level of activity of the virus in the community
    - the potential efficacy of the vaccine
    - the risk and potential severity of maternal disease, including the effects of disease on the fetus and newborn
    - the safety of the vaccine for the pregnant patient and the fetus.
- While a conversation with a clinician may be helpful, it should not be required prior to vaccination, as this may cause unnecessary barriers to access.
- Vaccines currently available under EUA have not been tested in pregnant women. Therefore, there are no safety data specific to use in pregnancy. See details about the Food and Drug Administration's (FDA) EUA process below.
- Pregnancy testing should not be a requirement prior to receiving Pfizer-BioNTech vaccine.

- Pregnant patients who decline vaccination should be supported in their decision. Regardless of their decision to receive or not receive the vaccine, these conversations provide an opportunity to remind patients about the importance of other prevention measures such as hand washing, physical distancing, and wearing a mask.
- Expected side effects should be explained as part of counseling patients, including that they are a normal part of the body's reaction to the vaccine and developing antibodies to protect against COVID-19 illness.
- The mRNA vaccines are not live virus vaccines, nor do they use an adjuvant to enhance vaccine efficacy. These vaccines do not enter the nucleus and do not alter human DNA in vaccine recipients. As a result, mRNA vaccines cannot cause any genetic changes.

COVID-19 Infection Risk in Pregnancy

Available data suggest that symptomatic pregnant patients with COVID-19 are at increased risk of more severe illness compared with nonpregnant peers (Ellington MMWR 2020, Collin 2020, Delahoy MMWR 2020, Panagiotakopoulos MMWR 2020, Zambrano MMWR 2020). Although the absolute risk for severe COVID-19 is low, these data indicate an increased risk of ICU admission, need for mechanical ventilation and ventilatory support (ECMO), and death reported in pregnant women with symptomatic COVID-19 infection, when compared with symptomatic non-pregnant women (Zambrano MMWR 2020). Pregnant patients with comorbidities such as obesity and diabetes may be at an even higher risk of severe illness consistent with the general population with similar comorbidities (Ellington MMWR 2020, Panagiotakopoulos MMWR 2020, Knight 2020, Zambrano MMWR 2020). Given the growing evidence, CDC has included pregnancy as a factor that leads to increased risk for severe COVID-19 illness (CDC). Similar to the general population, Black and Hispanic individuals who are pregnant appear to have disproportionately higher prevalence of COVID-19 infection and death (Ellington MMWR 2020, Moore MMWR 2020, Zambrano MMWR 2020). Further, risk (Zambrano MMWR 2020) of ICU admission was higher for pregnant Asian and Native Hawaiian/Pacific Islander individuals. These disparities are due to a range of social and structural factors including disparities in socioeconomic status, access to care, rates of chronic conditions, occupational exposure, systemic racism, and historic and continued inequities in the health care system.

COVID-19 Vaccines in Development

It is important to note that COVID-19 vaccine development and regulatory approval is a rapidly changing process, and information and recommendations will evolve as more data are collected about these vaccines and their use in specific populations.

Advisory Committee on Immunization Practices Recommendations

The Advisory Committee on Immunization Practices (ACIP) develops recommendations on how to use vaccines to control disease in the United States. The Committee's recommendations are sent to CDC's Director for approval. Once the ACIP recommendations have been reviewed and approved by the CDC Director and the U.S. Department of Health and Human Services, they are published in CDC's Morbidity and Mortality Weekly Report (MMWR). The MMWR publication represents the final and official CDC recommendations for immunization of the U.S. population (ACIP).

ACOG has representation on the ACIP, including on the ACIP COVID-19 working groups. On December 2, 2020 the ACIP voted to recommend that health care workers and long-term care facility residents be prioritized for vaccination in the initial deployment of COVID-19 vaccine (Phase 1a) (CDC 2020). As the availability of vaccine becomes more robust, ACIP will expand these recommendations to include additional priority populations (Phase 1b and Phase 1c).

On December 12, 2020, after an explicit, evidence-based review of all available data, the Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for use of the Pfizer-BioNTech COVID-19 vaccine in persons aged ≥16 years for the prevention of COVID-19 (CDC 2020). Following this vote, CDC released an MMWR outlining the recommendations. Additional clinical considerations developed by ACIP for the use of the vaccine in specific populations, including pregnant and lactating individuals, will be posted on the CDC's website shortly. Within these clinical considerations, it is expected that regarding pregnancy, CDC will state that a pregnant individual who is part of a group (e.g., healthcare personnel) recommended to receive a COVID-19 vaccine may choose to be vaccinated. A discussion with their healthcare provider can help the patient make an informed decision. Further, regarding lactation, it is expected that CDC will state that lactating individuals who are part of a group (e.g., healthcare personnel) recommended to receive a COVID-19 vaccine may choose to be vaccinated.

U.S. FDA Emergency Use Authorization and Approval

On December 11, 2020, the U.S. Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the Pfizer-BioNtech mRNA vaccine (BNT162b2) for use in individuals age 16 years and older as a 2-dose regimen given 3 weeks apart. This vaccine has been shown to be 95% effective at preventing COVID-19 illness after the second dose.

According to the EUA Fact Sheet for Health Care Professionals, available data on Pfizer-BioNTech COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy. The EUA Fact Sheet for Recipients and Caregivers states "If you are pregnant or breastfeeding, discuss your options with your healthcare provider".

The EUA authority allows the FDA to strengthen the nation's public health protections against chemical, biological, radiological, and nuclear (CBRN) threats by facilitating the availability and use of medical countermeasures needed during public health emergencies.

Under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), the FDA Commissioner may allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by CBRN threat agents when there are no adequate, approved, and available alternatives (FDA 2017).

Data on the safety and effectiveness of the vaccine(s) continues to be collected during the EUA period. (FDA, 2017).

Vaccine Information and Recommendations

At the time of this publication, one vaccine developed for the prevention of COVID-19 has received EUA from the FDA. However, COVID-19 vaccines are rapidly emerging and additional EUAs are likely to materialize. ACOG will strive to update this guidance as quickly as possible while maintaining accurate, evidence-based information.

mRNA COVID-19 Vaccines

The development and use of mRNA vaccines is relatively new. These vaccines consist of messenger RNA (mRNA) encapsulated by a lipid nanoparticle (LNP) for delivery into the host cells. These vaccines utilize the body's own cells to generate the coronavirus spike protein (the relevant antigens), which, similar to all other vaccines, stimulates immune cells to create antibodies against COVID-19. The mRNA vaccines are not live virus vaccines, nor do they use an adjuvant to enhance vaccine efficacy. These vaccines do not enter the nucleus and do not alter human DNA in vaccine recipients. As a result, mRNA vaccines cannot cause any genetic changes (CDC, Zhang 2019, Schlake 2012). Based on the mechanism of action of these vaccines and the demonstrated safety and efficacy in Phase II and Phase III clinical trials, it is expected that the safety and efficacy profile of the vaccine for pregnant individuals would be similar to that observed in non-pregnant individuals. That said, there are no safety data specific to mRNA vaccine use in pregnant or lactating individuals and the potential risks to a pregnant individual and the fetus are unknown.

Side Effects

Expected side effects should be explained as part of counseling patients, including that they are a normal part of the body's reaction to the vaccine and developing antibodies to protect against COVID-19 illness. Most study participants experienced mild side effects similar to influenza-like illness symptoms following vaccination such as injection site reactions (84.1%), fatigue (62.9%), chills (31.9%), muscle pain (38.3%), joint pain (23.6%), and headaches (55.1%). In the study subgroup of persons age 18-55 years fever greater than 38 C occurred in 3.7% after the first dose and 15.8% after the second dose (FDA 2020). Most of these symptoms resolved by day 3 after vaccination. Patients should be counseled about more severe side effects and when to seek medical care. For more information and details on side effects, see Local Reactions, Systemic Reactions, Adverse Events, and Serious Adverse Events: Pfizer-BioNTech COVID-19 Vaccine from the CDC.

Pregnancy Considerations

Despite ACOG's persistent advocacy for the inclusion of pregnant individuals in COVID-19 vaccine trials, none of the COVID-19 vaccines approved under EUA have been tested in pregnant individuals. However, studies in pregnant women are planned. Data from Developmental and Reproductive Toxicity (DART) studies for the Pfizer-BioNtech COVID-19 vaccine are anticipated in mid-December, according to the manufacturer. From what has been communicated so far regarding these forthcoming data, there have not been any major safety signals identified. These animal model studies provide the first safety data to help inform the future of clinical trials in pregnancy.

Among participants of Phase II/III clinical studies in non-pregnant adults, a few inadvertent pregnancies that have occurred are being followed to collect safety outcomes.

ACOG Recommendations

Pregnant Individuals

ACOG recommends that COVID-19 vaccines should not be withheld from pregnant individuals who meet criteria for vaccination based on ACIP-recommended priority groups. While safety data on the use of COVID-19 vaccines in pregnancy are not currently available, there are also no data to indicate that the vaccines should be contraindicated, and no safety signals generated from DART studies for the Pfizer-BioNtech vaccine. Therefore, in the interest of allowing pregnant individuals who would otherwise be considered a priority population for a vaccine approved for use under EUA, make their own decisions regarding their health, ACOG recommends that pregnant individuals should be free to make their own decision in conjunction with their clinical care team.

Individuals considering a COVID-19 vaccine should have access to available information about the safety and efficacy of the vaccine, including information about data that are not available. A conversation between the patient and their clinical team may assist with decisions regarding the use of vaccines approved under EUA for the prevention of COVID-19 by pregnant patients. Important considerations include the level of activity of the pandemic in the community, the potential efficacy of the vaccine, the potential risk and severity of maternal disease, including the effects of disease on the fetus and newborn, and the safety of the vaccine for the pregnant patient and the fetus. While a conversation with a clinician may be helpful, it should not be required prior to vaccination as this may cause unnecessary barriers to access.

Clinicians should review the available data on risks and benefits of vaccination with pregnant patients, including the risks of not getting vaccinated in the context of the individual patient's current health status, and risk of exposure, including the possibility for exposure at work or home and the possibility for exposing high-risk household members. Conversations about risk should take in to account the individual patient's values and perceived risk of various outcomes and should respect and support autonomous decision-making (ACOG 2013).

Pregnant women who experience fever following vaccination should be counseled to take acetaminophen, as fever has been associated with adverse pregnancy outcomes. Acetaminophen has been proven to be safe for use in pregnancy and does not appear to impact antibody response to COVID-19 vaccines.

Pregnant patients who decline vaccination should be supported in their decision. Regardless of their decision to receive or not receive the vaccine, these conversations provide an opportunity to remind patients about the importance of other prevention measures such as hand washing, physical distancing, and wearing a mask.

Lactating Individuals

ACOG recommends COVID-19 vaccines be offered to lactating individuals similar to non-lactating individuals when they meet criteria for receipt of the vaccine based on prioritization groups outlined by the ACIP. While lactating individuals were not included in most clinical trials, COVID-19 vaccines should not be withheld from lactating individuals who otherwise meet criteria for vaccination. Theoretical concerns regarding the safety of vaccinating lactating individuals do not outweigh the potential benefits of receiving the vaccine. There is no need to avoid initiation or discontinue breastfeeding in patients who receive a COVID-19 vaccine.

Individuals Contemplating Pregnancy

Vaccination is strongly encouraged for non-pregnant individuals within the ACIP prioritization group(s). Further, ACOG recommends vaccination of individuals who are actively trying to become pregnant or are contemplating pregnancy and meet the criteria for vaccination based on ACIP prioritization recommendations. Additionally, it is not necessary to delay pregnancy after completing both doses of the COVID-19 vaccine.

If an individual becomes pregnant after the first dose of the COVID-19 vaccine series, the second dose should be administered as indicated. If an individual receives a COVID-19 vaccine and becomes pregnant within 30 days of receipt of the vaccine, participation in CDC's V-SAFE program should be encouraged (see below for more information on CDC's V-SAFE program).

Importantly, routine pregnancy testing is not recommended prior to receiving a COVID-19 vaccine.

Health Equity Considerations and Racial and Ethnic Minority Groups

Racial and ethnic minority groups have been disproportionately affected by the COVID-19 pandemic. Individuals in racial and ethnic minority groups are more likely to have severe illness and even die from COVID-19 likely due to a range of social and structural factors including disparities in socioeconomic status, access to care, rates of chronic conditions, and occupational exposure, systemic racism, and historic and continued inequities in the health care system. Access to and confidence in COVID-19 vaccines is of critical importance for all communities, but willingness to consider vaccination varies by patient characteristics, in part due to historic injustices and systemic racism that has eroded trust in some communities of color. According to a recent Kaiser Family Foundation survey, only 50% of Black Americans compared with 65% of White Americans, would definitely or probably get vaccinated against COVID-19 even if the vaccine was free and determined safe by scientists, many citing distrust as a concern (Hamel 2020). When discussing COVID-19 vaccines with an individual who expresses concerns, it is critical to:

- Be aware of historical and current injustices perpetuated on communities of color
- Actively listen to and validate expressed fears and concerns
- Continue to support patients who decide not to be vaccinated, share resources, and encourage the continued use of prevention measures

If the patient is amenable to further discussion:

- Inform about the testing process, existing safety data and continued monitoring of safety and efficacy data on COVID-19 vaccines; there have not been shortcuts with the testing of this vaccine
- Discuss the increased incidence of infection and severe illness from COVID-19 in racial and ethnic minority groups
- Explain that individuals representing racial and ethnic minority groups were included in clinical trials (9.8% of Pfizer-BioNtech overall Phase II/III participants were Black and 26.2% were Hispanic/Latinx)

Additional Resources for Communicating with Communities of Color

- Centers for Disease Control and Prevention. Health Equity Considerations and Racial and Ethnic Minority Groups. Available at: https://www.cdc.gov/coronavirus/2019-ncov/community/health-equity/race-ethnicity.html. Retrieved December 13, 2020
- Chandler R, Guillaume D, Parker AG, Mack A, Hamilton J, Dorsey J, et al. The impact of COVID-19 among Black women: evaluating perspectives and sources of information [published online November 5, 2020]. Ethn Health. DOI: 10.1080/13557858.2020.1841120. Available at: https://www.tandfonline.com/doi/full/10.1080/13557858.2020.1841120. Retrieved December 11, 2020.
- Silverman E. STAT-Harris poll: the share of Americans interested in getting Covid-19 vaccine as soon as possible is dropping. STAT. October 19, 2020. Available at: https://www.statnews.com/pharmalot/2020/10/19/covid19-coronavirus-pandemic-vaccine-racial-disparities/. Retrieved December 11, 2020.
- Joint statement on ensuring racial equity in the development and distribution of a COVID-19 vaccine. Health Leads blog. October 26, 2020. Available at: https://healthleadsusa.org/communications-center/blog/joint-statement-on-covid19-vaccine-equity/ . Retrieved December 11, 2020.
- American College of Obstetricians and Gynecology. Addressing health equity during the COVID-19 pandemic. Position Statement. Washington, DC: ACOG; 2020. Available at: https://www.acog.org/clinical-information/policy-and-position-statements/position-statements/2020/addressing-health-equity-during-the-covid-19-pandemic. Retrieved December 11, 2020.

Vaccine Confidence

Vaccine hesitancy, particularly around COVID-19 vaccines, exists among all populations. When communicating with patients it is extremely important to underscore the general safety of vaccines and emphasize the fact that no steps were skipped in the development and evaluation of COVID-19 vaccines. This can be done by briefly highlighting the safety requirements of vaccines, and ongoing safety monitoring even after vaccines are made available. The following are some messages to consider using when discussing COVID-19 vaccines with patients:

Vaccines are one of the greatest public health achievements of the 20th century. Before the widespread use of vaccines, people routinely died from infectious diseases, several of which have since been eradicated thanks to robust immunization programs.

- Several vaccines have safely been given to pregnant and lactating individuals for decades.
- The rigor of COVID-19 vaccine clinical trials with regards to monitoring safety and efficacy meet the same high standards and requirements as with a typical vaccine approval process.
- While there has been a worldwide attempt to develop COVID-19 vaccines rapidly, this does not mean that any safety standards have been relaxed. In fact, there are additional safety monitoring systems to track and monitor these vaccines, including real-time assessment.
- Side effects such as influenza-like-illness can be expected with these vaccines, however this is a normal reaction as the body develops antibodies to protect itself against COVID-19. COVID-19 vaccines cannot cause COVID-19 infection. It is important not to be dissuaded by these side effects, because in order to get the maximum protection against COVID-19, patients need two doses of the vaccine.

  Safety monitoring continues well beyond the EUA administration.

  - CDC's V-SAFE: A new active surveillance smartphone-based after-vaccination health checker for people who receive COVID-19 vaccines. V-SAFE will use text messaging and web surveys from CDC to check in with vaccine recipients for health problems following COVID-19 vaccination. Information on pregnancy status at the time of vaccination and at subsequent follow up time points will also be collected. The system will provide telephone follow up to anyone who reports medically significant (important) adverse events or exposure to COVID-19 vaccines during pregnancy or periconception period.

    Vaccine Adverse Event Reporting System (VAERS): A national early warning system to detect possible safety problems in U.S.-licensed vaccines. VAERS is co-managed by the CDC and the FDA. Healthcare professionals are encouraged to report any clinically significant adverse events following vaccination to VAERS, even if they are

not sure if vaccination caused the event. In addition, we are anticipating that the following adverse events will be required to be reported to VAERS for COVID-19 vaccines administered under an Emergency Use Authorization (EUA):

  - Vaccine administration errors (whether associated with an adverse event or not)
  - Serious adverse events (irrespective of attribution to vaccination) (such as death, life-threatening adverse event, inpatient hospitalization)
  - Multisystem inflammatory syndrome (MIS) in children [if vaccine is authorized in children] or adults
  - Cases of COVID-19 that result in hospitalization or death

- CDC's National Healthcare Safety Network (NHSN): An acute care and long-term care facility monitoring system with reporting to the Vaccine Adverse Event Reporting System or VAERS
- Vaccines and Medications in Pregnancy Surveillance System (VAMPSS): A national surveillance system designed to monitor the use and safety of vaccines and asthma medications during pregnancy
- FDA is working with large insurer/payer databases on a system of administrative and claims-based data for surveillance and research
- Additional safety monitoring information can be found here: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html

---

References

1. Advisory Committee on Immunization Practices. ACIP recommendations. Available at: https://www.cdc.gov/vaccines/acip/recommendations.html. Retrieved December 11, 2020.

   Centers for Disease Control and Prevention. COVID-19 (coronavirus disease): people with certain medical conditions. Available

at: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html. Retrieved December 11, 2020.

3. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): people with certain medical conditions. Available at: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html. Retrieved December 7, 2020.

4. Centers for Disease Control and Prevention. Local reactions, systemic reactions, adverse events, and serious adverse events: Pfizer-BioNTech COVID-19 Vaccine. Available at: https://www.cdc.gov/vaccines/covid-19/info-by-manufacturer/pfizer/reactogenicity.html. Retrieved December 13, 2020

5. Centers for Disease Control and Prevention. Understanding mRNA COVID-19 Vaccines. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/mrna.html. Retrieved December 13, 2020

6. Centers for Disease Control and Prevention. Health equity considerations and racial and ethnic minority groups. Available at: https://www.cdc.gov/coronavirus/2019-ncov/community/health-equity/race-ethnicity.html. Retrieved December 13, 2020

7. Collin J, Byström E, Carnahan A, Ahrne M. Public Health Agency of Sweden's Brief Report: pregnant and postpartum women with severe acute respiratory syndrome coronavirus 2 infection in intensive care in Sweden. Acta Obstet Gynecol Scand 2020;99:819-22. Available at: https://obgyn.onlinelibrary.wiley.com/doi/full/10.1111/aogs.13901. Retrieved December 11, 2020.

Delahoy MJ, Whitaker M, O'Halloran A, Chai SJ, Kirley PD, Alden N, et al. Characteristics and maternal and birth outcomes of hospitalized pregnant women with laboratory-confirmed COVID-19 - COVID-NET, 13 states, March 1-August 22, 2020. COVID-NET Surveillance Team. MMWR Morb Mortal Wkly Rep 2020;69:1347-

54. Available at: https://www.cdc.gov/mmwr/volumes/69/wr/mm6938e1.htm. Retrieved December 11, 2020.

9. Ellington S, Strid P, Tong VT, Woodworth K, Galang RR, Zambrano LD, et al. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status - United States, January 22-June 7, 2020. MMWR Morb Mortal Wkly Rep 2020;69:769-75. Available at: https://www.cdc.gov/mmwr/volumes/69/wr/mm6925a1.htm. Retrieved December 11, 2020.

10. Ethical issues in pandemic influenza planning concerning pregnant women. Committee Opinion No. 563. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013;121:1138-43. Available at: https://journals.lww.com/greenjournal/Fulltext/2013/05000/Committee_Opinion__No__563__Ethical_Issues_in.47.aspx. Retrieved December 11, 2020.

11. Hamel L, Lopes L, Muñana C, Artiga S, Brodie B. The undefeated survey on race and health. San Francisco, CA: Kaiser Family Foundation; 2020. Available at: https://www.kff.org/report-section/kff-the-undefeated-survey-on-race-and-health-main-findings/. Retrieved December 11, 2020.

12. Knight M, Bunch K, Vousden N, Morris E, Simpson N, Gale C, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. UK Obstetric Surveillance System SARS-CoV-2 Infection in Pregnancy Collaborative Group. BMJ 2020;369:m2107. Available at: https://www.bmj.com/content/369/bmj.m2107. Retrieved December 11, 2020.

Moore JT, Ricaldi JN, Rose CE, Fuld J, Parise M, Kang GJ, et al. Disparities in incidence of COVID-19 among underrepresented racial/ethnic groups in counties identified as hotspots during June 5-18, 2020 - 22 states, February-June 2020. COVID-19 State, Tribal, Local, and Territorial Response Team. MMWR Morb Mortal Wkly Rep 2020;69:1122-6. Available

at: https://www.cdc.gov/mmwr/volumes/69/wr/mm6933e1.htm. Retrieved December 11, 2020.

14. Panagiotakopoulos L, Myers TR, Gee J, Lipkind HS, Kharbanda EO, Ryan DS, et al. SARS-CoV-2 infection among hospitalized pregnant women: reasons for admission and pregnancy characteristics - eight U.S. health care centers, March 1-May 30, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1355-9. Available at: https://www.cdc.gov/mmwr/volumes/69/wr/mm6938e2.htm. Retrieved December 11, 2020.

15. Pfizer-BioNTech COVID-19 vaccine (BNT162, PF-07302048). Vaccines and Related Biological Products Advisory Committee briefing document. Available at: https://www.fda.gov/media/144246/download. Retrieved December 11, 2020.

16. Schlake T, Thess A, Fotin-Mleczek M, Kallen KJ. Developing mRNA-vaccine technologies. RNA Biol. 2012;9(11):1319-1330. doi:10.4161/rna.22269. U.S. Food and Drug Administration. December 11, 2020 communication to Pfizer Inc. Available at: https://www.fda.gov/media/144412/download. Retrieved December 13, 2020

17. U.S. Food and Drug Administration. Fact sheet for healthcare providers administering vaccine (vaccination providers). Emergency Use Authorization (EUA) of the Pfizer-Biontech COVID-19 vaccine to prevent Coronavirus Disease 2019 (COVID-19). Available at: https://www.fda.gov/media/144413/download. Retrieved December 13, 2020

18. U.S. Food and Drug Administration. Fact Sheet for Recipients and Caregivers. Emergency Use Authorization (EUA) of the Pfizer-Biontech COVID-19 vaccine to prevent Coronavirus Disease 2019 (COVID-19) in individuals 16 years of age and older. Available at: https://www.fda.gov/media/144414/download. Retrieved December 13, 2020

U.S. Food and Drug Administration. Emergency Use Authorization of medical products and related authorities. Monitoring and reporting of adverse events.

Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities#monitoring. Retrieved December 13, 2020

20. Zambrano LD, Ellington S, Strid P, Galang RR, Oduyebo T, Tong VT, et al. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status - United States, January 22-October 3, 2020. CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team. MMWR Morb Mortal Wkly Rep 2020;69:1641-7. Available at: https://www.cdc.gov/mmwr/volumes/69/wr/mm6944e3.htm. Retrieved December 11, 2020.

21. Zhang C, Maruggi G, Shan H and Li J (2019) Advances in mRNA Vaccines for Infectious Diseases. Front. Immunol. 10:594. doi: 10.3389/fimmu.2019.00594

A Practice Advisory is issued when information on an emergent clinical issue (e.g. clinical study, scientific report, draft regulation) is released that requires an immediate or rapid response, particularly if it is anticipated that it will generate a multitude of inquiries. A Practice Advisory is a brief, focused statement issued within 24-48 hours of the release of this evolving information and constitutes ACOG clinical guidance. A Practice Advisory is issued only on-line for Fellows but may also be used by patients and the media. Practice Advisories are reviewed periodically for reaffirmation, revision, withdrawal or incorporation into other ACOG guidelines.

This information is designed as an educational resource to aid clinicians in providing obstetric and gynecologic care, and use of this information is voluntary. This information should not be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. It is not intended to substitute for the independent professional judgment of the treating clinician. Variations in practice may be warranted when, in the reasonable judgment of the treating clinician, such course of action is indicated by the condition of the patient, limitations of available resources, or advances in knowledge or technology. The American College of Obstetricians and Gynecologists reviews its publications regularly; however, its publications may not reflect the most recent evidence. Any updates to this document can be found on www.acog.org or by calling the ACOG Resource Center.

While ACOG makes every effort to present accurate and reliable information, this publication is provided "as is" without any warranty of accuracy, reliability, or otherwise, either express or implied. ACOG does not guarantee, warrant, or endorse the products or services of any firm, organization, or person. Neither ACOG nor its officers, directors, members, employees, or agents will be liable for any loss, damage, or claim with respect to any liabilities, including direct, special, indirect, or consequential damages, incurred in connection with this publication or reliance on the information presented.

Publications of the American College of Obstetrician and Gynecologists are protected by copyright and all rights are reserved. The College's publications may not be reproduced in any form or by any means without written permission from the copyright owner.

The American College of Obstetricians and Gynecologists (ACOG), is the nation's leading group of physicians providing health care for women. As a private, voluntary, nonprofit membership organization of more than 58,000 members, ACOG strongly advocates for quality health care for women, maintains the highest standards of clinical practice and continuing education of its members, promotes patient education, and increases awareness among its members and the public of the changing issues facing women's health care. www.acog.org

---

Topics **COVID-19** **Coronavirus** **Vaccine-preventable diseases** **Immunization** **Lactation**

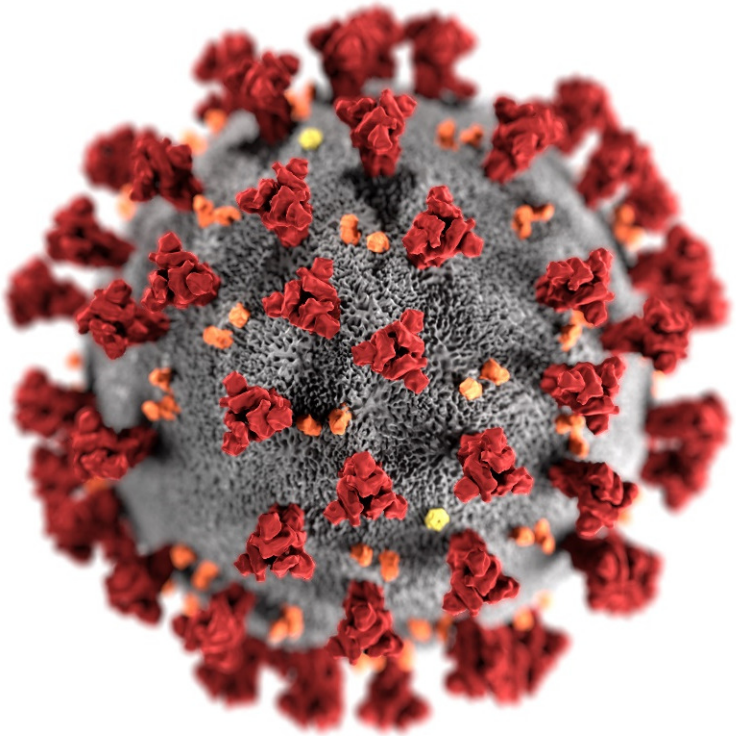
American College of Obstetricians and Gynecologists
409 12th Street SW, Washington, DC 20024-2188

Copyright 2020. All rights reserved.
Privacy Statement | Terms and Conditions of Use

What Clinicians Need to Know About the Pfizer-BioNTech COVID-19 Vaccine

Amanda Cohn, MD
Sarah Mbaeyi, MD, MPH

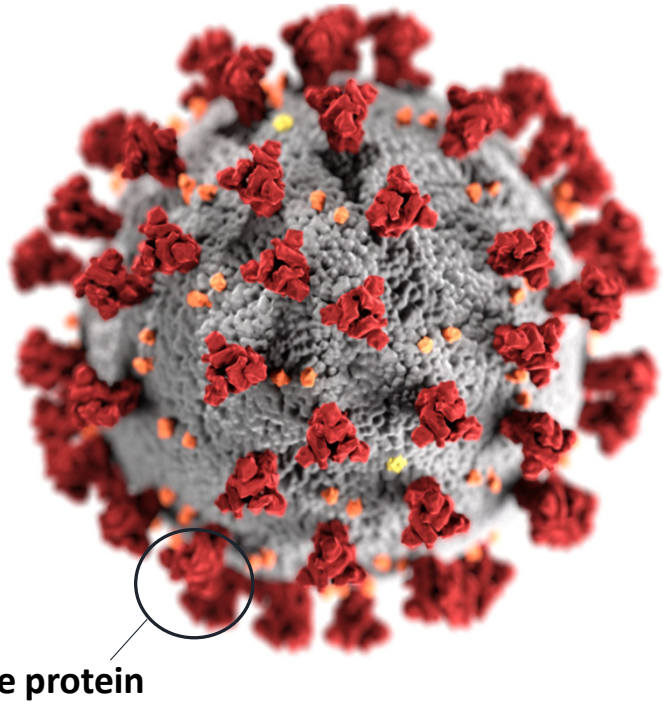
December 13, 2020



Pfizer-BioNTech COVID-19 Vaccine

Pfizer-BioNTech COVID-19 vaccine

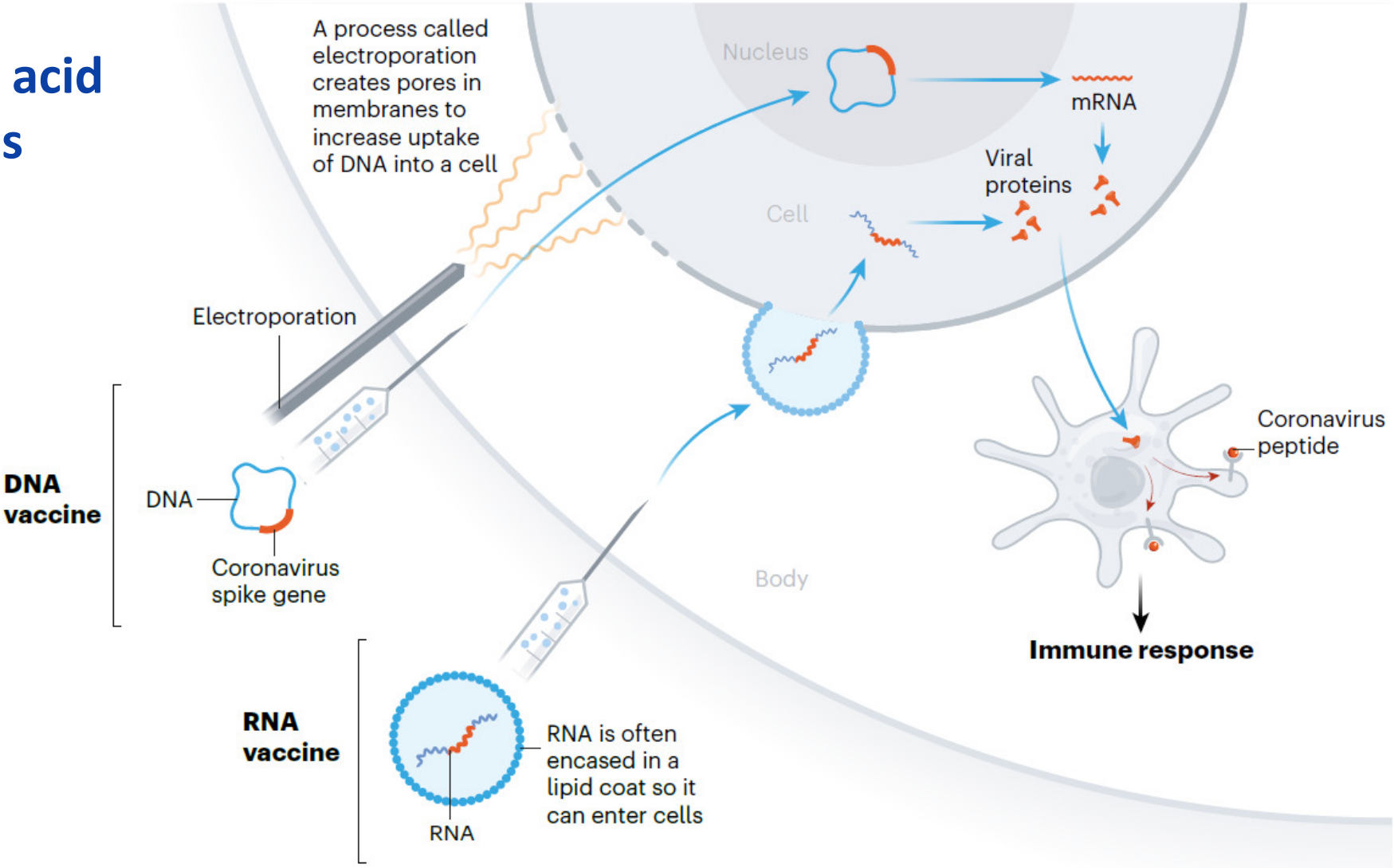
- Lipid nanoparticle-formulated mRNA vaccine encoding the spike protein
  - Spike protein: facilitates entry of virus into cells
- Vaccination induces antibodies that can block entry of SARS-CoV-2 into cells, thereby preventing infection
- FDA issued an Emergency Use Authorization on December 13, 2020 for use in persons aged ≥16 years



Explaining mRNA COVID-19 vaccines

- mRNA vaccines take advantage of the process that cells use to make proteins in order to trigger an immune response
  - Like all vaccines, COVID-19 mRNA vaccines have been **rigorously tested** for safety before being authorized for use in the United States
  - mRNA technology is **new, but not unknown**. They have been studied for more than a decade
  - mRNA vaccines **do not contain a live virus** and do not carry a risk of causing disease in the vaccinated person
  - mRNA from the vaccine never enters the nucleus of the cell and **does not affect or interact with a person's DNA**

Nucleic acid vaccines



Nature. Vol 580. April 30, 2020. https://media.nature.com/original/magazine-assets/d41586-020-01221-y/d41586-020-01221-y.pdf

Advisory Committee on Immunization Practices (ACIP) Recommendations

ACIP recommendations for use of COVID-19 vaccines

- On December 12, 2020, ACIP recommended use of the Pfizer-BioNTech COVID-19 vaccine in persons 16 years of age and older under the FDA's Emergency Use Authorization

- ACIP recommends that when a COVID-19 vaccine is authorized by FDA and recommended by ACIP, that 1) health care personnel and 2) residents of long-term care facilities be offered vaccination in the initial phase of the COVID-19 vaccination program

Vaccine Administration

Administration

- 2-dose series administered intramuscularly 3 weeks apart
- Administration of 2nd dose within 4-day grace period (e.g., day 17-21) considered valid
- If >21 days since 1st dose, 2nd dose should be administered at earliest opportunity (but no doses need to be repeated)
- Both doses are necessary for protection; efficacy of a single dose has not been systematically evaluated

Interchangeability with other COVID-19 vaccine products

- Pfizer-BioNTech COVID-19 vaccine not interchangeable with other COVID-19 vaccine products
  - Safety and efficacy of a mixed series has not been evaluated
- Persons initiating series with Pfizer-BioNTech COVID-19 vaccine should complete series with same product
- If two doses of different mRNA COVID-19 vaccine products inadvertently administered, no additional doses of either vaccine recommended at this time
  - Recommendations may be updated as further information becomes available or additional vaccine types authorized

Coadministration with other vaccines

- Pfizer-BioNTech COVID-19 vaccine should be administered alone with a minimum interval of 14 days before or after administration with any other vaccines
  - Due to lack of data on safety and efficacy of the vaccine administered simultaneously with other vaccines

- If Pfizer-BioNTech COVID-19 vaccine is inadvertently administered within 14 days of another vaccine, doses do not need to be repeated for either vaccine

Vaccination of Persons with Prior SARS-CoV-2 Infection or Exposure

Persons with a history of SARS-CoV-2 infection

- Vaccination should be offered to persons regardless of history of prior symptomatic or asymptomatic SARS-CoV-2 infection
  - Data from phase 2/3 clinical trials suggest vaccination safe and likely efficacious in these persons

- Viral or serologic testing for acute or prior infection, respectively, is not recommended for the purpose of vaccine decision-making

Persons with known current SARS-CoV-2 infection

- Vaccination should be deferred until recovery from acute illness (if person had symptoms) *and* criteria have been met to discontinue isolation

- No minimal interval between infection and vaccination

- However, current evidence suggests reinfection uncommon in the 90 days after initial infection, and thus persons with documented acute infection in the preceding 90 days may defer vaccination until the end of this period, if desired

https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-in-home-patients.html
https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html

Persons who previously received passive antibody therapy for COVID-19

- Currently no data on safety or efficacy of COVID-19 vaccination in persons who received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment

- Vaccination should be deferred for at least 90 days to avoid interference of the treatment with vaccine-induced immune responses
  - Based on estimated half-life of therapies and evidence suggesting reinfection is uncommon within 90 days of initial infection

Persons with a known SARS-CoV-2 exposure

- **Community or outpatient setting:**
  - Defer vaccination until quarantine period has ended to avoid exposing healthcare personnel (HCP) or other persons during vaccination visit

- **Residents of congregate healthcare settings (e.g., long-term care facilities):**
  - May be vaccinated, as likely would not result in additional exposures. HCP are already in close contact with residents and should employ appropriate infection prevention and control procedures

- **Residents of other congregate settings (e.g., correctional facilities, homeless shelters)**
  - May be vaccinated, in order to avoid delays and missed opportunities for vaccination
  - Where feasible, precautions should be taken to limit mixing of these individuals with other residents or non-essential staff

https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html
https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html

Vaccination of Special Populations

Persons with underlying medical conditions

- Vaccine may be administered to persons with underlying medical conditions who have no contraindications to vaccination

- Phase 2/3 clinical trials demonstrate similar safety and efficacy profiles in persons with underlying medical conditions, including those that place them at increased risk for severe COVID-19, compared to persons without comorbidities

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

Immunocompromised persons

- Persons with HIV infection, other immunocompromising conditions, or who take immunosuppressive medications or therapies might be at increased risk for severe COVID-19

- Data not currently available to establish safety and efficacy of vaccine in these groups

- These individuals may still receive COVID-19 vaccine unless otherwise contraindicated

- Individuals should be counseled about:
  - Unknown vaccine safety and efficacy profiles in immunocompromised persons
  - Potential for reduced immune responses
  - Need to continue to follow all current guidance to protect themselves against COVID-19

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

Pregnant women

- There are no data on the safety of COVID-19 vaccines in pregnant women
  - Animal developmental and reproductive toxicity (DART) studies are ongoing
  - Studies in humans are ongoing and more planned

- mRNA vaccines and pregnancy
  - Not live vaccines
  - They are degraded quickly by normal cellular processes and don't enter the nucleus of the cell

- COVID-19 and pregnancy
  - Increased risk of severe illness (ICU admission, mechanical ventilation and death)
  - Might be an increased risk of adverse pregnancy outcomes, such as preterm birth

- If a woman is part of a group (e.g., healthcare personnel) who is recommended to receive a COVID-19 vaccine and is pregnant, she may choose to be vaccinated. A discussion with her healthcare provider can help her make an informed decision.

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/pregnancy-breastfeeding.html

Pregnant women

- Considerations for vaccination:
  - level of COVID-19 community transmission (risk of acquisition)
  - her personal risk of contracting COVID-19 (by occupation or other activities)
  - the risks of COVID-19 to her and potential risks to the fetus
  - the efficacy of the vaccine
  - the known side effects of the vaccine
  - the lack of data about the vaccine during pregnancy

- Pregnant women who experience fever following vaccination should be counseled to take acetaminophen as fever has been associated with adverse pregnancy outcomes

- Routine testing for pregnancy prior to receipt of a COVID-19 vaccine is not recommended.

Breastfeeding/Lactating women

- There are no data on the safety of COVID-19 vaccines in lactating women or the effects of mRNA vaccines on the breastfed infant or milk production/excretion

- mRNA vaccines are not considered live virus vaccines and are not thought to be a risk to the breastfeeding infant

- If a lactating woman is part of a group (e.g., healthcare personnel) who is recommended to receive a COVID-19 vaccine, she may choose to be vaccinated

Patient Vaccine Counseling

Reactogenicity

- Before vaccination, providers should counsel vaccine recipients about expected local and systemic post-vaccination symptoms

- Unless a person develops a contraindication to vaccination, they should be encouraged to complete the series even if they develop post-vaccination symptoms in order to optimize protection against COVID-19

- Antipyretic or analgesic medications may be taken for treatment of post-vaccination symptoms
  - Routine prophylaxis for the purposes of preventing symptoms is not recommended at this time, due to lack of information on impact of use on vaccine-induced antibody responses

Vaccine efficacy

- Two doses required to achieve high efficacy
  - Efficacy after 2nd dose: 95.0% (95% CI: 90.3%, 97.6%)

- Patients should be counseled on importance of completing the 2-dose series in order to optimize protection

Public health recommendations for vaccinated persons

- Protection from vaccine is not immediate; vaccine is a 2-dose series and will take 1 to 2 weeks following the second dose to be considered fully vaccinated

- No vaccine is 100% effective

- Given the currently limited information on how well the vaccine works in the general population; how much it may reduce disease, severity, or transmission; and how long protection lasts, vaccinated persons should continue to follow all current guidance to protect themselves and others, including:
  - Wearing a mask
  - Staying at least 6 feet away from others
  - Avoiding crowds
  - Washing hands often
  - Following CDC travel guidance
  - Following quarantine guidance after an exposure to someone with COVID-19
  - Following any applicable workplace or school guidance

https://www.cdc.gov/coronavirus/2019-ncov/index.html

Contraindications and Precautions

Contraindications and precautions

- Package insert:
  - Severe allergic reaction (e.g., anaphylaxis) to any component of the Pfizer-BioNTech COVID-19 vaccine is a contraindication to vaccination
  - Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of the vaccine

- Because of reports of anaphylactic reactions in persons vaccinated outside of clinical trials, the additional following guidance is proposed:
  - A severe allergic reaction to any vaccine or injectable therapy (intramuscular, intravenous, or subcutaneous) is a precaution to vaccination at this time
  - Vaccine providers should observe patients after vaccination to monitor for the occurrence of immediate adverse reactions:
    - Persons with a history of anaphylaxis: 30 minutes
    - All other persons: 15 mins

Algorithm for the triage of persons presenting for Pfizer-COVID-19 vaccine

	PROCEED WITH VACCINATION	PRECAUTION TO VACCINATION	CONTRAINDICATION TO VACCINATION
CONDITIONS	**CONDITIONS** •Immunocompromising conditions •Pregnancy •Lactation **ACTIONS** •Additional counseling* •15-minute observation period	**CONDITIONS** •Moderate/severe acute illness **ACTIONS** •Risk assessment •Potential deferral of vaccination •15-minute observation period if vaccinated	**CONDITIONS** •None **ACTIONS** •N/A
ALLERGIES	**ALLERGIES** •History of food, pet, insect, venom, environmental, latex, etc., allergies •History of allergy to oral medications (including the oral equivalent of an injectable medication) •Non-serious allergy to vaccines or other injectables (e.g., no anaphylaxis) •Family history of anaphylaxis **ACTIONS** •15-minute observation period	**ALLERGIES** •History of severe allergic reaction (e.g., anaphylaxis) to another vaccine (not including Pfizer-BioNTech vaccine) •History of severe allergic reaction (e.g., anaphylaxis) to an injectable medication **ACTIONS:** •Risk assessment •Potential deferral of vaccination •30-minute observation period if vaccinated	**ALLERGIES** •History of severe allergic reaction (e.g., anaphylaxis) to any component of the Pfizer-BioNTech vaccine **ACTIONS** •Do not vaccinate

* See Special Populations section for information on patient counseling in these group

Interpretation of SARS-CoV-2 Test Results in Vaccinated Persons

SARS-CoV-2 tests

- **Viral tests:** Prior receipt of the Pfizer-BioNTech COVID-19 vaccine will not affect the results of SARS-CoV-2 nucleic acid amplification or antigen tests

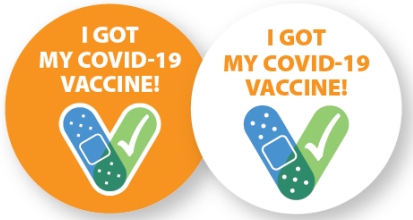
- **Antibody tests:**
  - Currently available antibody tests for SARS-CoV-2 assess IgM and/or IgG to spike or nucleocapsid proteins
  - Pfizer-BioNTech COVID-19 vaccine contains mRNA that encodes the spike protein; thus, a positive test for spike protein IgM/IgG could indicate either prior infection or vaccination
  - To evaluate for evidence of prior infection in an individual with a history of Pfizer-BioNTech COVID-19 vaccination, a test specifically evaluating IgM/IgG to the nucleocapsid protein should be used

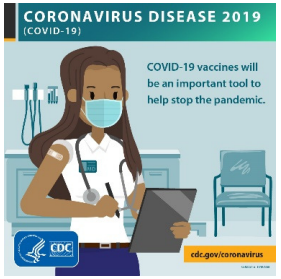
https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/eua-authorized-serology-test-performance

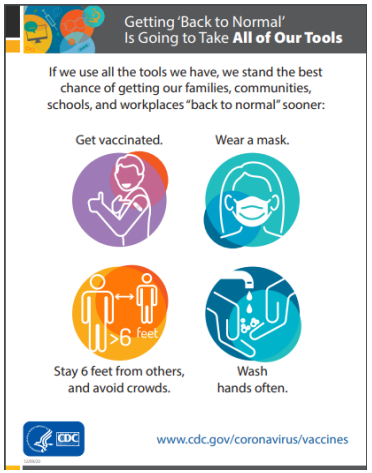
Clinical Resources

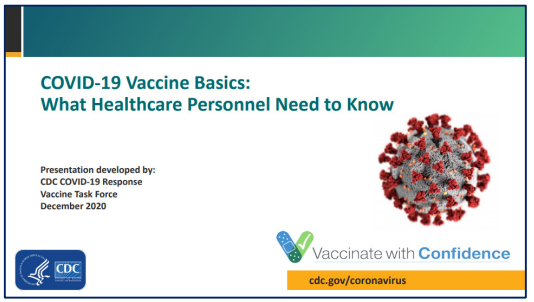
COVID-19 vaccine communication resources

- Engaging in Effective COVID-19 Vaccine Conversations
  - https://www.cdc.gov/vaccines/covid-19/hcp/engaging-patients.htm
- Toolkit for Medical Centers, Clinics, and Clinicians
  - https://www.cdc.gov/vaccines/covid-19/health-systems-communication-toolkit.html
- More toolkits coming soon
  - Long-term care facilities
  - Health departments
  - Community-based organizations
  - Employers of essential workers



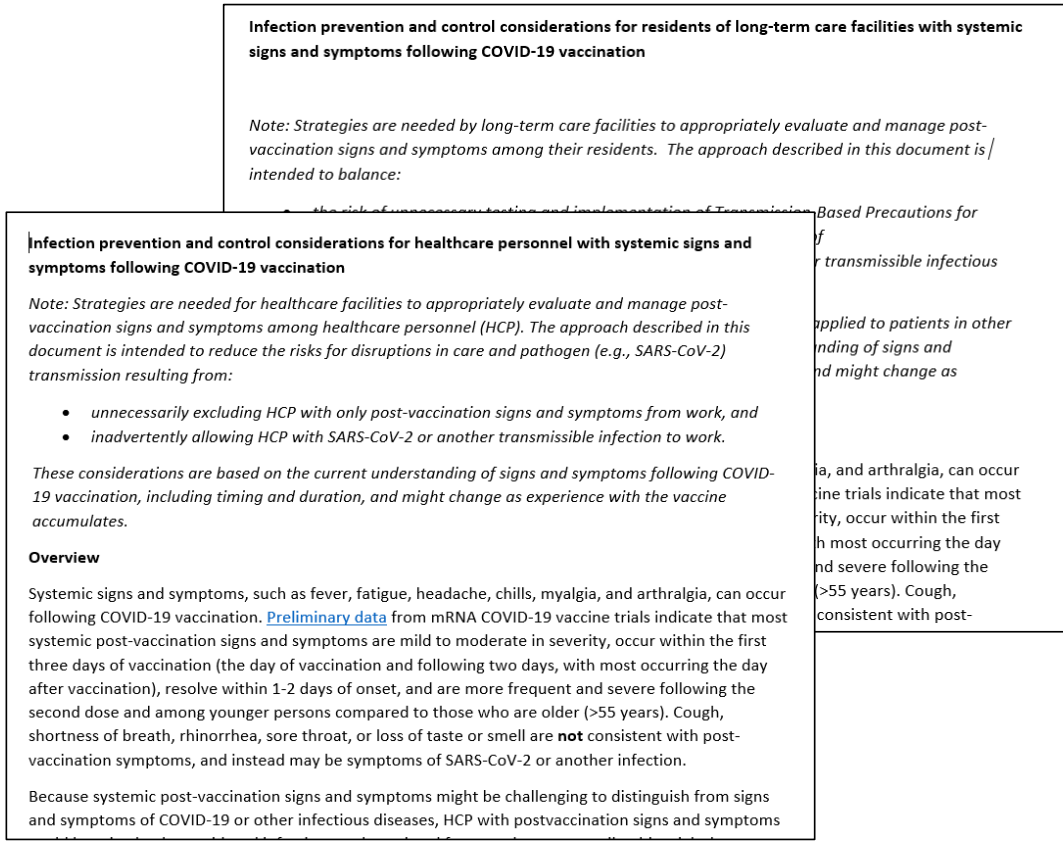






Infection prevention and control recommendations for persons with post-vaccination symptoms

- Healthcare personnel
- Long-term care facility residents



Infection prevention and control considerations for residents of long-term care facilities with systemic signs and symptoms following COVID-19 vaccination

Note: Strategies are needed by long-term care facilities to appropriately evaluate and manage post-vaccination signs and symptoms among their residents. The approach described in this document is intended to balance:

Infection prevention and control considerations for healthcare personnel with systemic signs and symptoms following COVID-19 vaccination

Note: Strategies are needed for healthcare facilities to appropriately evaluate and manage post-vaccination signs and symptoms among healthcare personnel (HCP). The approach described in this document is intended to reduce the risks for disruptions in care and pathogen (e.g., SARS-CoV-2) transmission resulting from:

- *unnecessarily excluding HCP with only post-vaccination signs and symptoms from work, and*
- *inadvertently allowing HCP with SARS-CoV-2 or another transmissible infection to work.*

These considerations are based on the current understanding of signs and symptoms following COVID-19 vaccination, including timing and duration, and might change as experience with the vaccine accumulates.

Overview

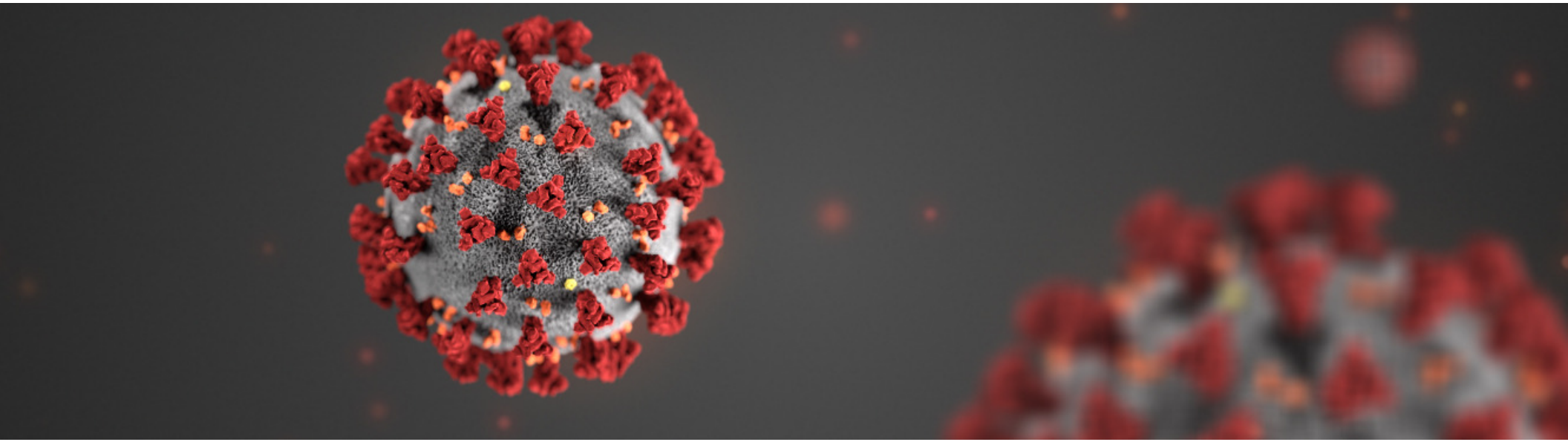
Systemic signs and symptoms, such as fever, fatigue, headache, chills, myalgia, and arthralgia, can occur following COVID-19 vaccination. Preliminary data from mRNA COVID-19 vaccine trials indicate that most systemic post-vaccination signs and symptoms are mild to moderate in severity, occur within the first three days of vaccination (the day of vaccination and following two days, with most occurring the day after vaccination), resolve within 1-2 days of onset, and are more frequent and severe following the second dose and among younger persons compared to those who are older (>55 years). Cough, shortness of breath, rhinorrhea, sore throat, or loss of taste or smell are **not** consistent with post-vaccination symptoms, and instead may be symptoms of SARS-CoV-2 or another infection.

Because systemic post-vaccination signs and symptoms might be challenging to distinguish from signs and symptoms of COVID-19 or other infectious diseases, HCP with postvaccination signs and symptoms

https://www.cdc.gov/vaccines/covid-19/index.html

FDA EUA resources

- FDA COVID-19 EUA
  - https://www.fda.gov/media/144412/download
- FDA COVID-19 Information
  - https://www.fda.gov/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-covid-19
- FDA EUA Guidance
  - https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#covid19euas



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Thank you

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

PROCÈS-VERBAL DE LA RENCONTRE DU COMITÉ SUR L'IMMUNISATION DU QUÉBEC
18 décembre 2020 – 9 h à 11 h
Réunion par Teams

Étaient présents :

Membres actifs :	Sapha Barkati, François Boucher, Nicholas Brousseau, Julie Bestman-Smith, Alex Carignan, Gaston De Serres, Philippe De Wals, Vladimir Gilca, Rodica Gilca, Maryse Guay, Chantal Sauvageau, Bruce Tapiéro.
Membres liaison :	Dominique Biron, Hélène Gagné, Catherine Guimond, Lyne Judd, Marc Lebel, Yen Bui.
Membres d'office :	Dominique Grenier, Nadine Sicard, Eveline Toth.
Secrétariat scientifique :	Dominique Gagnon, Maryse Guay, Marilou Kiely.
S'étaient excusés:	Patricia Hudson, Julien Michaud-Tétreault (médecin résident à l'Université de Sherbrooke).
Invités :	Nicole Boulianne (en soutien à la Cellule Vaccination-COVID-19), Ève Capistran, (médecin résidente en microbiologie et infectiologie à l'Université de Sherbrooke) Paule Clément (en soutien à la Cellule Vaccination-COVID-19), Gisèle Trudeau (en soutien à la Cellule Vaccination-COVID-19).

Objectif(s) de la rencontre :

- Répondre à des questions formulées par le GAV sur la vaccination contre la COVID-19 avec le vaccin de Moderna et sur l'utilisation du vaccin de Pfizer-BioNTech

	Point discuté + Éléments de discussion	Décision(s) + Action (P. responsable)
1.	**Question(s) du GAV sur l'intervalle minimal recommandé entre les doses du vaccin de Moderna et sur l'harmonisation de l'intervalle entre les doses du vaccin de Pfizer et celui de Moderna** ▪ Recommandation du CCNI : intervalle minimal de 21 jours entre les 2 doses et intervalle recommandé de 28 jours; ▪ Proposition de mettre 21 jours comme intervalle minimal dans le PIQ; ▪ Suggestion de formuler une recommandation uniforme pour les 2 vaccins pour l'instant notamment pour des questions d'harmonisation des pratiques. (c'est-à-dire similitude de la technologie des vaccins de Pfizer-BioNTech et Moderna). ▪ Nécessaire de préciser les intervalles pour la prise de R.-V. de la 2e dose qui se prend automatiquement avec Clic Santé; ▪ Avis sur le report de la 2e dose toujours sous embargo au MSSS.	▪ Recommandation d'un intervalle minimal de 21 jours pour le vaccin de Moderna (même pour Pfizer-BioNTech); ▪ Intervalle recommandé de 28 jours pour le vaccin de Moderna (21 pour Pfizer-BioNTech); ▪ Ajout de l'information au PIQ pour l'intervalle minimal; ▪ Ajout dans l'avis sur l'utilisation des vaccins contre la COVID-19 que des intervalles plus longs pourraient également être considérés (Maryse Guay).

	Point discuté + Éléments de discussion	Décision(s) + Action (P. responsable)
2.	**Question du GAV sur l'ajout de la précaution liée à l'hypersensibilité ou d'une allergie non anaphylactique aux composants du vaccin contre la COVID-19 dans le PIQ** ▪ Recommandation du CCNI d'une période d'observation post-vaccinale prolongée de 30 minutes dans les cas où l'on soupçonnerait une hypersensibilité ou une allergie non anaphylactique aux composants du vaccin contre la COVID-19; ▪ PIQ contient déjà une section sur les précautions générales et la conduite recommandée lors d'une manifestation compatible à ce qui est décrit précédemment (non spécifique au vaccin contre la COVID-19).	▪ Décision de ne pas ajouter d'éléments à cet effet au PIQ dans la section sur le vaccin contre la COVID-19; ▪ Ajout d'un hyperlien vers la section sur les précautions générales à la section du PIQ sur le vaccin contre la COVID-19; ▪ Aucune mention à faire dans l'avis sur l'utilisation des vaccins contre la COVID-19.
3.	**Question du GAV sur l'ajout d'information concernant la vaccination des femmes en âge de procréer** ▪ Différentes recommandations sont formulées pour la vaccination des femmes désirant devenir enceintes (par exemple report de la vaccination pour une période déterminée); ▪ CCNI va mentionner qu'il serait prudent d'attendre 28 jours après la vaccination avant de devenir enceinte; ▪ SOGC recommande aux femmes planifiant une grossesse de se faire vacciner et encourage la discussion avec un professionnel de la santé sur les risques et bénéfices de retarder la grossesse; ▪ 2 propositions sont présentées : ▪ 1) En l'absence de données, il pourrait être prudent de retarder la grossesse; ▪ 2) Une grossesse ne devrait pas être évitée avant ou après l'administration du vaccin.	▪ Recommandation : donner l'information concernant le peu de données disponibles. Pas de recommandation de retarder la grossesse. Discuter avec un professionnel de la santé au besoin pour la question de retarder la vaccination; ▪ Ajout dans l'avis sur l'utilisation des vaccins contre la COVID-19 (paragraphe sera proposé par Nicholas Brousseau).
4.	**Question du GAV sur l'interaction entre le vaccin contre la COVID-19 et les anticorps monoclonaux anti-SRAS-CoV-2 ou le plasma de convalescents** ▪ Recommandation du CCNI : En l'absence de données probantes, une évaluation devrait être faite par un spécialiste, avec précision sur une diminution possible de l'efficacité du vaccin ou des anticorps monoclonaux anti-SRAS-CoV-2 si ces 2 produits sont administrés de façon rapprochée; ▪ Recommandation de l'ACIP : Attente de 90 jours avant d'administrer le vaccin contre la COVID-19; ▪ Dans la province : faible nombre de patients ayant reçu du plasma ou pour qui on prévoit en donner; ▪ Proposition de réponse formulée par Rodica Gilca est présentée aux membres du CIQ.	▪ Approbation des membres du CIQ de la proposition formulée par Rodica Gilca : ➢ *À ce jour, l'interaction entre le vaccin contre la COVID-19 et les anticorps monoclonaux anti-SRAS-CoV-2 ou le plasma de convalescents est inconnue. Étant donné qu'il est possible que l'administration rapprochée de ces produits diminue l'efficacité du vaccin contre la COVID-19, et que la probabilité des réinfections est plus grande après 90 jours, le CIQ recommande d'espacer l'administration du vaccin de 90 jours. Pour l'administration de ces produits après le vaccin, il est préférable d'attendre 90 jours, mais la gestion devrait se faire cas par cas en fonction de la sévérité de la maladie.*

	Point discuté + Éléments de discussion	Décision(s) + Action (P. responsable)
		▪ Ajout de l'information au PIQ et dans l'avis sur l'utilisation des vaccins.
5.	**Question du GAV sur l'utilisation des analgésiques ou antipyrétiques oraux pour les réactions postvaccinales** ▪ Recommandation du CCNI : Ne pas systématiquement utiliser d'analgésiques ou d'antipyrétiques oraux en prophylaxie avant ou au moment de la vaccination. Les analgésiques ou antipyrétiques oraux peuvent être envisagés pour la gestion des effets indésirables, s'ils surviennent après la vaccination.	▪ Décision de référer aux consignes habituelles dans le PIQ et d'inclure cette information dans le Questions-Réponses; ▪ Aucune mention à faire dans l'avis sur l'utilisation des vaccins contre la COVID-19.
6.	**Recommandation pour l'âge minimal pour l'administration du vaccin de Moderna** ▪ CCNI s'appuie sur les recommandations des compagnies : 16 ans pour le vaccin de Pfizer-BioNTech et 18 ans pour celui de Moderna; ▪ Public Health England a mis 16 ans comme âge minimal pour les 2 vaccins (technologie similaire utilisée). ▪ 2 propositions sont présentées : ▪ 1) Harmoniser l'âge minimal pour les 2 vaccins; ▪ 2) Considérer 18 ans comme âge minimal pour recevoir le vaccin de Moderna.	▪ Recommandation de mettre 18 ans comme âge minimal pour recevoir le vaccin de Moderna en concordance avec le CCNI; ▪ Ajout de l'information au PIQ; ▪ Ajout dans l'avis sur l'utilisation des vaccins contre la COVID-19 qu'en l'absence de données, l'âge minimal recommandé pour recevoir le vaccin de Moderna est de 18 ans.
7.	**Autres questions du GAV sur la vaccination contre la COVID-19 avec le vaccin de Moderna** **1) Interchangeabilité des vaccins de Pfizer-BioNTech et de Moderna** ▪ Selon les membres du CIQ, question non urgente; ▪ Avis sera publié prochainement par le CCNI; ▪ Discussion sur l'interchangeabilité des 2 vaccins aura lieu une fois que les recommandations du CCNI seront publiées. **2) Précautions pour les vaccins de Pfizer-BioNTech et de Moderna** ▪ Discussion sur l'excès de cas de paralysie de Bell et de lymphadénopathie observé après l'administration des deux vaccins. Les membres du CIQ s'interrogent à savoir si des éléments devraient être inclus dans le PIQ ou dans l'avis sur l'utilisation des vaccins contre la COVID-19; ▪ Discussion qui amène les membres du CIQ à s'interroger également sur le fait de discuter de la surveillance des manifestations cliniques indésirables.	▪ Ajout d'un hyperlien vers la section sur le système de surveillance à la section du PIQ sur le vaccin contre la COVID-19; ▪ Ajout de l'information concernant la surveillance passive qui sera mise en place pour la vaccination COVID-19; ▪ Ajout dans l'avis sur l'utilisation des vaccins contre la COVID-19 concernant les cas de paralysie de Bell de la lymphadénopathie observés dans les essais cliniques (Maryse Guay). Ajout dans le PIQ à prévoir par la suite; ▪ Ajout dans l'avis que le CIQ restera à l'affût des données de surveillance des MCI (Maryse Guay).

	Point discuté + Éléments de discussion	Décision(s) + Action (P. responsable)
8.	**Prochaines étapes et prochaine rencontre** ▪ Dépôt dans Teams de documents pour lesquels une action est requise au plus tard le lundi 21 décembre 2020; ▪ Courriel envoyé aux membres du CIQ pour qu'ils consultent les documents; ▪ Approbation des documents lors de la rencontre du 23 décembre 2020; ▪ 3 avis du CIQ sont actuellement sous embargo et devraient être publiés prochainement; ▪ Chantal Sauvageau évoque des enjeux de compréhension sur le terrain par rapport au libellé actuellement inscrit dans les précautions de la section du PIQ sur les vaccins contre la COVID-19 pour les maladies auto-immunes. La mention "sauf si avis contraire du médecin traitant" pose problème à savoir si le médecin traitant doit être consulté avant la vaccination.	▪ Révision du libellé sur les précautions pour les maladies auto-immunes pour élargir à l'avis d'un professionnel de la santé, dont le médecin traitant (Nicholas Brousseau & Maryse Guay, en coll. avec Chantal Sauvageau)
9	**Autre :** ▪ Julie Bestman-Smith est d'avis qu'il faudrait avoir une discussion au CIQ concernant le retour au travail des personnes immunodéprimées ou malades chroniques qui seront vaccinées; ▪ Question qui ne concerne pas seulement le CIQ.	▪ Sera rediscuté éventuellement. Implication de l'équipe en santé au travail à prévoir.

Procès-verbal préparé par Dominique Gagnon, révisé par Nicholas Brousseau et Maryse Guay et Marilou Kiely le 7 janvier 2021.

Procès-verbal adopté tel quel par le CIQ lors de la réunion du 13 janvier 2021.

SOGC Statement on COVID-19 Vaccination in Pregnancy

Version date: December 18th, 2020

Pre-amble

The SOGC acknowledges the need for guidance related to the COVID-19 vaccine and pregnancy and during lactation. We recognize the difficulty facing women and their health care providers at this time, due to the absence of clinical trials that can support evidence-informed recommendations about the COVID-19 vaccine for pregnant and breastfeeding populations. Information related to COVID-19, the impact of the disease on pregnancy and data related to COVID-19 vaccines in development are rapidly evolving. The information contained herein is subject to change as further evidence becomes available and currently applies to all proposed COVID-19 vaccines.

Consensus Statement: For individuals who are at high risk of infection and/or morbidity from COVID-19, it is the SOGC's position that the documented risk of not getting the COVID-19 vaccine outweighs the theorized and undescribed risk of being vaccinated during pregnancy or while breastfeeding and vaccination should be offered.

SARS-CoV-2 and the impact on pregnancy

Most pregnant women who become infected with SARS-CoV-2 will have mild-to-moderate symptoms and many can be asymptomatic.[1] However, both Canadian and international data from large studies spanning multiple jurisdictions demonstrate that approximately 8-11% of pregnant women will require hospitalization for COVID-related morbidity and between 2-4% of pregnant women will require admission to an intensive care unit (ICU).[2, 3, 4] Compared to non-pregnant individuals with COVID-19, pregnant individuals are at increased risk of invasive ventilation with an equivalent mortality to age-matched peers.[2, 4] The risk of severe morbidity from COVID-19 in pregnant women appears to be associated with risk factors including age ≥ 35 years old, asthma, obesity, preexisting diabetes, preexisting hypertension and heart disease.[2, 4]

COVID-19 Vaccines

On December 9th, 2020, Health Canada authorized the first COVID-19 vaccine in Canada: Pfizer-BioNTech COVID-19 vaccine. [5] This vaccine is presently the only COVID-19 vaccine authorized for human use in Canada although several other companies have filed for approval with Health Canada including Moderna and AstraZenica who have an mRNA platform and an adenovirus vector platform, respectively. The Pfizer-BioNTech COVID-19 vaccine uses a new mRNA vaccine platform. This model consists of messenger RNA (mRNA) encapsulated by a lipid nanoparticle (LMP) which allows the mRNA entrance into host (human) cells. The mRNA in the vaccine codes for the SARS-CoV-2 spike protein, utilized by the virus to bind to human receptors and promote viral replication. The vaccine provides the host cell instructions to manufacture only this spike protein and express it on its surface. Recognizing the spike protein as a foreign antigen, the host immune system is then activated to produce an immune response.[6] The mRNA does not enter the nucleus or alter human DNA and human cells do not have the machinery to allow it to do so.

The Pfizer-BioNTech COVID-19 vaccine is administered as a series of two intramuscular injections administered 21-28 days apart.[7] The safety and efficacy Pfizer-BioNTech COVID-19 vaccine has been demonstrated for adults 16 years and older in Phase II and Phase III trials involving the randomization of approximately 44,000 individuals.[8] These trials demonstrated a vaccine efficacy of 94.6% for preventing symptomatic COVID-19 cases at least 7 days following the second dose.[8]

The available safety data is based on an interim analysis of 37,586 adults of whom approximately 9,500 individuals had at least 2 months of follow-up after receiving the vaccine. Safety monitoring will continue for 2 years following vaccine administration. There were no clinically meaningful differences in adverse events or severe adverse events in the vaccine group compared to control except for lymphadenopathy which occurred in 0.3% of the vaccine group compared to <0.1% of the placebo group. The most commonly reported side effects from the vaccine were pain at the injection site (66-83%), fatigue (51-59%) and headache (39-52%). Fever was reported in 11-16% of patients, particularly following the second dose.[8]

Pregnant and breastfeeding women were excluded from the Phase II and Phase III studies for the Pfizer-BioNTech COVID-19 vaccine. However, there were 23 women (12 in the vaccine arm and 11 in the placebo arm) who

reported pregnancies during the trial and are being followed for pregnancy outcomes with no reports of adverse effects to date. Currently, there are no other safety or efficacy data available for pregnant or breastfeeding women. The Developmental and Reproductive Toxicity (DART) animal studies for the Pfizer-BioNTech vaccine are ongoing and the results anticipated for mid-December 2020. According to the American College of Obstetricians & Gynecologists (ACOG), no major safety signals have been identified.[9]

To date, Phase III data is available for two other COVID-19 vaccines. The Moderna mRNA-1273 vaccine also utilizes mRNA vaccine technology with the SARS-CoV-2 spike protein as its antigenic target. In Phase III trials randomizing 30,000 individuals, the vaccine was reported to have 94.1% efficacy against symptomatic COVID-19 with no serious safety concerns identified during the initial 2 month follow-up period.[10] The Oxford-AstraZeneca ChAdOx1 nCoV-19 vaccine is not an mRNA vaccine, instead it utilizes a Chimpanzee adenovirus vector vaccine platform and preliminary Phase III data from 11,636 participants demonstrates an overall vaccine efficacy of 70.4% against symptomatic COVID-19 disease.[11] Unfortunately, all the vaccines for which Phase III results are available excluded pregnant or breastfeeding women from their trials.

Similarly, breastfeeding women were also excluded from the Phase III trials available at present. Therefore, there is no data on the safety of COVID-19 vaccines in lactating women or the effects of mRNA vaccines on the breastfed infant or on milk production. Because mRNA vaccines are not considered live virus vaccines, they are not hypothesized to be a risk to the breastfeeding infant.[12]

Considerations for COVID-19 Vaccination During Pregnancy and Breastfeeding

Decades of experience with other vaccines administered during pregnancy would suggest that we could expect a similar efficacy for the COVID-19 vaccines in pregnant women compared to non-pregnant women. Vaccines in general are immunogenic, safe, and efficacious when delivered to pregnant women. While there have been no red flags or hypothesized mechanisms for potential harm associated with administration of an mRNA vaccine during pregnancy, until more data is available, the potential risks of vaccination to a pregnant individual and fetus remain unknown. What *is* known, however, is that an unvaccinated pregnant individual remains at risk of COVID-19 infection and remains at heightened risk of severe morbidity if infected compared to non-pregnant counterparts. Severe infection with COVID-19 carries risks to both maternal and fetal health. While pregnancy itself does not appear to increase the risk of becoming infected with SARS-CoV-2, pregnant individuals may be in work-related

(e.g., health care worker, front line workers etc.) or community situations (e.g., caregiver, indigenous communities, outbreak setting, etc.) where the risk of infection is considerable. Owing to maternal age or underlying comorbidities, some pregnant individuals are at high risk of severe COVID-related morbidity.

NACI has advised "COVID-19 vaccine **should not** be offered to populations excluded from clinical trials until further evidence is available. ***However,*** if a risk assessment deems that the benefits of vaccine outweigh the potential risks for the individual (e.g., where the risk of severe outcomes of COVID-19 and risk of exposure to SARS-CoV-2 is high) or for the fetus/infant (in the case of pregnancy/breastfeeding) and if informed consent includes discussion about the insufficient evidence in this population, then a complete series of authorized COVID-19 vaccines **may be** offered to pregnant and breastfeeding individuals.[6]

We **recommend** that pregnant and breastfeeding individuals who are eligible for the COVID-19 vaccine due to exposure risk, medical status, or other circumstances should be able to make an informed decision by having access to up-to-date information about the safety and efficacy of the vaccine (including clear information about the data that is not yet available) and information about the risks of COVID-19 infection for them. The concern around vaccination in the absence of evidence of safety in pregnancy has been debated in the literature. The PREVENT Working Group state, "the absence of evidence and the mere theoretical or even documented risk of fetal harm is generally not sufficient to justify denying pregnant women access to a vaccine in an outbreak or epidemic." During an epidemic, the default should be to offer vaccines to pregnant women alongside other affected populations.[9, 13, 14]

Universal exclusion of pregnant women from receipt of the COVID-19 vaccine based on an undocumented and hypothetical risk to the fetus would leave pregnant women vulnerable to severe morbidity, which could also compromise fetal health. Conversely, lack of safety and efficacy data for this population precludes making a recommendation for routine COVID-19 vaccination for all pregnant and breastfeeding individuals.

Pregnant and breastfeeding individuals will likely look to their prenatal care provider to assist in making decisions weighing the risks and benefits so that they might arrive at a well informed and autonomous decision that is right for them as an individual. Such a discussion should prioritize patient autonomy and should include, but not be limited to assessment of:

- Local epidemiology and risk of community acquisition of COVID-19
- Workplace situation and risk of work-related acquisition of COVID-19
- Individual risk for COVID-related morbidity including consideration for comorbidities including advanced maternal age, immunosuppressive conditions, preexisting diabetes, preexisting hypertension, obesity or chronic respiratory conditions
- Gestational age
- Available data related to the safety of the vaccine during pregnancy and lactation
- Data that is not yet available related to the safety and efficacy of the vaccine for pregnant and breastfeeding women
- Individual beliefs and personal risk assessment of the available data.

Individuals who proceed with vaccination

Individuals should be informed of the expected side effects following vaccination. While pain at the injection site, fatigue and headache are the most commonly reported symptoms following vaccination, fever was reported 16% of the time for younger non-pregnant individuals.[8] Pregnant patients can be counselled to treat mild post-vaccination fevers with antipyretics (e.g., acetaminophen). Active surveillance is ongoing for the Pfizer-BioNTech COVID-19 vaccine. As such, prenatal care providers are encouraged to inform themselves on local procedures for active surveillance and notify the appropriate channels when a pregnant or breastfeeding mother is receiving a dose of the vaccine.

Inadvertent pregnancy following vaccination

Individuals who are discovered to be pregnant during their vaccine series or shortly afterward should *not* be counselled to terminate pregnancy based on having received the vaccine. If conception is presumed to predate the first dose, it is recommended to follow the same procedures for active surveillance (as available) as would be activated if the pregnancy was known at the time of vaccination.

Where pregnancy is detected during the vaccine series (i.e. following the first dose, but ahead of the second dose), the decision of whether to complete the vaccine series during pregnancy should be based on an assessment of the potential risks of not being completely vaccinated during pregnancy vs. the potential risks of receiving the vaccine during pregnancy (as discussed above).

Individuals contemplating pregnancy

For an individual planning a pregnancy, it is recommended to complete the entire COVID-19 vaccination series (where possible) to achieve maximal vaccine efficacy ahead of pregnancy. It is not known whether an individual should delay pregnancy following receipt of the vaccine and a risk-benefit discussion for those planning pregnancy should occur similar to the discussion for pregnant and breastfeeding women.

Future research

As the evidence evolves, it is becoming clear that pregnant and postpartum women may represent a population at increased risk of COVID-related morbidity. Severe COVID-19 infection during pregnancy has important implications for both maternal and fetal health. NACI acknowledges that people of reproductive age constitute a substantial proportion of the Canadian population, yet no data on the use of COVID-19 vaccine in pregnancy are available. We support NACI's recommendation for the inclusion of pregnant women in clinical trials of COVID-19 vaccines to ensure that this population has equitable access to COVID-19 vaccine options informed by robust safety, immunogenicity, and efficacy data.[15]

This statement has been endorsed by The Canadian Fertility and Andrology Society (CFAS).

References

1. Maru S, Patil U, Carroll-Bennett R, et al. Universal screening for sars-cov-2 infection among pregnant women at elmhurst hospital center, queens, new york. PLoS One. 2020;15:e0238409. Available at https://www.ncbi.nlm.nih.gov/pubmed/33301498.

2. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: Living systematic review and meta-analysis. BMJ. 2020;370:m3320. Available at https://www.ncbi.nlm.nih.gov/pubmed/32873575.

3. Money D. Canadian surveillance of covid-19 in pregnancy: Epidemiology, maternal and infant outcomes. Report #1: Released december 2nd, 2020early release: Maternal and infant outcomes (march 1, 2020 to september 30, 2020) from three canadian provinces 2020. Available at https://med-fom-ridresearch.sites.olt.ubc.ca/files/2020/12/CANCOVID-Preg-report-1-BC-AB-ON-data_02DEC2020-V2.pdf.

4. Zambrano LD, Ellington S, Strid P, et al. Update: Characteristics of symptomatic women of reproductive age with laboratory-confirmed sars-cov-2 infection by pregnancy status - united states, january 22-october 3, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:1641-7. Available at https://www.ncbi.nlm.nih.gov/pubmed/33151921.

5. Health Canada. Drug product database online query. Available at https://health-products.canada.ca/dpd-bdpp/index-eng.jsp.

6. National Advisory Committee on Immunization. Vaccines and treatments for covid-19: Progress. Health Canada. Available at https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/prevention-risks/covid-19-vaccine-treatment.html.

7. Pfizer-biontech covid-19 vaccine: Covid-19 mrna vaccine, suspension for intramuscular injection (product monograph). Available at https://covid-vaccine.canada.ca/info/pdf/pfizer-biontech-covid-19-vaccine-pm1-en.pdf.

8. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the bnt162b2 mrna covid-19 vaccine. N Engl J Med. 2020. Available at https://www.ncbi.nlm.nih.gov/pubmed/33301246.

9. The American College of Obstetricians and Gynecologists. Vaccinating pregnant and lactating patients against covid-19. 2020. Available at https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/vaccinating-pregnant-and-lactating-patients-against-covid-19.

10. Moderna announces primary efficacy analysis in phase 3 cove study for its covid-19 vaccine candidate and filing today with u.S. Fda for emergency use authorization. Moderna. 2020. Available at https://investors.modernatx.com/node/10421/pdf.

11. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the chadox1 ncov-19 vaccine (azd1222) against sars-cov-2: An interim analysis of four randomised controlled trials in brazil, south africa, and the uk. Lancet. 2020. Available at https://www.ncbi.nlm.nih.gov/pubmed/33306989.

12. Cohn A, Mbaeyi S. What clinicians need to know about the pfizer-biontech covid-19 vaccine. Centers for Disease Control and Prevention (CDC). 2020.

13. The PREVENT Working Group. Pregnant women & vaccines against emerging epidemic threats: Ethics guidance for preparedness, research, and response. 2018. Available at https://www.who.int/immunization/sage/meetings/2018/october/1_PREVENT_Recs_Excerpts_for_SAGE.PDF.

14. Advisory Committee on Immunization Practices. Interim considerations for covid-19 vaccination of healthcare personnel and long-term care facility residents. Centers for Disease Control and Prevention (CDC). 2020. Available at https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19/clinical-considerations.html.

15. National Advisory Committee on Immunization. Research priorities for covid-19 vaccines to support public health decisions. Health Canada. 2020. Available at https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/research-priorities-covid-19-vaccines.html.

Projet d'ordre du jour

Comité COVID-19| Mère-enfant

Mardi 23 février 2021
14 h à 15 h

Points à l'ordre du jour :

1. Mot de bienvenue

2. État de situation :
   - Données

3. Directive visiteurs – proches aidants : pédiatrie
   - Directives générales : https://publications.msss.gouv.qc.ca/msss/fichiers/directives-covid/dgaumip-001-rev1_details.pdf
   - Travaux en cours

4. Point d'information :
   - Position de la SOGC sur la vaccination des femmes enceintes (p.j.)

5. Divers

INSPQ INSTITUT NATIONAL DE SANTÉ PUBLIQUE DU QUÉBEC

Avis intérimaire sur l'utilisation des vaccins à ARN messager contre la COVID-19

AVIS DU COMITÉ SUR L'IMMUNISATION DU QUÉBEC

3 septembre 2021, version 13.0 – Modifications apportées en jaune

Introduction

Le présent avis est rédigé dans le but de soutenir la campagne de vaccination contre la COVID-19 qui a débuté en décembre 2020 au Québec. Il se veut complémentaire à l'avis du Comité sur l'immunisation du Québec (CIQ) sur les groupes prioritaires pour la vaccination contre la COVID-19 au Québec(1) et relate les recommandations du CIQ concernant l'utilisation des vaccins à ARN messager (ARNm) contre la COVID-19.

Étant donné l'état des connaissances scientifiques, cet avis est adapté et modifié au fil du temps, en fonction de leur évolution. Les changements qui sont apportés dans la mise à jour de l'avis sont surlignés en jaune pour en faciliter la lecture. D'autres aspects plus opérationnels relatifs à la vaccination contre la COVID-19 sont couverts tant par le Protocole d'immunisation du Québec (PIQ)(2) que par les documents « Questions-réponses » mis à disposition des personnes vaccinatrices et qui sont également mis à jour régulièrement.

Le premier vaccin contre la COVID-19 qui a été rendu disponible est le vaccin à ARNm BNT162b2 de Pfizer/BioNTech ou tozinaméran (vaccin PB COVID-19) dont l'autorisation d'utilisation a été donnée par Santé Canada le 9 décembre 2020(3). Le deuxième, le vaccin de Moderna contre la COVID-19 (vaccin MOD COVID-19), autorisé par Santé Canada le 23 décembre 2020(4), s'appuie sur une technologie semblable au vaccin PB COVID-19(5). Le présent avis traite des sujets suivants :

1) l'âge minimal d'administration des vaccins à ARNm;
2) les contre-indications et les précautions;
3) les populations particulières;
4) l'interchangeabilité des vaccins à ARNm contre la COVID-19;
5) l'intervalle pour la 2e dose des vaccins à ARNm contre la COVID-19;
6) la co-administration et l'interaction entre les vaccins à ARNm et d'autres produits;
7) la vaccination des personnes ayant eu un diagnostic confirmé de COVID-19;
8) les manifestations cliniques après la vaccination contre la COVID-19.

Québec

1 Âge minimal de l'administration des vaccins à ARNm

Le vaccin PB COVID-19 a été autorisé au départ pour administration aux personnes âgées de 16 ans et plus étant donné que dans les premiers essais cliniques de phase III de ce vaccin, un nombre très restreint de jeunes âgés de 12 à 15 ans avait été inclus et aucun résultat concernant l'immunogénicité ou l'efficacité du vaccin dans ce groupe d'âge n'était disponible(6,7). Des données d'efficacité et d'innocuité pour ce groupe spécifique sont devenues disponibles ultérieurement(8).

Le 5 mai 2021, le vaccin PB COVID-19 a été autorisé par Santé Canada pour administration aux enfants de 12 à 15 ans(9). Cette autorisation s'appuie sur une extension de l'étude de phase III initiale dans laquelle 2 260 sujets âgés de 12 à 15 ans recrutés depuis octobre 2020 ont été répartis aléatoirement. Ainsi, 1 131 adolescents ont reçu deux doses du vaccin PB COVID-19, alors que les 1 129 autres ont reçu un placébo, et ce, à 21 jours d'intervalle. Tant chez les sujets sans preuve d'infection antérieure au SRAS-CoV-2 que chez ceux avec ou sans preuve d'infection antérieure, l'efficacité vaccinale a été de 100 % pour la période débutant le 7e jour après l'administration de la 2e dose. Après la 1re dose, trois cas de COVID-19 ont été observés parmi les jeunes vaccinés alors qu'il y en a eu 35 dans le groupe placébo. Tous les cas du groupe vacciné sont apparus moins de 11 jours après cette 1re dose, correspondant à la période où la réponse immunitaire au vaccin est encore incomplète(10). Aucun des cas de COVID-19 identifié en cours d'étude n'a été grave (aucune hospitalisation, admission aux soins intensifs, intubation ou ventilation mécanique ou décès)(10). De plus, la réponse humorale des 12-15 ans observée après l'administration de la 2e dose était robuste, voire supérieure à celle observée chez les 16 à 25 ans.

Les données dans ce groupe des 12-15 ans n'indiquent aucun enjeu majeur d'innocuité, les manifestations locales ou systémiques après la vaccination qui ont été signalées étant équivalentes à ce qui a été observé chez les jeunes adultes de 16-25 ans(9). Toutefois la fréquence des réactions systémiques s'est avérée plus élevée chez les plus jeunes, en comparaison des personnes de 18 à 55 ans; la proportion de jeunes de 12 à 15 ans ayant fait une réaction fébrile (≥ 38 °C) a été de 10 % après la première dose et de 20 % après la seconde, alors que ces proportions chez les plus âgés étaient respectivement de 4 et 16 %(6). On ne dispose pas pour le moment de données sur la fréquence des réactions après la vaccination spécifiquement chez les jeunes qui avaient des antécédents d'infection au SRAS-CoV-2. Il faut rappeler que ces observations s'appuient sur un nombre limité de sujets, dont le suivi est toujours en cours. La question des cas de myocardite et de péricardite identifiés après l'administration des vaccins à ARNm, qui apparaissent plus fréquemment chez les jeunes hommes après la 2e dose, est traitée à la section 2.2 du présent document.

À la lumière de ces données, l'âge minimal pour administrer le vaccin PB COVID-19 peut être abaissé à l'âge de 12 ans. Comme les jeunes de 12-15 ans ainsi que plusieurs de ceux de 16-17 ans se retrouvent en milieu scolaire, il pourrait être opportun de profiter de ce contexte pour mieux les joindre(11,12). Il faudra également adapter les messages lors de la vaccination considérant la réactogénicité plus importante dans ce groupe.

Le 27 août 2021, le vaccin MOD COVID-19 a été autorisé par Santé Canada pour administration aux enfants de 12 à 17 ans(13), autorisation qui s'ajoute à celle pour les personnes de 18 ans et plus. L'essai clinique de phase III a inclus 3 732 adolescents qui ont reçu le vaccin (n = 2 486) ou le placébo (n = 1 240). Dans un avis distinct(14), le CIQ a précisé que la majorité des enfants de 12 à 17 ans avaient déjà été vaccinés avec le PB COVID-19 et que ce dernier vaccin pourrait être associé à une fréquence moindre de myocardites/péricardites par rapport au vaccin MOD COVID-19. Le CIQ a recommandé de poursuivre la campagne avec le vaccin PB COVID-19 chez les jeunes de 12 à 17 ans.

2 Contre-indications et précautions

Les contre-indications et précautions à prendre avant d'administrer un vaccin à ARNm sont mentionnées au PIQ. L'information additionnelle présentée ici se veut complémentaire et dans le but de donner plus de détails justifiant ces contre-indications et précautions.

2.1 Antécédents d'anaphylaxie

Une histoire de réaction allergique grave antérieure (ex. : anaphylaxie) à tout composant ou à une dose d'un vaccin contre la COVID-19 représente une contre-indication à la vaccination contre la COVID-19. Les personnes qui ont de tels antécédents devraient être référées à un allergologue. Le CIQ formule cette recommandation qui correspond à celle des monographies(6,15), de Santé Canada(16) et à celle du Comité consultatif national de l'immunisation (CCNI)(17). Cette contre-indication est renforcée du fait que les cas d'anaphylaxie semblent plus fréquents pour les vaccins à ARNm contre la COVID-19 que pour d'autres types de vaccins(18), cela étant observé aussi au Québec(19). Une des explications possibles à la survenue de ces cas est qu'une allergie au polyéthylène glycol (PEG), un composant des vaccins à ARNm, soit en cause(20).

Le CIQ émet ci-bas certaines recommandations additionnelles qui sont en conformité avec les orientations de l'Association des Allergologues et Immunologues du Québec(21).

Toute personne ayant présenté une réaction allergique au PEG devrait être dirigée vers un allergologue avant de recevoir un vaccin contre la COVID-19.

Les personnes ayant présenté une réaction allergique immédiate (dans l'heure après l'administration) à un vaccin contenant du polysorbate devraient recevoir un vaccin à ARNm contre la COVID-19. Cette vaccination devrait être suivie d'une période d'observation de 30 minutes en raison de la possibilité théorique de réaction croisée entre le polysorbate et le PEG.

Les personnes qui ont présenté des réactions allergiques immédiates (dans l'heure après l'administration) légères à modérées donc non anaphylactiques après une dose précédente de vaccins contre la COVID-19 pourraient être revaccinées après une évaluation des risques et bénéfices pour l'individu et un consentement éclairé. Cette vaccination devrait être suivie d'une période d'observation de 30 minutes. Aucune précaution particulière n'est recommandée pour les personnes ayant présenté des réactions localisées au site d'injection (ex. présence seulement d'une urticaire au site d'injection).

Les personnes ayant d'autres antécédents d'allergie peuvent recevoir les vaccins contre la COVID-19 sans aucune précaution particulière et dans les conditions habituelles incluant une période d'observation post-vaccination de 15 minutes. Il s'agit par exemple des personnes ayant des antécédents d'allergies aux aliments, aux médicaments (incluant la chimiothérapie et les produits de contraste), au venin d'insecte ou aux allergènes environnementaux.

2.2 Myocardite ou péricardite après la vaccination

De rares cas de myocardite ou de péricardite ont été observés dans les 7 jours après l'administration des vaccins à ARNm(22,23). Les symptômes incluent entre autres la dyspnée, une douleur thoracique et des palpitations. Ces cas sont principalement observés après la 2e dose chez les jeunes hommes âgés de moins de 30 ans. Aux États-Unis, le risque après la 2e dose de vaccin à ARNm est évalué respectivement chez les hommes et chez les femmes à 1/15 000 et 1/100 000 chez les adolescents, à 1/20 000 et 1/200 000 chez les 18-24 ans, et à 1/50 000 et 1/400 000 chez les 25-29 ans. Bien qu'un traitement à l'hôpital soit requis la majorité du temps, les cas présentent le plus souvent une atteinte légère et récupèrent rapidement. La surveillance se poursuit à l'échelle internationale et des travaux sont en cours pour mieux comprendre la fréquence des myocardites/péricardites après la vaccination, l'évolution clinique des cas et les facteurs de risque associés. Un avis du CIQ spécifique à cette question est disponible(14).

Outre l'âge et le sexe, les facteurs de risque pour ces cas de myocardite/péricardite suivant la vaccination ne sont pas connus. À titre de précaution, les personnes ayant eu une myocardite ou une péricardite à la suite de leur 1re dose de vaccin à ARNm ne devraient pas recevoir la seconde dose pour le moment, d'ici à ce que plus d'information soit disponible à ce sujet(24). En ce qui concerne les personnes avec histoire de myocardite sans lien avec un vaccin à ARNm contre la COVID-19, la vaccination devrait être considérée après discussion avec l'équipe clinique, notamment pour s'assurer que la myocardite n'est plus évolutive. Si le diagnostic est lointain et que la personne n'est plus suivie pour ce problème, la vaccination devrait être proposée d'emblée(25). En ce qui concerne les personnes avec antécédent de péricardite sans lien avec un vaccin à ARNm, la vaccination devrait être proposée d'emblée.

Par ailleurs, toutes les personnes vaccinées devraient être informées de la possibilité de survenue d'une myocardite ou d'une péricardite dans les jours suivant la vaccination, de la fréquence plus élevée chez les jeunes hommes après la 2e dose, et de l'importance de consulter un médecin en cas de dyspnée, de douleurs thoraciques ou de palpitations.

3 Populations particulières

Des recommandations spécifiques se rapportent à certains sous-groupes de personnes étant donné qu'elles n'ont pas participé aux essais cliniques sur les vaccins contre la COVID-19 venant surtout du fait qu'elles en étaient exclues.

3.1 Personnes avec antécédents de maladies auto-immunes ou démyélinisantes et d'immunosuppression

3.1.1 Maladies auto-immunes ou démyélinisantes

Les maladies auto-immunes ou démyélinisantes constituent un groupe hétérogène de pathologies en termes de mécanisme physiopathologique et d'expression clinique(26). Dans l'essai de phase III du vaccin PB COVID-19, peu de personnes vivant avec une maladie auto-immune ou démyélinisante ont été incluses. Or, des données provenant d'études observationnelles sont maintenant disponibles. Les réponses immunitaires après la vaccination étaient plus faibles seulement chez les participants qui recevaient un traitement immunosuppresseur. Diverses études indiquent que la fréquence et la sévérité des manifestations cliniques inhabituelles chez les personnes avec maladie auto-immune ou démyélinisante est comparable à celle retrouvée chez les personnes qui ne présentent pas de tel problème(17). La vaccination devrait être recommandée aux personnes avec antécédent de maladies auto-immunes ou démyélinisantes. Au besoin, il peut être encouragé de discuter de la question de la vaccination avec un professionnel de la santé, par exemple avec le médecin traitant.

3.1.2 Immunosuppression

Les personnes immunosupprimées ou qui seront immunosupprimées de façon imminente, en raison de traitements qu'elles recevront, sont à risque plus élevé de complications de la COVID-19(27,28). Ces personnes n'ont pas été incluses dans les essais de phase III des vaccins à ARNm, mais des données d'études observationnelles sont maintenant disponibles et montrent l'efficacité et l'innocuité des vaccins à ARNm contre la COVID-19 chez les personnes immunosupprimées(17). La vaccination est donc recommandée pour cette population, comme cela l'a d'ailleurs été recommandé au Royaume-Uni(7), aux États-Unis(27) et plus particulièrement par l'*American Society of Transplantation* pour les personnes ayant bénéficié d'une greffe d'organe solide(29). L'efficacité et l'immunogénicité des vaccins à ARNm sont toutefois plus faibles chez les personnes immunosupprimées que chez les personnes immunocompétentes. Un avis distinct du CIQ décrit les recommandations vaccinales spécifiques aux personnes immunosupprimées, incluant l'offre d'une troisième dose de vaccin dans la cadre de la série primaire pour améliorer la réponse immunitaire(30).

3.2 Personnes enceintes ou qui allaitent

Le risque de complications de la COVID-19 chez les femmes enceintes, bien que moindre que celui observé chez les personnes âgées, est plus élevé en comparaison du risque pour les femmes du même âge qui ne le sont pas(31–34). Ce risque est plus élevé pour les femmes enceintes ayant des problèmes de santé préexistants (ex. : diabète, obésité)(32,33). Le risque de complications de la grossesse comme la prématurité est plus élevé pour la femme enceinte ayant la COVID-19(32,35,36).

De plus en plus de données observationnelles sont aussi disponibles à propos de l'immunogénicité et de l'innocuité des vaccins contre la COVID-19 chez les femmes enceintes(17). Ainsi, la vaccination contre la COVID-19 devrait être recommandée à une femme enceinte. Pour ces femmes, un vaccin à ARNm est à privilégier étant donné la disponibilité de plus de données de sécurité avec ce type de produit(37,38). Avant de se présenter au site de vaccination, la femme enceinte pourra, si elle le désire, choisir d'en parler avec un professionnel de la santé, par exemple avec son médecin traitant pour discuter plus spécifiquement de son risque personnel d'exposition ou de complications, des risques théoriques de la vaccination chez la femme enceinte et des avantages potentiels de la vaccination(17).

Les femmes qui allaitent ont aussi été exclues des essais cliniques initiaux sur les vaccins contre la COVID-19(17). Les données sur l'excrétion des vaccins à ARNm dans le lait maternel et les risques associés pour le bébé allaité sont rassurantes(6,15,39). La vaccination contre la COVID-19 devrait être recommandée à une femme qui allaite. Il n'y a pas de risque connu associé à l'utilisation d'un vaccin non vivant chez les femmes enceintes ou qui allaitent.

En ce qui concerne les femmes désirant devenir enceintes, très peu de données sont disponibles sur l'innocuité des vaccins à ARNm en début de grossesse. La Société des obstétriciens et gynécologues du Canada recommande aux individus planifiant une grossesse de procéder à la vaccination contre la COVID-19 et encourage une discussion avec un professionnel de la santé sur les risques et les bénéfices de retarder la grossesse(40). L'*American College of Obstetricians and Gynecologists* émet une recommandation similaire, et propose aussi de ne pas retarder une éventuelle grossesse(41). Le CIQ propose de fournir l'information appropriée sur le peu de données disponibles, mais considère que les bénéfices attendus de la vaccination dépassent les risques potentiels chez les femmes planifiant une grossesse.

4 Interchangeabilité des vaccins contre la COVID-19

Le vaccin PB COVID-19 ainsi que le vaccin MOD COVID-19 s'appuient sur une technologie semblable comportant un ARNm qui encode la protéine spiculaire du SRAS-CoV-2 (ou protéine S) qui va générer ultimement une réponse immunitaire(42). Leur profil d'efficacité, d'immunogénicité et de réactogénicité sont très similaires. Il est très probable que l'effet de rappel soit aussi bon dans un calendrier mixte, c'est-à-dire un calendrier qui emploierait une dose de chacun des vaccins. Il devrait en être de même pour un calendrier mixte comportant deux produits utilisant des plateformes technologiques différentes. En ce qui concerne les vaccins à ARNm, à partir des données disponibles sur l'interchangeabilité des vaccins, il est recommandé d'utiliser le même vaccin pour la seconde dose si le même vaccin à ARNm est facilement disponible. Lors de l'administration de la 2e dose du vaccin contre la COVID-19, si le même vaccin à ARNm utilisé lors de la première dose n'est pas facilement disponible ou est inconnu, il est recommandé d'administrer le vaccin à ARNm disponible. Le CIQ considère donc qu'une personne qui a reçu sa première dose de vaccin à ARNm et qui est admissible à sa seconde peut recevoir un vaccin à ARNm différent si celui reçu lors de la première dose n'est pas disponible. Les vaccins à ARNm seront alors considérés interchangeables, les deux doses reçues seront considérées valides et il ne sera pas nécessaire d'administrer une 3e dose. Cela est conforme à la conduite proposée par le CCNI(43). Un avis distinct du CIQ décrit par ailleurs la conduite pertinente en ce qui concerne le vaccin AstraZeneca(44).

5 Intervalle pour la 2e dose des vaccins ARNm contre la COVID-19

5.1 Intervalle minimal

Selon la posologie du vaccin PB COVID-19 recommandée par le fabricant, les deux doses de la série vaccinale s'administrent à 21 jours d'intervalle(6). Une seconde dose qui aurait été administrée à compter du jour 19, devrait tout de même être considérée valide étant donné que l'intervalle minimal déterminé selon le protocole de l'étude de phase III était de 19 jours et que des sujets de l'étude ont été vaccinés selon cet intervalle plus court(17). Cependant, une 2e dose donnée en deçà de 19 jours ne peut pas être considérée valide. Pour des considérations opérationnelles, il est probablement plus simple de donner la 2e dose selon un intervalle minimal de 21 jours, bien que des intervalles plus longs pourraient également être considérés(7,17,45).

Selon la posologie du vaccin MOD COVID-19 recommandée par le fabricant, les deux doses de la série vaccinale s'administrent à 28 jours d'intervalle(46). Dans le protocole de l'étude de phase III, la 2e dose du vaccin de MOD COVID-19 devait être administrée 28 jours après la première dose, mais il était acceptable qu'elle le soit 25 jours après la première dose(46). Certains sujets auraient tout de même reçu la deuxième dose 21 jours après la première dose(17).

Pour des considérations opérationnelles, il est jugé plus simple d'harmoniser l'intervalle minimal de la 2e dose des vaccins PB et MOD COVID-19 étant donné qu'ils s'appuient sur la même technologie de l'ARNm. La 2e dose du vaccin MOD COVID-19 peut donc être donnée selon un intervalle minimal de 21 jours, bien que des intervalles plus longs pourraient également être considérés(7,17,45,46). Cependant, contrairement au vaccin PB COVID 19, une 2e dose du vaccin MOD COVID-19 donnée avant 21 jours ne peut être considérée valide, car aucun des participants aux essais de phase III de Moderna n'ont reçu la 2e dose en deçà de 21 jours de la première dose. Ces recommandations pourront être ajustées selon la disponibilité de nouvelles données à ce sujet.

5.2 Intervalle recommandé

En décembre 2020, devant la pénurie de vaccins contre la COVID-19, la circulation élevée du SRAS-CoV-2 et la bonne efficacité d'une 1re dose de vaccin à ARNm, le CIQ a proposé d'offrir une 1re dose au plus grand nombre de personnes appartenant aux six premiers groupes prioritaires (essentiellement les personnes de 70 ans et plus et les travailleurs de la santé les plus exposés) et de retarder l'administration de la 2e dose prévue au calendrier(45). Le CCNI a par la suite proposé un intervalle allongé allant jusqu'à 16 semaines entre les deux doses de vaccin prévues(47), ce qui a été adopté par le MSSS. En lien notamment avec l'augmentation du nombre de doses disponibles, le CIQ a proposé le 2 juin 2021 un intervalle de 8 semaines ou plus entre les doses, ce qui a été retenu par le MSSS. Depuis le début du mois de juillet 2021, la disponibilité des vaccins à ARNm est importante et le Québec n'est plus en contexte de pénurie.

L'efficacité terrain d'une première dose des vaccins à ARN messager contre la COVID-19 symptomatique est appréciable et varie de 55 % à 80 % selon les études(48,49). La protection perdure durant au moins 16 semaines(50). Des données du Royaume-Uni et de l'Ontario suggèrent une efficacité légèrement plus faible d'une seule dose des vaccins à ARNm contre le variant Delta (B.1.617.2), plus contagieux et en émergence dans plusieurs pays, comparativement aux autres variants(51,52). Une deuxième dose de vaccin à ARNm augmente la protection à environ 90 % pour la COVID-19 symptomatique dans les études terrain et cette efficacité semble relativement préservée même contre le variant Delta (B.1.617.2)(49,51).

Une meilleure immunogénicité après la 2e dose a été notée lorsqu'un intervalle allongé entre les doses était utilisé plutôt qu'un intervalle de 3 semaines(53). La concentration moyenne d'anticorps contre le SRAS-CoV-2 après la 2e dose était de 1 138 U/ml avec un intervalle de 3 semaines entre les doses et de 4 030 U/ml avec un intervalle de 12 semaines entre les doses, ce qui correspond à des titres 3,5 fois plus élevés. Il est plausible que l'efficacité vaccinale après la 2e dose soit plus durable lorsqu'un intervalle allongé est utilisé. Nous ne disposons toutefois d'aucune donnée indiquant à partir de quel intervalle l'allongement du délai pour l'administration de la 2e dose n'augmenterait plus significativement la réponse immunitaire ou la protection.

La situation épidémiologique de la COVID-19 au début juillet 2021 est sous contrôle au Québec. Toutefois, le variant Delta (B.1.617.2) a fait son apparition et circule sur le territoire québécois(54). De par sa contagiosité élevée, il est possible qu'il devienne rapidement le variant prédominant au Québec, à l'instar de ce qui a été observé dans plusieurs autres juridictions. Des travaux de modélisation faits au Canada suggèrent qu'une vague importante de COVID-19 pourrait survenir en cas de prédominance du variant Delta (B.1.617.2)(55).

En lien avec les préoccupations concernant le variant Delta (B.1.617.2) et le caractère explosif de sa transmission, de l'efficacité légèrement plus faible d'une seule dose contre ce variant, de la disponibilité importante des vaccins à ARNm et malgré la meilleure réponse avec un intervalle de 8 semaines ou plus entre les doses, il apparaît opportun d'utiliser un intervalle de 4 semaines ou plus entre les doses des vaccins à ARNm. Cette recommandation concernant l'intervalle entre les doses sera révisée au besoin selon l'évolution de la situation épidémiologique, de la circulation des variants du SRAS-CoV-2 et des nouvelles données qui deviendront disponibles sur les vaccins contre la COVID-19 et leurs caractéristiques.

6 Co-administration et interaction entre les vaccins à ARNm et d'autres produits

La pandémie de COVID-19 a perturbé les activités liées au Programme québécois d'immunisation, notamment la vaccination scolaire (ex. vaccins VPH, Men-C-C et dT) qui a été beaucoup ralentie. La co-administration des vaccins à ARNm contre la COVID-19 avec d'autres vaccins pourrait faciliter les activités de rattrapage en optimisant l'utilisation des ressources déjà en place pour la vaccination de masse contre la COVID-19. Il n'existe cependant aucune donnée sur l'interaction des vaccins à ARNm avec d'autres vaccins (ex. réduction potentielle

de l'immunogénicité ou augmentation de la réactogénicité) en cas de co-administration bien que des études soient planifiées(56,57). Dans plusieurs juridictions, la co-administration des vaccins à ARNm avec d'autres vaccins n'est pas recommandée; un intervalle minimal de 7, 14 ou 28 jours entre les doses est alors recommandé(17,58,59). Il existe une exception, aux États-Unis la co-administration est permise de même que la vaccination sans intervalle minimal avant ou après un autre type de vaccin(60,61). En l'absence de données, il s'avère raisonnable de ne pas administrer un vaccin à ARNm en même temps qu'un autre vaccin. Il est recommandé d'attendre au minimum 14 jours avant ou après l'administration de tout autre vaccin, inactivé ou vivant atténué. Ces délais minimaux permettraient notamment de faciliter l'évaluation des manifestations cliniques inhabituelles pouvant survenir après la vaccination(7,17). Il sera essentiel de rester à l'affût des études de co-administration qui évalueront l'immunogénicité et l'innocuité de cette stratégie.

Dans la mesure du possible, il est recommandé de respecter les délais indiqués plus haut pour tout vaccin. Cependant, les connaissances générales montrent qu'il n'y a que peu ou pas d'interactions entre des vaccins inactivés contenant des antigènes différents(2,7). Ainsi, ces délais ne s'appliquent pas si un vaccin est requis en prophylaxie post-exposition ou si l'administration rapide de plusieurs vaccins est requise avant le début d'un traitement immunodépresseur ou d'une greffe. Aussi, l'administration de la vaccination contre la COVID-19 ne devrait en aucun cas être retardée chez une personne qui aurait reçu le vaccin antigrippal, le vaccin antipneumococcique ou tout autre vaccin inactivé récemment. Il en va de même pour la situation inverse. On ne devrait pas retarder l'administration d'un vaccin antigrippal, antipneumococcique ou inactivé chez une personne ayant reçu le vaccin contre la COVID-19 parce que le délai entre les vaccins est trop court, et ce, pour éviter les occasions manquées. Par ailleurs, dans les 14 jours suivant la vaccination contre la COVID-19, une femme enceinte peut recevoir le vaccin dcaT pour que ce dernier soit administré à 32 semaines ou moins de grossesse. Pour tous les vaccins, si l'intervalle minimal de 14 jours n'est pas respecté, la dose serait considérée comme valide et n'aurait pas à être redonnée.

À ce jour, l'interaction entre les vaccins à ARNm et les anticorps monoclonaux anti-SRAS-CoV-2 ou le plasma de convalescents est inconnue. Étant donné qu'il est possible que l'administration rapprochée de ces produits diminue l'efficacité du vaccin contre la COVID-19, et que le risque des réinfections par le SRAS-CoV-2 est plus faible à l'intérieur des 90 jours suivants le premier épisode, le CIQ recommande d'attendre 90 jours après l'administration d'anticorps anti-SRAS-CoV-2 ou de plasma de convalescents avant de donner un vaccin contre la COVID-19. En ce qui concerne l'administration de ces produits après un vaccin contre la COVID-19, il est préférable d'attendre 90 jours, mais la gestion d'une telle situation devrait se faire au cas par cas en fonction de la sévérité de la maladie de la personne chez qui il serait indiqué de donner des anticorps anti-SRAS-CoV-2 ou le plasma de convalescents.

En ce qui concerne le test cutané à la tuberculine (TCT), l'administration de certains vaccins vivants atténués (notamment celui contre la rougeole) peut réduire la réponse à un TCT effectué par la suite(62). Il est possible que ce soit aussi le cas du test de libération de l'interféron gamma (TLIG), mais cela n'a pas été étudié. Les vaccins inactivés n'interfèrent pas avec le TCT. Aucune donnée n'est disponible concernant l'interférence entre les vaccins contre la COVID-19 et le TCT ou le TLIG. En l'absence de données, il apparaît prudent d'éviter d'effectuer un TCT ou un TLIG dans les 28 jours suivant l'administration d'un vaccin contre la COVID-19. Mais dans certaines situations, notamment lors de l'investigation d'un contact d'un cas de tuberculose contagieuse, il pourrait être considéré d'effectuer le TCT durant l'intervalle de 28 jours de la vaccination contre la COVID-19, s'il est jugé que les bénéfices dépassent les inconvénients et après discussion avec un professionnel de la santé apte à le faire, par exemple le médecin traitant. Si le résultat est considéré non significatif, un autre TCT au moins 28 jours après la vaccination devrait être envisagé.

7 Vaccination des personnes avec diagnostic confirmé de COVID-19

Une infection par le SRAS-CoV-2 induit une réponse immunitaire adaptative cellulaire et humorale dirigée contre de nombreux constituants du virus(63,64). Les vaccins à ARNm et ceux à vecteur viral sont quant à eux conçus pour générer une immunité dirigée spécifiquement contre la protéine de spicule(65). Dans une étude portant sur le vaccin PB-COVID-19, les anticorps qui ont été produits étaient principalement dirigés contre des épitopes situés dans le domaine de fixation du récepteur (Receptor Binding Domain ou RBD) et le domaine N-terminal (N-Terminal Domain ou NTD)(66). Ces anticorps sont caractérisés par une activité neutralisante inhibant l'attachement du virus à la cellule hôte, mais possèdent d'autres fonctions contribuant à la protection(63).

De nombreuses études ont montré un effet d'une dose unique de vaccin pour élever les titres d'anticorps dirigés contre la protéine spiculaire ainsi que l'intensité de la réponse cellulaire chez des personnes préalablement infectées(67–84). Les titres d'anticorps observés chez les individus préalablement infectés par le SRAS-CoV-2 ayant reçu une dose de vaccin à ARNm sont semblables voire plus élevés que chez les personnes naïves ayant reçu deux doses de vaccin(85). Une dose de vaccin à ARNm chez des individus préalablement infectés génère une réponse en anticorps humoraux capable de neutraliser in vitro des souches appartenant à des variants comme ceux de la lignée Beta (B.1.351) identifiée en Afrique du Sud ou de la lignée Gamma (P.1) identifiée au Brésil(86,87). Cette augmentation de la capacité de la réponse immunitaire à neutraliser les variants a été également constatée dans une étude où des personnes infectées avaient reçu une ou deux doses de vaccin à ARNm, sans que l'analyse ne fasse de distinction en fonction du nombre de doses(88).

Il existe également un grand nombre d'études ayant mis en évidence la quasi-absence d'effet immunitaire supplémentaire d'une deuxième dose de vaccin chez des personnes immunocompétentes préalablement infectées(69,70,76,83,85,89,90). Dans une étude, il a été rapporté qu'une deuxième dose de vaccin à ARNm chez des personnes ayant eu une infection pouvait être associée à une diminution de la réponse cellulaire(68). Une exception quant à l'absence de bénéfice significatif d'une deuxième dose de vaccin pour les personnes préalablement infectées pourrait être celle des personnes ayant fait une infection asymptomatique, bien que les résultats de toutes les études ne soient pas concordants. Dans une étude chez des travailleurs de la santé aux États-Unis, les anticorps de liaison et les titres neutralisants ont été mesurés chez des individus naïfs et chez ceux ayant fait une infection asymptomatique ou symptomatique documentée par une sérologie et une histoire clinique(75). Avant toute vaccination, les titres étaient plus élevés chez les individus ayant fait une infection symptomatique que chez ceux ayant fait une infection asymptomatique. Après une première dose de vaccin à ARNm, l'augmentation des titres a été plus forte dans le groupe des asymptomatiques que dans le groupe des symptomatiques pour arriver à des titres d'anticorps aussi élevés chez les personnes asymptomatiques. Dans une autre étude chez des travailleurs de la santé ayant été infectés, les niveaux d'anticorps mesurés après une première dose de vaccin PB-COVID-19 s'est traduite par un niveau d'anticorps plus élevé chez les personnes symptomatiques, qu'asymptomatiques, et la deuxième dose a augmenté légèrement les titres dans le groupe des symptomatiques et davantage dans le groupe des asymptomatiques(80).

Les résultats de l'étude prospective de cohorte SIREN parmi des travailleurs de la santé au Royaume-Uni indiquent une protection de 72 % (IC95 % : 58 à 85) après une première dose de vaccin PB-COVID-19 chez les individus séronégatifs au départ et de 86 % (IC95 % : 76 à 97) après la deuxième dose(91). Chez les personnes séropositives au départ (antécédent d'infection), la protection conférée par la primo-infection s'élevait à 90 % (IC95 % : 88 à 92). Dans ce dernier groupe, il n'a pas été possible de modéliser l'effet d'une première dose de vaccin vu le nombre restreint de cas incidents, mais on peut supposer que cela s'est ajouté à une protection déjà très élevée.

Par ailleurs, la réactogénicité après l'administration d'une dose d'un vaccin à ARNm contre la COVID-19 des personnes ayant déjà fait une infection à la COVID-19 est plus importante que ce qui est noté chez les personnes n'ayant jamais été infectées par le SRAS-CoV-2(92,93). Cela se manifeste par des fréquences de réactions systémiques statistiquement plus élevées comme de la fatigue, des céphalées ou des myalgies(92). L'Agence nationale de sécurité du médicament et des produits de santé a également noté, dans le cadre de la surveillance renforcée pour le vaccin PB-COVID-19, une fréquence plus élevée de réactions systémiques chez les personnes avec antécédents de COVID-19 comparativement à celles sans de tels antécédents(94). Cependant, les informations disponibles restent rassurantes quant à l'innocuité d'une première et deuxième dose de vaccin chez les personnes ayant déjà fait une infection. Par exemple, dans l'essai de phase III du vaccin de Moderna, la 1re et la 2e dose ont été bien tolérées chez les individus avec infection au SRAS-CoV-2 avant la vaccination(95). De plus, dans toutes les études d'immunogénicité citées plus haut, aucun problème de sécurité n'a été évoqué.

Devant ces faits, il appert qu'une seule dose de vaccin contre la COVID-19 soit suffisante pour les personnes immunocompétentes ayant un antécédent de COVID-19 confirmée par un test d'amplification des acides nucléiques (TAAN) pour le SRAS-CoV-2, étant donné qu'elles ont déjà élaboré une mémoire immunitaire lors de l'infection. Cela est cohérent avec les recommandations de diverses autorités de santé publique, notamment en France, en Allemagne et en Italie(96), mais diffère de celle du CCNI qui mentionne que deux doses de vaccin peuvent être offertes aux personnes ayant fait la COVID-19 dans le passé(17). Certaines nuances doivent cependant être apportées. L'existence ou non d'une histoire d'infection par le SRAS-CoV-2 ne devrait pas modifier le nombre de doses à recommander aux personnes immunodéprimées ou dialysées pour qui des recommandations spécifiques ont été émises(30). Par ailleurs, le CIQ recommande une 2e dose pour les personnes avec antécédent de COVID-19 qui planifient un voyage et doivent répondre à l'exigence sanitaire d'une double vaccination. Finalement, toute personne avec diagnostic confirmé de COVID-19 qui désire une deuxième dose de vaccin pourrait la recevoir sans avoir à fournir de justification puisqu'aucun enjeu majeur d'innocuité n'a été identifié en lien avec l'administration d'une telle 2e dose.

Dans le cas d'une personne dont l'épisode d'infection au SRAS-CoV-2 coïncide avec le moment où elle aurait reçu une première dose d'un vaccin contre la COVID-19 ou qui surviendrait après avoir reçu une première dose, il n'est pas possible de déterminer si cette première dose de vaccin a pu être efficace ou si elle serait suffisante, particulièrement si la vaccination a été donnée durant la période d'incubation ou trop précocement pendant la phase de guérison de la maladie ou encore avant que la protection conférée par le vaccin ait pu s'installer. Devant de telles situations, un calendrier de vaccination à deux doses est préconisé selon celui en vigueur au Québec. De manière opérationnelle, il est défini qu'une personne dont l'épisode d'infection au SRAS-CoV-2 a débuté moins de 21 jours avant d'avoir reçu un vaccin contre la COVID-19 ou dont l'épisode a débuté après avoir reçu un vaccin contre la COVID-19, doit recevoir au total deux doses de vaccin contre la COVID-19 selon le calendrier en vigueur au Québec. En ce qui concerne le meilleur moment pour vacciner les personnes qui ont fait la COVID-19, il est nécessaire d'attendre la fin de l'épisode aigu de COVID-19 avant de procéder à la vaccination, notamment pour éviter de confondre les conséquences de la maladie avec les manifestations cliniques qui peuvent survenir à la suite de la vaccination(17). Pour des raisons de sécurité évidentes, il est également préférable d'attendre après la fin de la période de contagiosité d'un cas de COVID-19 avant de le vacciner, correspondant généralement aux 10 jours d'isolement[1] après la date de début des symptômes(97). En cohérence avec le délai de 4 semaines ou plus recommandé entre les 2 doses des vaccins contre la COVID-19 prévues au calendrier de vaccination québécois, la vaccination devrait être offerte 4 semaines ou plus après le diagnostic.

[1] Cette période d'isolement peut varier en fonction de certains facteurs. Se référer aux recommandations du Comité sur la gestion des cas et des contacts de COVID-19 pour déterminer la période d'isolement à respecter(97).

Pour des raisons de faisabilité et de contraintes opérationnelles, il est parfois complexe de retracer les antécédents d'infection à la COVID-19 au sein de certains groupes (ex. : milieux d'hébergement) et de faire le tri des personnes avec ou sans antécédents avant de procéder à la vaccination. Dans ces cas, il pourrait être plus judicieux de vacciner contre la COVID-19 toutes les personnes de ces groupes sans tenir compte des antécédents d'infection. Peu importe les situations, il n'est aucunement recommandé de disposer d'une preuve de présence ou d'absence d'infection antérieure à la COVID-19 pour décider d'administrer un vaccin à ARNm.

La situation épidémiologique au Québec continue d'être surveillée de très près relativement à la circulation des variants du SRAS-CoV-2 et à l'efficacité vaccinale contre la COVID-19. De plus, la littérature scientifique évolue rapidement et les nouveaux écrits sont également surveillés. Les dernières recommandations au sujet de la vaccination des personnes ayant des antécédents de COVID-19 pourront donc être ajustées en fonction de cette surveillance continue.

8 Manifestations cliniques après la vaccination

Les manifestations après la vaccination contre la COVID-19 survenues chez les personnes vaccinées lors des études de phase III, soit des réactions locales au site d'injection (ex. : douleur) ou des réactions systémiques (ex. : fatigue, céphalée, myalgie), sont décrites en détail dans le PIQ(98). Elles correspondent à des manifestations que l'on retrouve assez souvent après avoir reçu un vaccin.

En ce qui a trait aux manifestations plus inhabituelles, une lymphadénopathie a été rapportée rarement après avoir reçu les vaccins PB ou MOD COVID-19, soit chez 1 % ou moins des sujets(5,99). Par ailleurs, lors des études de phase III, des cas de paralysie de Bell ont été observés, soit trois cas chez les personnes ayant reçu le vaccin MOD COVID-19 et quatre cas chez celles ayant reçu le vaccin PB COVID-19 alors qu'aucun cas n'est survenu dans le groupe placebo de l'essai du vaccin PB COVID-19(100) et un seul cas dans le groupe placebo de l'essai du vaccin de Moderna(5). Dans ces études pré-homologation, pour les deux vaccins combinés, l'incidence des cas de paralysie de Bell chez les vaccinés a été estimée à environ 17,7 par 100 000 et n'était pas supérieure à l'incidence attendue selon la *U.S. Food and Drug administration* et *l'American Academy of Otolaryngology–Head and Neck Surgery*. Un cas survenu à la suite du vaccin de Moderna avait une autre cause attribuable et n'a pas été comptabilisé dans l'incidence. Ces manifestations reliées dans le temps à la vaccination contre la COVID-19 survenues chez peu de personnes ne permettent pas actuellement de départager ce qui pourrait être relié au vaccin de ce qui pourrait être le fruit du hasard. Le CIQ reste très à l'affût des données de surveillance des manifestations cliniques après la vaccination, afin d'ajuster ses recommandations selon leur évolution(19), et ce, tout en tenant compte des changements des données scientifiques.

Références

1. Comité sur l'immunisation du Québec. Avis préliminaire sur les groupes prioritaires pour la vaccination contre la COVID-19 au Québec 2021 [Internet]. 2021. Disponible sur: https://www.inspq.qc.ca/publications/3085-groupes-prioritaires-vaccination-covid

2. Ministère de la Santé et des Services sociaux. Protocole d'immunisation du Québec (PIQ): Gouvernement du Québec; 2021 [Internet]. Disponible sur: https://www.msss.gouv.qc.ca/professionnels/vaccination/protocole-d-immunisation-du-quebec-piq/

3. Santé Canada. Santé Canada autorise le premier vaccin contre la COVID-19 - Déclaration. Ottawa: Gouvernement du Canada; 2020 [Internet]. Disponible sur: https://www.canada.ca/fr/sante-canada/nouvelles/2020/12/sante-canada-autorise-le-premier-vaccin-contre-la-covid-190.html

4. Gouvernement of Canada. Varicella (Chickenpox) [Internet]. [cité 8 mai 2019]. Disponible sur: https://www.canada.ca/en/public-health/services/immunization/vaccine-preventable-diseases/varicella-chickenpox.html

5. Moderna. FDA Briefing Document - Moderna COVID-19 Vaccine [Internet]. Disponible sur: https://www.fda.gov/media/144452/download

6. Pfizer Canada SRI. Monographie - Vaccin contre la COVID-19 de Pfizer-BioNTech - Vaccin à ARNm contre la COVID-19, suspension pour injection intramusculaire [Internet]. Disponible sur: https://pdf.hres.ca/dpd_pm/00060739.PDF

7. Medicines and Healthcare products Regulatory Agency. COVID-19: the green book, chapter 14a (Provisional guidance subject to MHRA approval of vaccine supply) 2020 [Internet]. Disponible sur: https://www.medbox.org/document/covid-19-the-green-book-chapter-14a-provisional-guidance-subject-to-mhra-approval-of-vaccine-supply#GO

8. Pfizer Canada. Pfizer-Biontech announce positive topline results of pivotal COVID-19 vaccine study in adolescents [Internet]. Disponible sur: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-biontech-announce-positive-topline-results-pivotal

9. Santé Canada. Sommaire de décision réglementaire - Vaccin contre la COVID-19 de Pfizer-BioNTech - Santé Canada [Internet]. 2021 [cité 7 mai 2021]. Disponible sur: https://covid-vaccine.canada.ca/info/sommaire-decision-reglementaire-detailTwo.html?linkID=RDS00802&pType=rds&lang=fr

10. Comité consultatif national de l'immunisaton. Recommandation sur l'utilisation du vaccin contre la COVID-19 de Pfizer-BioNTech chez les adolescents de 12 à 18 ans [Internet]. 2021. Disponible sur: https://www.canada.ca/fr/sante-publique/services/immunisation/comite-consultatif-national-immunisation-ccni/recommandations-utilisation-vaccins-covid-19-pfizer-biontech-adolescents.html

11. The Community Guide. Vaccination Programs: Schools and Organized Child Care Centers [Internet]. 2021 [cité 8 mai 2021]. Disponible sur: https://www.thecommunityguide.org/findings/vaccination-programs-schools-and-organized-child-care-centers

12. Guay M, Clouâtre A-M, Blackburn M, Baron G, De Wals P, Roy C, et al. Effectiveness and cost comparison of two strategies for hepatitis B vaccination of schoolchildren. Can J Public Health. févr 2003;94(1):64-7.

13. Gouvernement du Canada. Vaccin de Moderna contre la COVID-19 [Internet]. 2021. Disponible sur: https://www.canada.ca/fr/sante-canada/services/medicaments-produits-sante/covid19-industrie/medicaments-vaccins-traitements/vaccins/moderna.html

14. Comité sur l'immunisation du Québec. Avis préliminaire concernant la vaccination des jeunes contre la COVID-19 dans le contexte du signal de survenues de myocardites et de péricardites après l'administration des vaccins à ARN messager [Internet]. 2021. Disponible sur: https://www.inspq.qc.ca/publications/3153-vaccination-jeunes-covid-19-myocardites-pericardites-vaccin-arn

15. Moderna. Monographie de produit - COVID-19 Vaccine Moderna [Internet]. Disponible sur: https://www.modernacovid19global.com/ca/fr/product-monograph-french.pdf

16. Santé Canada. Vaccin contre la COVID-19 de Pfizer-BioNTech : recommandations de Santé Canada pour les personnes qui ont de graves allergies: Gouvernement du Canada; 2020 [Internet]. Disponible sur: https://canadiensensante.gc.ca/recall-alert-rappel-avis/hc-sc/2020/74543a-fra.php

17. Comité consultatif national de l'immunisation. Recommandations sur l'utilisation des vaccins contre la COVID-19: Agence de la santé publique du Canada - Gouvernement du Canada; mise à jour le 22 juillet 2021 [Internet]. Disponible sur: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines.html

18. Centers for Disease Control and Prevention. Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine — United States, December 14–23, 2020 [Internet]. Disponible sur: https://www.cdc.gov/mmwr/volumes/70/wr/mm7002e1.htm

19. Institut national de santé publique du Québec. Données de vaccination contre la COVID-19 au Québec [Internet]. 2021. Disponible sur: https://www.inspq.qc.ca/covid-19/donnees/vaccination

20. Stone CA, Liu Y, Relling MV, Krantz MS, Pratt AL, Abreo A, et al. Immediate Hypersensitivity to Polyethylene Glycols and Polysorbates: More Common Than We Have Recognized. J Allergy Clin Immunol Pract. juin 2019;7(5):1533-1540.e8.

21. Association des Allergologues et Immunologues du Québec. Vaccination COVID-19 chez patients avec histoire d'allergie. Document de travail. 2021.

22. Shimabukuro C. COVID-19 Vaccine safety updates [Internet]. 2021 juin 23. Disponible sur: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/03-COVID-Shimabukuro-508.pdf

23. Marshall M, Ferguson ID, Lewis P, Jaggi P, Gagliardo C, Collins JS, et al. Symptomatic Acute Myocarditis in Seven Adolescents Following Pfizer-BioNTech COVID-19 Vaccination. Pediatrics. 2021;e2021052478.

24. National Advisory Committee, on Immunization (NACI). Recommendations on the use of COVID-19 Vaccines [Internet]. 2021. Disponible sur: https://www.canada.ca/content/dam/phac-aspc/documents/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines/recommendations-use-covid-19-vaccines-en.pdf

25. Comité consultatif national de l'immunisation. Recommandation sur l'utilisation des vaccins à ARNm contre la COVID-19 chez les adolescents de 12 à 17 ans [Internet]. 2021. Disponible sur: https://www.canada.ca/fr/sante-publique/services/immunisation/comite-consultatif-national-immunisation-ccni/recommandations-utilisation-vaccins-covid-19/arnm-adolescents.html

26. Cho JH, Feldman M. Heterogeneity of autoimmune diseases: pathophysiologic insights from genetics and implications for new therapies. Nat Med. juill 2015;21(7):730-8.

27. Centers for Disease Control and Prevention. Interim Clinical Considerations for Use of mRNA COVID-19 Vaccines Currently Authorized in the United States [Internet]. Disponible sur: https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

28. Simard M, de Montigny C, Jean S, Fortin E, Blais C, Théberge I, et al. Impact des comorbidités sur les risques de décès et d'hospitalisation chez les cas confirmés de la COVID-19 durant les premiers mois de la pandémie au Québec [Internet]. Québec: Institut national de santé publique du Québec; 2020, 39 p. Disponible sur: https://www.inspq.qc.ca/publications/3082-impact-comorbidites-risque-deces-covid19

29. American Society of Transplantation. COVID-19 Vaccine FAQ Sheet 2020 [Internet]. Disponible sur: https://www.myast.org/sites/default/files/2020%2012%2008%20COVID19%20VACCINE%20FAQS_FINAL.pdf

30. Comité sur l'immunisation du Québec. Avis portant sur la pertinence d'une dose additionnelle de vaccin contre la COVID-19 pour les personnes ayant une immunodépression [Internet]. 2021. Disponible sur: https://www.inspq.qc.ca/sites/default/files/publications/3163-pertinence-dose-additionnelle-vaccin-covid-19-immunodeprimes.pdf

31. Money D. Canadian surveillance of COVID-19 in pregnancy: epidemiology, maternal and infant outcomes - Report #2: Released January 15, 2021 [Internet]. Disponible sur: http://med-fom-ridprogram.sites.olt.ubc.ca/files/2021/01/CANCOVID_Preg-report-2-ON-AB-BC-QC-data_15JAN2021_FINAL.pdf

32. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ. 2020;370:m3320.

33. Zambrano LD, Ellington S, Strid P, Galang RR, Oduyebo T, Tong VT, et al. Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-October 3, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(44):1641-7.

34. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, et al. Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The INTERCOVID Multinational Cohort Study. JAMA Pediatr [Internet]. 2021; Disponible sur: https://jamanetwork.com/journals/jamapediatrics/fullarticle/2779182?utm_campaign=articlePDF%26utm_medium=articlePDFlink%26utm_source=articlePDF%26utm_content=jamapediatrics.2021.1050

35. Chmielewska B, Barratt I, Townsend R, Kalafat E, van der Meulen J, Gurol-Urganci I, et al. Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis. The Lancet Global Health. 2021;S2214109X21000796.

36. Wei SQ, Bilodeau-Bertrand M, Liu S, Auger N. The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. CMAJ. 2021;193(16):E540-8.

37. Centers for Disease Control and Prevention. V-safe COVID-19 Vaccine Pregnancy Registry [Internet]. 2021. Disponible sur: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafepregnancyregistry.html

38. Shimabukuro TT, Kim SY, Myers TR, Moro PL, Oduyebo T, Panagiotakopoulos L, et al. Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. N Engl J Med. 2021;NEJMoa2104983.

39. Golan Y, Prahl M, Cassidy A, Lin CY, Ahituv N, Flaherman VJ, et al. COVID-19 mRNA vaccine is not detected in human milk [Internet]. Pediatrics; 2021. Disponible sur: http://medrxiv.org/lookup/doi/10.1101/2021.03.05.21252998

40. Société des obstétriciens et gynécologues du Canada. Déclaration de la SOGC sur la vaccination contre la COVID-19 pendant la grossesse - Mise à jour le 25 mai 2021 [Internet]. Disponible sur: https://www.sogc.org/common/Uploaded%20files/Latest%20News/FR_SOGC_Statement_COVID_19_Vaccination_in_Pregnancy.pdf

41. The American College of Obstetricians and Gynecologists. Vaccinating Pregnant and Lactating Patients Against COVID-19 [Internet]. Disponible sur: https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/vaccinating-pregnant-and-lactating-patients-against-covid-19

42. Comité sur l'immunisation du Québec. Caractéristiques des vaccins candidats contre la COVID-19 et enjeux relatifs à leur utilisation au Québec 2020 [Internet]. 2020. Disponible sur: https://www.inspq.qc.ca/sites/default/files/publications/3069-caracteristiques-vaccins-candidats-enjeux-covid19.pdf

43. Comité consultatif national de l'immunisation. Réponse rapide du CCNI : Interchangeabilité des vaccins autorisés contre la COVID-19 [Internet]. 2021. Disponible sur: https://www.canada.ca/content/dam/phac-aspc/documents/services/immunization/national-advisory-committee-on-immunization-naci/reponse-rapide-ccni-interchangeabilite-vaccins-authorises-covid-19-fr.pdf

44. Comité sur l'immunisation du Québec. Utilisation du vaccin AstraZeneca contre la COVID-19 dans le contexte du signal de thromboses avec thrombocytopénie suite à la vaccination - Mise à jour 7 mai 2021 [Internet]. Québec: Institut national de santé publique du Québec; p. 8. Disponible sur: https://www.inspq.qc.ca/publications/3124-thromboses-astrazeneca-covishield

45. Comité sur l'immunisation du Québec. Stratégie de vaccination contre la COVID-19 : report de la 2e dose en contexte de pénurie [Internet]. 2020. Disponible sur: https://www.inspq.qc.ca/publications/3098-strategie-vaccination-2e-dose-covid

46. Moderna. A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older [Internet]. Disponible sur: https://www.modernatx.com/sites/default/files/mRNA-1273-P301-Protocol.pdf

47. Comité consultatif national de l'immunisation. Archived 5: NACI rapid response: Extended dose intervals for COVID-19 vaccines to optimize early vaccine rollout and population protection in Canada [2021-03-03] [Internet]. 2021. Disponible sur: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/rapid-response-extended-dose-intervals-covid-19-vaccines-early-rollout-population-protection.html

48. Pilishvili T, Fleming-Dutra KE, Farrar JL, Gierke R, Mohr NM, Talan DA, et al. Interim Estimates of Vaccine Effectiveness of Pfizer-BioNTech and Moderna COVID-19 Vaccines Among Health Care Personnel - 33 U.S. Sites, January-March 2021. MMWR Morb Mortal Wkly Rep. 21 mai 2021;70(20):753-8.

49. Public Health England. COVID-19 vaccine surveillance report Week 20 [Internet]. 2021. Disponible sur: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/990089/Vaccine_surveillance_report_-_week_20.pdf

50. Institut national de santé publique du Québec. Efficacité du vaccin contre la COVID-19 chez les travailleurs de la santé du Québec [Internet]. 2021. Disponible sur: https://www.inspq.qc.ca/publications/3145-efficacite-vaccin-covid-19-travailleurs-sante

51. Bernal JL, Andrews N, Gower C, Gallagher E, Simmons R, Thelwall S, et al. Effectiveness of COVID-19 vaccines against the B.1.617.2 variant [Internet]. Epidemiology; 2021 mai. Disponible sur: https://www.medrxiv.org/content/10.1101/2021.05.22.21257658v1

52. Nasreen S, He S, Chung H, Brown KA, Gubbay JB, Buchan SA, et al. Effectiveness of COVID-19 vaccines against variants of concern, Canada [Internet]. Public and Global Health; 2021. Disponible sur: http://medrxiv.org/lookup/doi/10.1101/2021.06.28.21259420

53. Parry H, Bruton R, Stephens C, Brown K, Amirthalingam G, Hallis B, et al. Extended interval BNT162b2 vaccination enhances peak antibody generation in older people [Internet]. Infectious Diseases (except HIV/AIDS); 2021 [cité 2 juin 2021]. Disponible sur: https://www.medrxiv.org/content/10.1101/2021.05.15.21257017v1

54. Institut national de santé publique du Québec. Données sur les variants du SRAS-CoV-2 au Québec [Internet]. 2021. Disponible sur: https://www.inspq.qc.ca/covid-19/donnees/variants

55. Public Health Agency of Canada. Update on COVID-19 in Canada: Epidemiology and Modelling [Internet]. 2021. Disponible sur: https://www.canada.ca/content/dam/phac-aspc/documents/services/diseases-maladies/coronavirus-disease-covid-19/epidemiological-economic-research-data/update-covid-19-canada-epidemiology-modelling-20210625-en.pdf

56. Clinical Trials. COVID-19: A Trial Studying the SARS-CoV-2 mRNA Vaccine CVnCoV to Learn About the Immune Response, the Safety, and the Degree of Typical Vaccination Reactions When CVnCoV is Given at the Same Time as a Flu Vaccine Compared to When the Vaccines Are Separately Given in Adults 60 Years of Age and Older (CV-NCOV-011) [Internet]. 2021. Disponible sur: https://clinicaltrials.gov/ct2/show/NCT04848467

57. Clinical Trials. Safety and Immunogenicity Study of 20vPnC When Coadministered With a Booster Dose of BNT162b2 [Internet]. 2021. Disponible sur: https://clinicaltrials.gov/ct2/show/NCT04887948

58. UK Goverment. Greenbook, chapter 14a - COVID-19 - SARS-CoV-2 [Internet]. 2021. Disponible sur: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/984310/Greenbook_chapter_14a_7May2021.pdf

59. World Health Organization. Interim recommendations for use of the Pfizer–BioNTech COVID-19 vaccine, BNT162b2, under Emergency Use Listing [Internet]. 2021. Disponible sur: https://apps.who.int/iris/bitstream/handle/10665/338484/WHO-2019-nCoV-vaccines-SAGE_recommendation-BNT162b2-2021.1-eng.pdf

60. Centers for Disease Control and Prevention. Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Authorized in the United States [Internet]. 2021. Disponible sur: https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

61. Centers for Disease Control and Prevention. Coadministration with other vaccines [Internet]. 2021. Disponible sur: https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html#Coadministration

62. Centers for Disease Control and Prevention. Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013: Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP) [Internet]. Disponible sur: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6204a1.htm

63. Sette A, Crotty S. Adaptive immunity to SARS-CoV-2 and COVID-19. Cell. 2021;184(4):861-80.

64. Jagannathan P, Wang TT. Immunity after SARS-CoV-2 infections. Nat Immunol. mai 2021;22(5):539-40.

65. Klingler J, Lambert GS, Itri V, Liu S, Bandres JC, Enyindah-Asonye G, et al. SARS-CoV-2 mRNA vaccines induce a greater array of spike-specific antibody isotypes with more potent complement binding capacity than natural infection [Internet]. Infectious Diseases (except HIV/AIDS); 2021 mai. Disponible sur: http://medrxiv.org/lookup/doi/10.1101/2021.05.11.21256972

66. Amanat F, Thapa M, Lei T, Sayed Ahmed SM, Adelsberg DC, Carreno JM, et al. The plasmablast response to SARS-CoV-2 mRNA vaccination is dominated by non-neutralizing antibodies and targets both the NTD and the RBD [Internet]. Infectious Diseases (except HIV/AIDS); 2021 [cité 6 juill 2021]. Disponible sur: http://medrxiv.org/lookup/doi/10.1101/2021.03.07.21253098

67. Eyre DW, Lumley SF, Wei J, Cox S, James T, Justice A, et al. Quantitative SARS-CoV-2 anti-spike responses to Pfizer–BioNTech and Oxford–AstraZeneca vaccines by previous infection status. Clinical Microbiology and Infection. 2021;S1198743X21002895.

68. Camara C, Lozano-Ojalvo D, Lopez-Granados E, Paz-Artal E, Pion M, Correa-Rocha R, et al. Differential effects of the second SARS-CoV-2 mRNA vaccine dose on T cell immunity in naïve and COVID-19 recovered individuals [Internet]. Immunology; 2021. Disponible sur: http://biorxiv.org/lookup/doi/10.1101/2021.03.22.436441

69. Krammer F, Srivastava K, Alshammary H, Amoako AA, Awawda MH, Beach KF, et al. Antibody Responses in Seropositive Persons after a Single Dose of SARS-CoV-2 mRNA Vaccine. N Engl J Med. 8 avr 2021;384(14):1372-4.

70. Callegaro A, Borleri D, Farina C, Napolitano G, Valenti D, Rizzi M, et al. Antibody response to SARS-CoV-2 vaccination is extremely vivacious in subjects with previous SARS-CoV-2 infection. J Med Virol. 2021;93(7):4612-5.

71. Angyal A, Longet S, Moore S, Payne RP, Harding A, Tipton T, et al. T-Cell and Antibody Responses to First BNT162b2 Vaccine Dose in Previously SARS-CoV-2-Infected and Infection-Naive UK Healthcare Workers: A Multicentre, Prospective, Observational Cohort Study. SSRN Journal [Internet]. 2021; Disponible sur: https://www.ssrn.com/abstract=3812375

72. Anichini G, Terrosi C, Gandolfo C, Gori Savellini G, Fabrizi S, Miceli GB, et al. SARS-CoV-2 Antibody Response in Persons with Past Natural Infection. N Engl J Med. 2021;385(1):90-2.

73. Parry HM, Bruton R, Tut G, Ali M, Stephens C, Faustini S, et al. Single Vaccination with BNT162b2 or ChAdOx1 in Older People Induces Equivalent Antibody Generation but Enhanced Cellular Responses after ChAdOx1. SSRN Journal [Internet]. 2021; Disponible sur: https://www.ssrn.com/abstract=3825573

74. Taubel J, Spencer CS, Freier A, Camilleri D, Garitaonandia I, Lorch U. Can a second booster dose be delayed in patients who have had COVID-19? [Internet]. Infectious Diseases (except HIV/AIDS); 2021 avr. Disponible sur: http://medrxiv.org/lookup/doi/10.1101/2021.04.09.21255200

75. Saadat S, Rikhtegaran Tehrani Z, Logue J, Newman M, Frieman MB, Harris AD, et al. Binding and Neutralization Antibody Titers After a Single Vaccine Dose in Health Care Workers Previously Infected With SARS-CoV-2. JAMA. 2021;325(14):1467.

76. Mazzoni A, Di Lauria N, Maggi L, Salvati L, Vanni A, Capone M, et al. First-dose mRNA vaccination is sufficient to reactivate immunological memory to SARS-CoV-2 in subjects who have recovered from COVID-19. Journal of Clinical Investigation. 2021;131(12):e149150.

77. Ciccone EJ, Zhu DR, Ajeen R, K. Lodge E, Shook-Sa BE, Boyce RM, et al. SARS-CoV-2 seropositivity after infection and antibody response to mRNA-based vaccination [Internet]. Infectious Diseases (except HIV/AIDS); 2021. Disponible sur: http://medrxiv.org/lookup/doi/10.1101/2021.02.09.21251319

78. Bradley T, Grundberg E, CODIEFY study team, Selvarangan R. Antibody responses boosted in seropositive healthcare workers after single dose of SARS-CoV-2 mRNA vaccine [Internet]. Infectious Diseases (except HIV/AIDS); 2021. Disponible sur: http://medrxiv.org/lookup/doi/10.1101/2021.02.03.21251078

79. Ebinger JE, Fert-Bober J, Printsev I, Wu M, Sun N, Prostko JC, et al. Antibody responses to the BNT162b2 mRNA vaccine in individuals previously infected with SARS-CoV-2. Nat Med. 2021;27(6):981-4.

80. Levi R, Azzolini E, Pozzi C, Ubaldi L, Lagioia M, Mantovani A, et al. One dose of SARS-CoV-2 vaccine exponentially increases antibodies in individuals who have recovered from symptomatic COVID-19. Journal of Clinical Investigation. 2021;131(12):e149154.

81. Zollner A, Watschinger C, Rössler A, Farcet MR, Penner A, Böhm V, et al. B and T Cell Response to SARS-CoV-2 Vaccination in Health Care Professionals With and Without Previous COVID-19. SSRN Journal [Internet]. 2021; Disponible sur: https://www.ssrn.com/abstract=3827863

82. Sasikala M, Shashidhar J, Deepika G, Ravikanth V, Krishna VV, Sadhana Y, et al. Immunological memory and neutralizing activity to a single dose of COVID-19 vaccine in previously infected individuals. International Journal of Infectious Diseases. juill 2021;108:183-6.

83. Ontañón J, Blas J, de Cabo C, Santos C, Ruiz-Escribano E, García A, et al. Influence of past infection with SARS-CoV-2 on the response to the BioTech/Pfizer BNT162b2 mRNA vaccine in health care workers: kinetics and durability of the humoral response [Internet]. Infectious Diseases (except HIV/AIDS); 2021. Disponible sur: http://medrxiv.org/lookup/doi/10.1101/2021.05.25.21257788

84. Abu Jabal K, Ben-Amram H, Beiruti K, Batheesh Y, Sussan C, Zarka S, et al. Impact of age, ethnicity, sex and prior infection status on immunogenicity following a single dose of the BNT162b2 mRNA COVID-19 vaccine: real-world evidence from healthcare workers, Israel, December 2020 to January 2021. Euro Surveill. 2021;26(6):2100096.

85. Ibarrondo FJ, Hofmann C, Fulcher JA, Goodman-Meza D, Mu W, Hausner MA, et al. Primary, Recall, and Decay Kinetics of SARS-CoV-2 Vaccine Antibody Responses. ACS Nano. 23 juin 2021;acsnano.1c03972.

86. Stamatatos L, Czartoski J, Wan Y-H, Homad LJ, Rubin V, Glantz H, et al. mRNA vaccination boosts cross-variant neutralizing antibodies elicited by SARS-CoV-2 infection. Science. 2021;372(6549):1413-8.

87. Nadesalingam A, Cantoni D, Wells DA, Aguinam ET, Ferrari M, Smith P, et al. Breadth of neutralising antibody responses to SARS-CoV-2 variants of concern is augmented by vaccination following prior infection: studies in UK healthcare workers and immunodeficient patients [Internet]. Infectious Diseases (except HIV/AIDS); 2021. Disponible sur: http://medrxiv.org/lookup/doi/10.1101/2021.06.03.21257901

88. Wang Z, Muecksch F, Schaefer-Babajew D, Finkin S, Viant C, Gaebler C, et al. Naturally enhanced neutralizing breadth against SARS-CoV-2 one year after infection. Nature [Internet]. 2021; Disponible sur: http://www.nature.com/articles/s41586-021-03696-9

89. Goel RR, Apostolidis SA, Painter MM, Mathew D, Pattekar A, Kuthuru O, et al. Longitudinal Analysis Reveals Distinct Antibody and Memory B Cell Responses in SARS-CoV2 Naïve and Recovered Individuals Following mRNA Vaccination [Internet]. Infectious Diseases (except HIV/AIDS); 2021. Disponible sur: http://medrxiv.org/lookup/doi/10.1101/2021.03.03.21252872

90. Samanovic MI, Cornelius AR, Wilson JP, Karmacharya T, Gray-Gaillard SL, Allen JR, et al. Poor antigen-specific responses to the second BNT162b2 mRNA vaccine dose in SARS-CoV-2-experienced individuals. medRxiv. 9 févr 2021;2021.02.07.21251311.

91. Hall VJ, Foulkes S, Saei A, Andrews N, Oguti B, Charlett A, et al. COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study. The Lancet. mai 2021;397(10286):1725-35.

92. Krammer F, Srivastava K, the PARIS team, Simon V. Robust spike antibody responses and increased reactogenicity in seropositive individuals after a single dose of SARS-CoV-2 mRNA vaccine [Internet]. Allergy and Immunology; 2021. Disponible sur: http://medrxiv.org/lookup/doi/10.1101/2021.01.29.21250653

93. National Collaborating Centre for Methods and Tools. Rapid Review: What is the effectiveness, immunogenicity and safety of COVID-19 vaccines in persons who have had a prior, confirmed COVID-19 infection? [Internet]. 2021. Disponible sur: https://www.nccmt.ca/covid-19/covid-19-rapid-evidence-service/36

94. Agence nationale de sécurité du médicament et des produits de santé. Point de situation sur la surveillance des vaccins contre la COVID-19 [Internet]. Disponible sur: https://ansm.sante.fr/S-informer/Actualite/Point-de-situation-sur-la-surveillance-des-vaccins-contre-la-COVID-192

95. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 4 févr 2021;384(5):403-16.

96. Dolgin E. Is one vaccine dose enough if you've had COVID? What the science says [Internet]. 2021. Disponible sur: https://www.nature.com/articles/d41586-021-01609-4

97. Comité sur la gestion des cas et des contacts de COVID-19. COVID-19 : Mesures pour la gestion des cas et des contacts dans la communauté : recommandations intérimaires- Version 9.0 : Institut national de santé publique du Québec; 2021. [Internet]. 2021. Disponible sur: https://www.inspq.qc.ca/sites/default/files/publications/2902-mesures-gestion-cas-contacts-communaute_0.pdf

98. Ministère de la Santé et des Services sociaux. COVID-19 : vaccin à ARN messager contre la COVID-19 [Internet]. Disponible sur: https://www.msss.gouv.qc.ca/professionnels/vaccination/piq-vaccins/covid-19-vaccin-a-arn-messager-contre-la-covid-19/

99. Medicines and Healthcare products Regulatory Agency. Confirmation of guidance to vaccination centres on managing allergic reactions following COVID-19 vaccination with the Pfizer/BioNTech vaccine: Governement of United Kindom; 2020 [Internet]. Disponible sur: https://www.gov.uk/government/news/confirmation-of-guidance-to-vaccination-centres-on-managing-allergic-reactions-following-covid-19-vaccination-with-the-pfizer-biontech-vaccine

100. Food and Drug Administration. Fact sheet for healthcare providers administering vaccine (vaccination providers) emergency use authorization (eua) of the pfizer -biontech covid-19 vaccine to prevent Coronavirus disease 2019 (COVID-19) [Internet]. Disponible sur: https://www.fda.gov/media/144413/download

Avis intérimaire sur l'utilisation des vaccins à ARN messager contre la COVID-19

AUTEUR

Comité sur l'immunisation du Québec

RÉDACTEURS

Maryse Guay
Nicholas Brousseau
Philippe De Wals
Rodica Gilca
Marilou Kiely
Gisèle Trudeau
Chantal Sauvageau
Direction des risques biologiques et de la santé au travail

MISE EN PAGE

Marie-France Richard, agente administrative
Direction des risques biologiques et de la santé au travail

Ce document est disponible intégralement en format électronique (PDF) sur le site Web de l'Institut national de santé publique du Québec au : http://www.inspq.qc.ca.

Les reproductions à des fins d'étude privée ou de recherche sont autorisées en vertu de l'article 29 de la Loi sur le droit d'auteur. Toute autre utilisation doit faire l'objet d'une autorisation du gouvernement du Québec qui détient les droits exclusifs de propriété intellectuelle sur ce document. Cette autorisation peut être obtenue en formulant une demande au guichet central du Service de la gestion des droits d'auteur des Publications du Québec à l'aide d'un formulaire en ligne accessible à l'adresse suivante : http://www.droitauteur.gouv.qc.ca/autorisation.php, ou en écrivant un courriel à : droit.auteur@cspq.gouv.qc.ca.

Les données contenues dans le document peuvent être citées, à condition d'en mentionner la source.

© Gouvernement du Québec (2021)

N° de publication : 3093

Institut national de santé publique Québec

De :	Lauriane Padet
À :	Marie-Claude Gariépy
Cc :	Isabelle Rouleau
Objet :	Efficacité et sécurité vaccinale chez les femmes enceintes et allaitantes
Date :	23 septembre 2021 14:02:43
Pièces jointes :	Efficacité et sécurité vaccinale chez les femmes enceintes.docx

---

Bonjour Isabelle,

Marie-Claude m'a demandé cette semaine de faire une recherche sur **l'efficacité et la sécurité vaccinale chez la femme enceinte.**

Tu trouveras en pièce jointe mon document qui inclut les données sur l'efficacité vaccinale chez les femmes enceintes, l'immunogénicité induite suite à la vaccination de femmes enceintes ou allaitantes et les issues de grossesses suite à la vaccination. Pour chaque article, un bref résumé des résultats et/ou conclusion est inclus. Les articles sont rapportés du plus récents au plus anciens.

A noter que seules données en lien avec les vaccins à ARNm (Pfizer-BioNTech et Moderna) et les vaccin d'AstraZeneca et de Janssen ont été regardés.

J'Ai également inclus les recommandations actuelles pour la vaccination des femmes enceintes ainsi que les signaux sous surveillance suite à la vaccination des femmes enceintes.

En espérant le tout utile, n'hésite pas à communiquer avec moi si tu as des questions.

Bonne journée,

Lauriane

Lauriane Padet, Ph.D.
Conseillère scientifique spécialisée
Direction Risques Biologiques et Santé au Travail (RBST)
Unité Immunisation et infections nosocomiales
Institut national de santé publique du Québec
190, boulevard Crémazie Est, Montréal (Québec), H2P 1E2
lauriane.padet@inspq.qc.ca
INSPQ Centre d'expertise et de référence en santé publique
www.inspq.qc.ca

AVIS DE CONFIDENTIALITÉ
Ce message peut renfermer des renseignements protégés ou des informations confidentielles. Si vous l'avez reçu par erreur, ou s'il ne vous est pas destiné, veuillez en prévenir immédiatement l'expéditeur et effacer ce courriel. Par respect pour l'environnement, imprimer ce courriel seulement si nécessaire.

Mise en contexte

- Bien que les femmes enceintes courent un risque élevé de maladie grave et de décès liés à la COVID-19, en raison des craintes de tératogénicité potentielle ou d'effet indésirable sur la physiologie maternelle, la grossesse a été un critère d'exclusion spécifique pour la plupart des essais de vaccins, à l'exception de deux études :
  - Phase III Double-blind, Placebo-controlled Study of AZD1222 for the Prevention of COVID-19 in Adults
  - PFIZER AND BIONTECH COMMENCE GLOBAL CLINICAL TRIAL TO EVALUATE COVID-19 VACCINE IN PREGNANT WOMEN

    En février 2021, Pfizer a annoncé qu'un essai mondial de phase 2/3 allait être réalisé pour évaluer l'innocuité, la tolérabilité et l'immunogénicité du vaccin COVID-19 chez les femmes enceintes. L'essai de phase 2/3 est conçu comme une étude randomisée, contrôlée par placebo et porte sur environ 4 000 femmes enceintes en bonne santé âgées de 18 ans ou plus, vaccinées après 24 à 34 semaines de gestation. L'étude a pour objectif d'évaluer l'innocuité, la tolérabilité et l'immunogénicité de deux doses de vaccin BNT162b2 ou de placebo, administrées à 21 jours d'intervalle. Chaque femme participera à l'étude pendant environ 7 à 10 mois, selon qu'elle a été randomisée pour recevoir le vaccin ou le placebo. L'étude évaluera la sécurité chez les nourrissons des femmes enceintes vaccinées et le transfert d'anticorps potentiellement protecteurs à leurs nourrissons. Les nourrissons seront surveillés jusqu'à l'âge de six mois environ.

- Dues au manque de données sur la sécurité des vaccins, très peu de pays permettent actuellement la vaccination sans restriction des femmes enceintes ou allaitantes.

- A l'heure actuelle, le CDC, le comité consultatif sur les pratiques d'immunisation (ACIP), le collège américain des obstétriciens et gynécologues (ACOG), la société de médecine maternelle et fœtale (SMFM), l'Organisation mondiale de la santé (OMS), l'agence européenne des médicaments (EMA) et le Comité mixte de la vaccination et de l'immunisation (JCVI) recommandent que toutes les personnes enceintes ou allaitantes, ainsi que celles qui tentent de tomber enceintes, soient vaccinées contre la COVID-19.

Demande du 20 septembre 2021

- Quelle est l'efficacité vaccinale et la sécurité vaccinale chez les femmes enceintes ou les femmes allaitantes?
- Dans ce document, les données en lien avec l'efficacité vaccinale chez les femmes enceintes ont été rapportées. L'immunogénicité induite suite à la vaccination de femmes enceintes ou allaitantes a aussi été rapportée. Finalement, les articles rapportant l'absence ou la présence d'effet secondaire ont été recensés. Pour chaque article, un bref résumé des résultats et/ou conclusion est inclus. Les articles sont rapportés du plus récents au plus anciens.

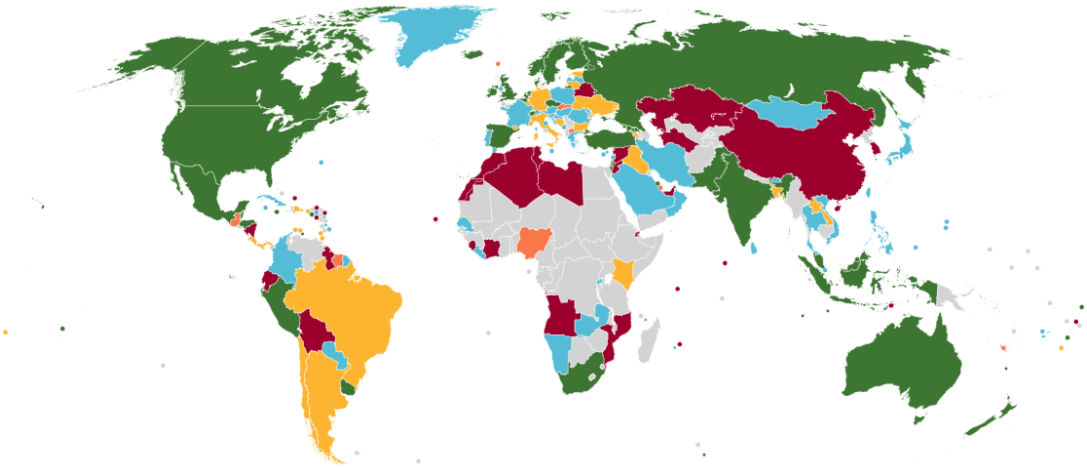
  A noter que seules données en lien avec les vaccins à ARNm (Pfizer-BioNTech et Moderna) et les vaccin d'AstraZeneca et de Janssen ont été regardés.

Covid-19 vaccine policies on pregnancy (switch to lactation)

Showing the most permissive policy position at present for each country for all vaccines.

Filter by vaccine / policy position

Change date



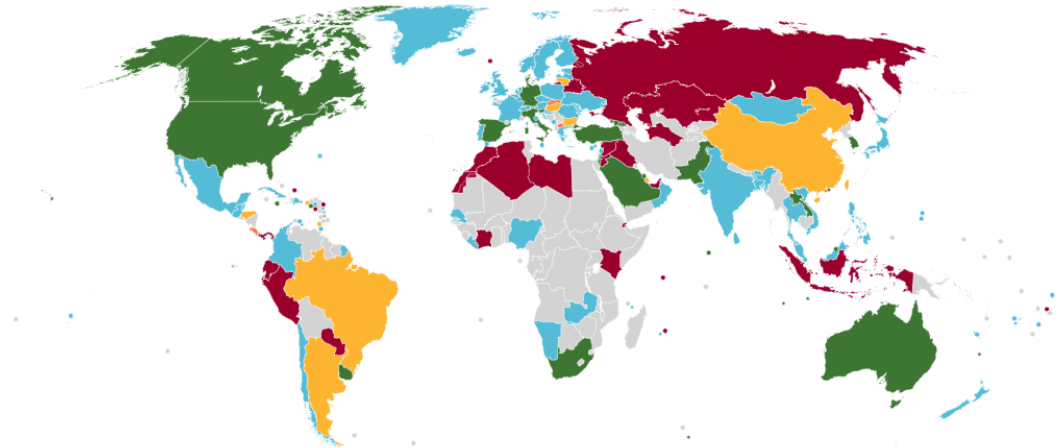
39	50	28	9	31	67
Recommended for some or all	Permitted	Permitted with qualifications	Not recommended but with exceptions	Not recommended	No position found

Covid-19 vaccine policies on lactation (switch to pregnancy)

Showing the most permissive policy position at present for each country for all vaccines.

Filter by vaccine / policy position

Change date



23	70	10	4	26	91
Recommended for some or all	Permitted	Permitted with qualifications	Not recommended but with exceptions	Not recommended	No position found

Source: [Covid-19 Maternal Immunization Tracker (Comit) - COVID-19 Vaccine policies for pregnant and lactating people worldwide.]

Efficacité vaccinale chez les femmes enceintes

Seules deux études observationnelles menées en Israël ont jusqu'à présent rapportées des données sur l'efficacité vaccinale chez les femmes enceintes. Ces études concernent uniquement l'efficacité du vaccin BNT162b2 de Pfizer-BioNTech

Il a été rapporté que la vaccination avec le vaccin BNT162b2 est associée à un risque significativement plus faible d'infection par le SRAS-CoV-2 par rapport à l'absence de vaccination (**Golshtein et al.**).

Une autre étude (**Dagan et al.**) montre que le vaccin à ARNm BNT162b2 est très efficace chez les femmes enceintes contre:

- Les infections (71%, 95% CI : 33-94% > 21 jours après 1 dose ; 96% (95% CI : 89–100%) > 7 jours après 2 doses)
- Les formes symptomatiques de la maladie (76%, 95% CI : 30-100% > 21 jours après 1 dose ; 97% (95% CI : 91–100%) > 7 jours après 2 doses).
- Les hospitalisations (89% (95% CI : 43–100%) > 7 jours après 2 doses).

L'efficacité vaccinale est comparable à celle de la population générale.

1- Goldshtein et al (24 août 2021) Association Between BNT162b2 Vaccination and Incidence of SARS-CoV-2 Infection in Pregnant Women
Résultats: The cohort included 7530 vaccinated and 7530 matched unvaccinated women, 46% and 33% in the second and third trimester, respectively (…) The hazards of infection were 0.33% vs 1.64% in the vaccinated and unvaccinated groups, respectively, representing an absolute difference of 1.31% (95% CI, 0.89%-1.74%), with an adjusted hazard ratio of 0.22 (95% CI, 0.11-0.43). Vaccine-related adverse events were reported by 68 patients; none was severe. The most commonly reported symptoms were headache (n = 10, 0.1%), general weakness (n = 8, 0.1%), non-specified pain (n = 6, <0.1%), and stomachache (n = 5, <0.1%). **Conclusion:** In this retrospective cohort study of pregnant women, BNT162b2 mRNA vaccination compared with no vaccination was associated with a significantly lower risk of SARS-CoV-2 infection. Interpretation of study findings is limited by the observational design.

2- Dagan et al. (07 septembre 2021) Effectiveness of the BNT162b2 mRNA COVID-19 vaccine in pregnancy
Résultats: The estimated vaccine effectiveness for documented infections was 67% (95% confidence interval (CI) = 40–84%) in days 14–20 after the first dose, 71% (33–94%) in days 21–27 after the first dose and 96% (89–100%) in days 7–56 after the second dose (Table 1). The estimated vaccine effectiveness for symptomatic infection was 66% (95% CI = 32–86%) in days 14–20 after the first dose, 76% (30–100%) in days 21–27 after the first dose and 97% (91–100%) in days 7–56 after the second dose. Vaccine effectiveness for COVID-19-related hospitalization was 89% (43–100%) in days 7–56 after the second dose. Vaccine effectiveness could not be meaningfully estimated for the other outcomes and time periods due to the small number of events. **Conclusion:** The results of this study indicate that the BNT162b2 mRNA COVID-19 vaccine is highly effective in pregnant women for the variants circulating in Israel at the time of the study, with vaccine effectiveness that was comparable to that estimated in the general population.

Revue de littérature

1- Damayanti et al. (21 août 2021) A Literature Review on the Vaccination of COVID-1 in Pregnant and Breastfeeding Women: Effectiveness and Safety
2- Garg et al. (31 juillet 2021) COVID-19 Vaccine in Pregnant and Lactating Women: A Review of Existing Evidence and Practice Guidelines

Immunogénicité induite par la vaccination contre la COVID-19 chez les femmes enceintes ou allaitantes

- L'ensemble des études citées ci-dessous rapporte une immunité humorale élevée contre le virus du SRAS-Cov-2 chez les femmes enceintes et les femmes allaitantes suite à la vaccination avec un vaccin à ARNm. L'immunogénicité et la réactogénicité semblent similaires à celles observées chez les femmes non enceintes (**Gray et al., Atyeo et al.).** Cependant, une étude a rapporté une baisse du niveau d'IgG anti-SARS-CoV-2 IgG par rapport aux femmes non-enceintes (**Peretz et al.**).

- La présence d'anticorps spécifiques au SRAS-Cov-2 dans le lait (**Charepe et al.**, **Gray et al.**, **Valcarce et al.**, **Baird et al.**, **Juncker et al.**, **Collier et al.**, **Perl et al.**, **Atyeo et al.**) sang de cordon ou placenta (**Gray et al.**, **Douxfils et al.**, **Beharier et al.**, **Zdanowski et al., Gill et al.**, **Collier et al.**, **Prabhu et al.**), suite à la vaccination avec des vaccins à ARNm (Pfizer-BioNTech ou Moderna), suggère un transfert immunitaire de la mère à l'enfant pendant la grossesse et durant l'allaitement.

1- Charepe et al. (17 septembre 2021) COVID-19 mRNA vaccine and antibody response in lactating women: a prospective cohort study

Vaccin(s): Pfizer-BioNTech (n= 14 femmes allaitantes) **Results:** All women showed immunity after vaccination with positive antibodies for IgM, IgA and IgG antibodies. The dominant serum antibody response was IgG. Modest levels of antibodies in breastmilk of lactating mothers were observed in this study, especially IgG in 42.9%. There was a moderate association between higher titers of IgG and a longer duration of breastfeeding (R= 0.55, p=0.041). **Conclusions:** Evidence of antibody transfer in human milk after COVID-19 vaccination is scarce. The presence of antibodies in human milk is reported, but immunization through breastfeeding is still to be established.

2- Gray et al. (01 septembre 2021) COVID-19 vaccine response in pregnant and lactating women: A cohort study
Vaccin(s): Pfizer-BioNTech (n=41 femmes enceintes, n=16 femmes allaitantes), Moderna (n=43 femmes enceintes, n=15 femmes allaitantes) **Résumé :** Les vaccins à ARN messager contre la maladie à coronavirus 2019 ont généré une immunité humorale robuste chez les femmes enceintes et allaitantes, avec une immunogénicité et une réactogénicité similaires à celles observées chez les femmes non enceintes. Les réponses immunitaires induites par les vaccins étaient statistiquement significativement supérieures à la réponse à l'infection naturelle. Le transfert immunitaire aux nouveau-nés s'est produit via le placenta et le lait maternel.

3- Valcarce et al. (20 août 2021) Detection of SARS-CoV-2-Specific IgA in the Human Milk of COVID-19 Vaccinated Lactating Health Care Workers

Vaccin(s): Pfizer-BioNTech (n=14 femmes allaitantes), Moderna (n=7 femmes allaitantes) **Results:** We found significant secretion of SARS-CoV-2-specific IgA and IgG in human milk and plasma after SARS-CoV-2 vaccination. **Conclusions:** Our results show that the mRNA-based COVID-19 vaccines induce SARS-CoV-2-specific IgA and IgG secretion in human milk. Further studies are needed to determine the duration of this immune response, its capacity to neutralize the COVID-19 virus, the transfer of passive immunity to breastfeeding infants, and the potential therapeutic use of human milk IgA to combat SARS-CoV-2 infections and COVID-19.

4- Douxfils et al. (15 août 2021) Efficient Maternal to Neonate Transfer of Neutralizing Antibodies after SARS-CoV-2 Vaccination with BNT162b2: A Case-Report and Discussion of the Literature

Vaccin(s): Pfizer-BioNTech (n=1 femme allaitante) **Conclusion:** This case reports on the successful maternal to fetal transfer of neutralizing antibodies after vaccination with BNT162b2 in a pregnant woman at 25 weeks of gestation. The levels of neutralizing antibodies were approximately 5-fold higher in the umbilical cord than in the maternal blood, while the level of total antibodies showed only a 2-fold increase. This suggests that the antibodies that crossed the syncytiotrophoblast cell barrier have specific characteristics that correlate to

functional neutralizing capacity. Although pregnant and lactating woman have been excluded from clinical trials for several reasons including ethical concerns about fetal exposure, accumulating evidence has now revealed that these vaccines are safe and efficient for both the fetus and the woman.

5- Baird et al (août 2021) SARS-CoV-2 Antibodies Detected in Mother's Milk Post-Vaccination
Vaccin(s): Pfizer-BioNTech ou Moderna (n=7) **Results:** We observed significantly elevated levels of SARS-CoV-2 specific IgG and IgA antibodies in human milk beginning approximately 7 days after the initial vaccine dose, with an IgG-dominant response. **Conclusions:** Maternal vaccination results in SARS-CoV-2 specific immunoglobulins in human milk that may be protective for infants.

6- Juncker et al. (août 2021) The Levels of SARS-CoV-2 Specific Antibodies in Human Milk Following Vaccination
Vaccin(s): Pfizer-BioNTech (n=26 femmes allaitantes) **Results:** In total, 366 human milk samples from 26 lactating women were analyzed. A biphasic response was observed, with SARS-CoV-2 specific immunoglobulin A (IgA) starting to increase between day 5 and 7 after the first dose of the vaccine. After the second dose, an accelerated IgA antibody response was observed. **Conclusion:** After vaccination with the mRNA-based BNT162b2 vaccine, a SARS-CoV-2 specific antibody response was observed in human milk. The presence of SARS-CoV-2 specific IgA after vaccination is important as antibodies are transferred via human milk, and thereby might provide protection to infants against COVID-19.

7- Peretz et al (09 août 2021) Short-term outcome of pregnant women vaccinated with BNT162b2 mRNA COVID-19 vaccine
Vaccin(s): Pfizer-BioNTech (n=390 femmes enceintes) **Résults:** All serum samples in both groups were positive for SARS-CoV-2 IgG. However, pregnant women had significantly lower serum SARS-CoV-2 IgG levels compared to non-pregnant women (signal-to-cut-off ratio, 27.03 vs 34.35, respectively; $P < 0.001$) (…) **Conclusion:** The vaccine is effective in generating a humoral immune response in pregnant women, although SARS-CoV-2 IgG levels were lower than those observed in non-pregnant vaccinated women.

8- Beharier et al. (01 juillet 2021) Efficient maternal to neonatal transfer of antibodies against SARS-CoV-2 and BNT162b2 mRNA COVID-19 vaccine
Vaccin(s): Pfizer-BioNTech (n=86 femmes enceintes) **Résults:** The BNT162b2 mRNA vaccine elicits strong maternal humoral IgG response (anti-S and RBD) that crosses the placenta barrier and approaches maternal titers in the fetus within 15 days following the first dose. Maternal to neonatal anti-COVID-19 antibodies ratio did not differ when comparing sensitization (vaccine vs. infection). IgG transfer ratio at birth was significantly lower for third-trimester as compared with second trimester infection. Lastly, fetal IgM response was detected in 5 neonates, all in the infected group. **Conclusion:** Antenatal BNT162b2 mRNA vaccination induces a robust maternal humoral response that effectively transfers to the fetus, supporting the role of vaccination during pregnancy.

9- Zdanowski et al. (19 juin 2021) Evaluation of SARS-CoV-2 Spike Protein Antibody Titers in Cord Blood after COVID-19 Vaccination during Pregnancy in Polish Healthcare Workers: Preliminary Results
Vaccin(s): Pfizer-BioNTech (n=150 femmes enceintes) **Results:** The results of the current study document high anti-S total IgG antibody titers in cord serum at birth in all mother-infant pairs analyzed. The mean umbilical cord blood sample IgG antibody titer anti-S protein was 1026.51 U/mL (±SD 769.25). The mean cord-to-maternal anti-S IgG antibody ratio was 1.28 (±SD 0.798). A significant positive correlation was observed between the week of gestation at which the first dose was administered and the week of gestation at which the second dose was administered, and the respective cord-to-maternal ratio ($r = 0.48$; $p = 0.0029$) for the first dose and ($r = 0.39$; $p = 0.0102$) for the second dose. **Conclusions:** To date, despite the prevalence of COVID-19 vaccination, there is a lack of conclusive evidence supporting the safety and efficacy of vaccination of pregnant women. Therefore, the results we present are complementary. Our study suggests that maternal immunization may provide neonatal protection through the transplacental transfer of antibodies. Of particular importance is the demonstration that antibody transfer is correlated with the time from vaccination to delivery, which may allow future determination of the optimal timing of COVID-19 vaccination in pregnant women.

10- Gill et al. (mai 2021) Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Antibodies in Neonatal Cord Blood After Vaccination in Pregnancy

Vaccin(s): Pfizer-BioNTech (n=1 femme enceinte) **Results:** (Case report) A 34-year-old multigravid patient working in health care received the Pfizer-BioNTech (BNT162b2) mRNA vaccine for SARS-CoV-2 in the third trimester of pregnancy. Uncomplicated spontaneous vaginal delivery of a female neonate with Apgar scores of 9 and 9 occurred at term. The patient's blood as well as neonatal cord blood were evaluated for SARS-CoV-2–specific antibodies. Both the patient and the neonate were positive for antibodies at a titer of 1:25,600. **Conclusion:** In this case, passage of transplacental antibodies for SARS-CoV-2 was shown after vaccination in the third trimester of pregnancy.

11- Collier et al. (13 mai 2021) Immunogenicity of COVID-19 mRNA Vaccines in Pregnant and Lactating Women

Vaccin(s): Pfizer-BioNTech (n=11 femmes enceintes, n=11 femmes allaitantes), Moderna (n=19 femmes enceintes, n=5 femmes allaitantes) **Results:** In this cohort study involving 103 women who received a COVID-19 mRNA vaccine, 30 of whom were pregnant and 16 of whom were lactating, immunogenicity was demonstrated in all, and vaccine-elicited antibodies were found in infant cord blood and breast milk. Pregnant and nonpregnant vaccinated women developed cross-reactive immune responses against SARS-CoV-2 variants of concern. **Conclusion:** In a small convenience sample, COVID-19 mRNA vaccines were immunogenic in pregnant and lactating women and induced immune responses against SARS-CoV-2 variants.

12- Perl at al (12 avril 2021) SARS-CoV-2–Specific Antibodies in Breast Milk After COVID-19 Vaccination of Breastfeeding Women

Vaccin(s): Pfizer-BioNTech (n=84 femmes allaitantes) **Results:** Mean levels of anti–SARS-CoV-2-specific IgA antibodies in the breast milk increased rapidly and were significantly elevated at 2 weeks after the first vaccine (2.05 ratio; P < .001), when 61.8% of samples tested positive, increasing to 86.1% at week 4 (1 week after the second vaccine). Mean levels remained elevated for the duration of follow-up, and at week six, 65.7% of samples tested positive. Anti–SARS-CoV-2-specific IgG antibodies remained low for the first 3 weeks, with an increase at week 4 (20.5 U/mL; P = .004), when 91.7% of samples tested positive, increasing to 97% at weeks 5 and 6.

No mother or infant experienced any serious adverse event during the study period. Forty-seven women (55.9%) reported a vaccine-related adverse event after the first vaccine dose and 52 (61.9%) after the second vaccine dose, with local pain being the most common complaint (Table). Four infants developed fever during the study period 7, 12, 15, and 20 days after maternal vaccination. All had symptoms of upper respiratory tract infection including cough and congestion, which resolved without treatment except for 1 infant who was admitted for neonatal fever evaluation due to his age and was treated with antibiotics pending culture results. No other adverse events were reported. **Conclusion:** This study found robust secretion of SARS-CoV-2 specific IgA and IgG antibodies in breast milk for 6 weeks after vaccination. IgA secretion was evident as early as 2 weeks after vaccination followed by a spike in IgG after 4 weeks (a week after the second vaccine).

13- Prabhu et al. (06 avril 2021) Antibody response to SARS-CoV-2 mRNA vaccines in pregnant women and their neonates

Vaccin(s): Pfizer-BioNTech (n=85), Moderna (n=37) **Results:** All women and their neonates, except for one neonate, had detectable IgG antibodies by 4 weeks after maternal first dose of vaccination (Figure 1A). 43.6% (24/55) of neonates born to women that received only one vaccine dose had detectable IgG, while 98.5% (65/67) of neonates born to women that received both vaccine doses had detectable IgG. The IgG levels in pregnant women increased weekly from two weeks after first vaccine dose (p=0.0047;0.019), as well as between the first and second weeks after the second vaccine dose (p=2e-07) (Figure 1B). Maternal IgG levels were linearly associated with neonatal IgG levels (R=0.89, p<2.2e-16) (Figure 2A). Placental transfer ratio correlated with the weeks that elapsed since maternal second dose of vaccine (R=0.8, p=2.6e-15) (Figure 2B). **Conclusion:** mRNA-based COVID-19 vaccines in pregnant women lead to maternal antibody production as early as 5 days after the first vaccination dose, and passive immunity to the neonate as early as 16 days after the first vaccination dose. The increasing levels of maternal IgG over time, and the increasing placental IgG transfer ratio over time suggest that timing between vaccination and birth may be an important factor to consider in the vaccination strategies of pregnant women.

14- Atyeo et al. (05 avril 2021) COVID-19 mRNA vaccines drive differential Fc-functional profiles in pregnant, lactating, and non-pregnant women

Vaccin(s): Pfizer-BioNTech (n=65) et Moderna (n=66) (n=84 femmes enceintes et n= 31 femmes allaitantes), **Results:** Vaccine-specific titers were comparable, albeit slightly lower, between pregnant and lactating women, compared to non-pregnant controls. Among pregnant women, we found higher antibody titers and functions in those vaccinated with the Moderna vaccine. FcR-binding and antibody effector functions were induced with delayed kinetics in both pregnant and lactating women compared to non-pregnant women. Antibody boosting resulted in high FcR-binding titers in breastmilk. These data point to an immune resistance to generate highly inflammatory antibodies during pregnancy and lactation, and a critical need to follow prime/boost timelines in this vulnerable population to ensure full immunity is attained. **Conclusion:** Overall, our data have demonstrated that while antibody titers are similar, pregnant and lactating women respond to vaccination in qualitatively and kinetically distinct manners compared to non-pregnant women. While this study largely profiled responses in women vaccinated later in pregnancy, these data point to the importance of profiling women receiving COVID-19 vaccines throughout pregnancy to begin to understand how distinct platforms, vaccines, populations, and timing affect the quality and quantity of immunity induced across the mother:fetal dyad.

Revue de littérature

1- Zipursky et al. (01 mars 2021) Pregnancy, breastfeeding and the SARS-CoV-2 vaccine: an ethics-based framework for shared decision-making
2- Atyeo et al (04 février) Compromised SARS-CoV-2-specific placental antibody transfer

Sécurité vaccinale des femmes enceintes ou allaitantes

- 6 articles ont rapporté qu'il n'y a pas de différence significative entre les femmes enceintes vaccinées et celles non vaccinées pour ce qui est des effets indésirables ou d'autres complications maternelles ou néonatales y compris les événements thromboemboliques et accouchement prématuré (**Theiler et al.** (Pfizer-BioNTech, Moderna et Janssen), **Shimabukuro et al.** (Pfizer-BioNTech et Moderna), **Golan et al.** (Pfizer-BioNTech et Moderna), **Blakeway et al.** (Pfizer-BioNTech, Moderna et AstraZeneca), **Peretz et al.** (Pfizer-BioNTech), **Kachikis et al.** (Pfizer-BioNTech et Moderna).

- Une étude a cependant rapporté le cas d'une femme qui a développé une thrombocytopénie immune après avoir reçu une dose du vaccin de Moderna au cours du premier trimestre et qui a été résolu après un traitement oral avec des corticostéroïdes (**Bennett et al.**).

- Le taux d'avortement spontané est le signal principal suivi par les instances de santé publique chez les femmes enceintes vaccinées contre la COVID-19. Cinq études rapportées ci-dessous montrent que la vaccination de femmes enceintes contre la COVID-19 n'est pas associée avec un risque augmenté d'avortement spontané ou de naissance prématurée (**Trostle et al.** (vaccin Pfizer-BioNTech et Moderna), **FDA Briefing document** (vaccin Janssen), **Zauche et al.** (vaccin de Pfizer-BioNTech et Moderna), **Kharbanda et al.** (vaccin de Pfizer-BioNTech, Moderna et Janssen), **Rose et al.** (vaccin de Pfizer-BioNTech et Moderna).

- Une étude brésilienne a rapporté qu'une femme de 35 ans a développé une thrombocytopénie thrombotique associée à une hémorragie intracérébrale suite à l'administration du vaccin d'AstraZeneca. La femme a perdu son fœtus et est décédée 17 jours après la vaccination (**Mendes-de-Almeida et al.).** Suite à cet événement, le Brésil a suspendu toute vaccination de femme enceinte avec le vaccin d'AstraZeneca (**Foncesca et al.**).

- Deux études ont montré que les vaccins à ARNm (Pfizer-BioNTech et Moderna) ne sont pas détectés dans le lait maternel. Ces résultats renforcent les recommandations selon lesquelles les femmes qui allaitent et qui reçoivent un vaccin à ARNm anti-COVID-19, devraient continuer à allaiter leur nourrisson (**Mattar et al., Golan et al.**).

1- Theiler et al. (03 Novembre 2021) Pregnancy and birth outcomes after SARS-CoV-2 vaccination in pregnancy
Vaccin(s): Janssen (n=1 femme enceinte), Moderna (n=12 femmes enceintes), Pfizer-BioNTech (n=127 femmes enceintes). **Results:** Of 2002 patients in the delivery cohort, 140 (7.0%) received a COVID-19 vaccine during pregnancy, and 212 (10.6%) experienced a COVID-19 infection during pregnancy. The median gestational age at first vaccination was 32 weeks (range, 13 6/7–40 4/7 weeks), and patients vaccinated during pregnancy were less likely than unvaccinated patients to experience COVID-19 infection before delivery (2/140 [1.4%] vs 210/1862 [11.3%]; P<.001). No maternal COVID-19 infection occurred after the vaccination of pregnant patients. Factors significantly associated with increased likelihood of vaccination in a multivariable logistic regression model included older age, higher level of maternal education, being a non-smoker, use of infertility treatment for the current pregnancy, and lower gravidity. Compared with unvaccinated patients, no significant difference in the composite adverse outcome (7/140 [5.0%] vs 91/1862 [4.9%]; P=.95) or other maternal or neonatal complications, including thromboembolic events and preterm birth, was observed in vaccinated patients. **Conclusion:** In this birth cohort, vaccinated pregnant women were less likely than unvaccinated pregnant patients to experience COVID-19 infection, and COVID-19 vaccination during pregnancy was not associated with increased pregnancy or delivery complications. The cohort was skewed toward late pregnancy vaccination, and thus, findings may not be generalizable to vaccination during early pregnancy.

3- Golan et al. (16 septembre 2021) COVID-19 mRNA Vaccination in Lactation: Assessment of adverse events and vaccine related antibodies in mother-infant dyads

Vaccin(s): Pfizer-BioNTech (n=27 femmes allaitantes), Moderna (n=21 femmes allaitantes). **Results:** No severe maternal or infant adverse events were reported in this cohort. Two mothers and two infants were diagnosed with COVID-19 during the study period. PEGylated proteins, were not found at significant levels in milk after vaccination.

After vaccination, levels of anti-SARS-CoV-2 IgG and IgM significantly increased in maternal plasma and there was significant transfer of anti-SARS-CoV-2-Receptor Binding Domain (anti-RBD) IgA and IgG antibodies to milk. Milk IgA levels after the 2nd dose were negatively associated with infant age. Anti-SARS-CoV-2 IgG antibodies were not detected in the plasma of infants whose mothers were vaccinated during lactation. **Conclusion:** COVID-19 mRNA vaccines generate robust immune responses in plasma and milk of lactating individuals without severe adverse events reported.

4- Kharbanda et al. (08 septembre 2021) Spontaneous Abortion Following COVID-19 Vaccination During Pregnancy
Vaccin(s): Pfizer-BioNTech (n=8225 femmes enceintes), Moderna (n=6 327 femmes enceintes), Janssen (n=527 femmes enceintes) **Results:** Of 105 446 unique pregnancies, 13 160 spontaneous abortions and 92 286 ongoing pregnancies were identified. Overall, 7.8% of women received 1 or more BNT162b2 (Pfizer-BioNTech) vaccines; 6.0% received 1 or more mRNA-1273 (Moderna) vaccines; and 0.5% received an Ad26.COV.2.S (Janssen) vaccine during pregnancy and before 20 weeks' gestation. The proportion of women aged 35 through 49 years with spontaneous abortions was higher (38.7%) than with ongoing pregnancies (22.3%). A COVID-19 vaccine was received within 28 days prior to an index date among 8.0% of ongoing pregnancy periods vs 8.6% of spontaneous abortions (Table 1). Spontaneous abortions did not have an increased odds of exposure to a COVID-19 vaccination in the prior 28 days compared with ongoing pregnancies (adjusted odds ratio, 1.02; 95% CI, 0.96-1.08). Results were consistent for mRNA-1273 and BNT162b2 and by gestational age group (Table 2). **Conclusion:** Among women with spontaneous abortions, the odds of COVID-19 vaccine exposure were not increased in the prior 28 days compared with women with ongoing pregnancies. Strengths of this surveillance include the availability of a multisite diverse population with robust data capture. Several limitations should be noted. First, gestational age of spontaneous abortions and ongoing pregnancies were not chart confirmed; pregnancy dating may be inaccurate early in pregnancy. Second, although vaccination status was identified using multiple data sources, the COVID-19 vaccine rollout has been complex and some vaccines may have been missed, potentially biasing findings to the null. Third, data on important confounders, such as prior pregnancy history, were not available. Fourth, it was not possible to assess risks specific to the Ad26.COV.2.S vaccine given the small number of exposures. Despite limitations, these data can be used to inform vaccine recommendations and to counsel patients.

5- Rose et al. (08 septembre 2021) Receipt of mRNA Covid-19 Vaccines and Risk of Spontaneous Abortion
Vaccin(s): Pfizer-BioNTech (n=1294 femmes enceintes), Moderna (n=1162 femmes enceintes). **Results:** (…) As compared with data from two historical cohorts that represent the lower and upper ranges of spontaneous-abortion risk,2,4 the cumulative risks of spontaneous abortion from our primary and sensitivity analyses were within the expected risk range (…). **Conclusion:** (…) our findings suggest that the risk of spontaneous abortion after mRNA Covid-19 vaccination either before conception or during pregnancy is consistent with the expected risk of spontaneous abortion; these findings add to the accumulating evidence about the safety of mRNA Covid-19 vaccination in pregnancy.

6- Bennett et al. (22 août 2021) Newly diagnosed immune thrombocytopenia in a pregnant patient after coronavirus disease 2019 vaccination
Vaccin(s): Moderna (n=1 femme enceinte) **Results:** We report a case of immune thrombocytopenia in the first trimester, which occurred 13 days after initiating the COVID-19 vaccination series. Thorough evaluation, including hematology consultation, established the diagnosis. High-dose oral corticosteroids were started, and she was discharged home with significant improvement in platelet count on her fourth day of hospitalization with no subsequent complications. **Conclusion:** To conclude, in this case report, we describe a case of ITP following COVID-19 vaccination in a pregnant patient in the first trimester, with resolved symptoms following treatment with oral corticosteroids. At present, a causal relationship between COVID-19 vaccination and ITP has not been established, but providers must remain vigilant to infrequent complications. Nonetheless, we advocate that the benefits of COVID-19 vaccination outweigh the risks of SARS-CoV-2 infection during pregnancy.

7- Trostle et al. (16 août 2021) COVID-19 vaccination in pregnancy: early experience from a single institution
Vaccin(s): Pfizer-BioNTech (n=332 femmes enceintes), Moderna (n=92 femmes enceintes) **Results:** We identified 424 pregnant women who received an mRNA vaccination. Of those, 348 (82.1%) received both doses and 76 (17.9%) received only 1 dose. The maternal characteristics and vaccination information are shown in Table 1. Of the included

women, 4.9% had a history of a confirmed COVID-19 diagnosis before vaccination. After vaccination, no patient in our cohort was diagnosed with COVID-19. In terms of the pregnancy outcomes, 9 women had spontaneous abortions, 3 terminated their pregnancies, and 327 have ongoing pregnancies. Of the women included, 85 delivered liveborn infants. There were no stillbirths in our population. Of the 9 spontaneous abortions, 8 occurred during the first trimester at a range of 6 to 13 weeks' gestation. There was 1 second trimester loss. The rate of spontaneous abortion among women vaccinated in the first trimester was 6.5%. The 327 women with ongoing pregnancies have been followed for a median of 4.6 weeks (range, 0-17 weeks) following their most recent dose. A total of 113 (34.6%) women, initiated vaccination during the first trimester, 178 (54.4%) initiated vaccination during the second trimester, and 36 (11.0%) during the third trimester. Following the vaccination, 2 fetuses (0.6%) developed intrauterine growth restriction, whereas 5 (1.5%) were diagnosed with anomalies. Outcomes for the 85 women who delivered are shown in Table 2. Of the women who delivered, 18.8% were diagnosed with a hypertensive disorder of pregnancy. The rate of preterm birth was 5.9%. One preterm delivery was medically indicated, whereas the remaining 3 were spontaneous. A total of 15.3% of neonates required admission to the neonatal intensive care unit (NICU). Of the NICU admissions, 61.5% were because of hypoglycemia or an evaluation for sepsis. Other reasons for admission included prematurity, hypothermia, and transient tachypnea of the newborn. Of all the neonates, 12.2% were small for gestational age (SGA) per the World Health Organization standards. **Conclusion:** There were no stillbirths. Our 6.5% rate of spontaneous abortion is within the expected rate of 10%,3 and our preterm birth rate of 5.9% is below the national average of 9.5%.4 Our rate of pregnancy-related hypertensive disorders is higher than our baseline institutional rate of 9.5%, however, this may be because of the underlying characteristics of our study population or skewing of our small sample size. Our 12.2% rate of SGA neonates is near the expected value based on the definition that 10% of neonates will be SGA at birth.

8- Blakeway et al. (10 août 2021) COVID-19 Vaccination During Pregnancy: Coverage and Safety

Vaccin(s): Pfizer-BioNTech (n=110 femmes enceintes), Moderna (n=-18 femmes enceintes), AstraZeneca (n=13 femmes enceintes). **Results:** Data were available for 1328 pregnant women of whom 141 received at least one dose of vaccine before giving birth and 1187 women who did not; 85.8% of those vaccinated received their vaccine in the third trimester and 14.2% in the second trimester. Of those vaccinated, 128 (90.8%) received an mRNA vaccine and 13 (9.2%) a viral vector vaccine. There was evidence of reduced vaccine uptake in younger women (P=0.002), those with high levels of deprivation (i.e., fifth quintile of Index of Multiple Deprivation, P=0.008) and women of Afro-Caribbean or Asian ethnicity, compared to Caucasian ethnicity (P<0.001). Women with pre-pregnancy diabetes had increased vaccine uptake (P=0.008). In the multivariable model adjusting for variables that had a significant effect according to the univariable analysis, fifth deprivation quintile (most deprived) was significantly associated with lower antenatal vaccine uptake (adjusted OR 0.09, 95% CI 0.02-0.39, P=0.002), while pre-pregnancy diabetes was significantly associated with higher antenatal vaccine uptake (adjusted OR 11.1, 95% CI 2.01-81.6, P=0.008). In a propensity score matched cohort, compared with non-vaccinated pregnant women, 133 women who received at least one dose of the COVID-19 vaccine in pregnancy (vs. those unvaccinated) had similar rates of adverse pregnancy outcomes (P>0.05 for all): stillbirth (0.0% vs 0.3%), fetal abnormalities (2.2% vs 2.7%), intrapartum pyrexia (3.7% vs 1.5%), postpartum hemorrhage (9.8% vs 9.5%), cesarean section (30.8% vs. 30.6%), small for gestational age (12.0% vs 15.8%), maternal high dependency unit or intensive care admission (6.0% vs 3.5%) or neonatal intensive care unit admission (5.3% vs 5.4%). Mixed-effects Cox regression showed that vaccination was not significantly associated with birth <40 weeks' gestation (hazard ratio 0.93, 95% CI 0.71-1.23, P=0.630). **Conclusion:** Of pregnant women eligible for COVID-19 vaccination, less than one third accepted COVID-19 vaccination during pregnancy and they experienced similar pregnancy outcomes. This study contributes to the body of evidence that having COVID-19 vaccination in pregnancy does not alter perinatal outcomes. Clear communication to improve awareness among pregnant women and healthcare professionals on vaccine safety is needed, alongside strategies to address vaccine hesitancy. This includes post-vaccination surveillance to gather further data on pregnancy outcomes, particularly after first trimester vaccination, as well as long-term infant follow-up.

9- Peretz et al (09 août 2021) Short-term outcome of pregnant women vaccinated with BNT162b2 mRNA COVID-19 vaccine

Vaccin(s): Pfizer-BioNTech (n=390 femmes enceintes) **Results:** The rates of rash, fever and severe fatigue following vaccination among pregnant women were comparable to those in non-pregnant women. Myalgia, arthralgia and headache were significantly less common among pregnant women after each dose, local pain or swelling and axillary lymphadenopathy were significantly less common among pregnant women after the first and second doses, respectively, while paresthesia was significantly more common among the pregnant population after the second dose. Among pregnant women, there were no significant differences in the rates of side effects according to whether the vaccine was administered during the first, second or third trimester of pregnancy, except for local pain/swelling, which was significantly less common after the first dose when administered during the third trimester, and uterine contractions, which were significantly more common after the second dose when administered during the third trimester (…) **Conclusion:** The adverse-effect profile and short-term obstetric and neonatal outcomes among pregnant women who were vaccinated with the BNT162b2 vaccine at any stage of pregnancy do not indicate any safety concerns.

10- Zauche et al. (09 août 2021) Receipt of mRNA COVID-19 vaccines preconception and during pregnancy and risk of self-reported spontaneous abortions, CDC v-safe COVID-19 Vaccine Pregnancy Registry 2020-21

Vaccin(s): Pfizer-BioNTech (n=1294 femmes enceintes), Moderna (n=1294 femmes enceintes) **Results:** Among 2,456 pregnant persons who received an mRNA COVID-19 vaccine preconception or prior to 20 weeks' gestation, the cumulative risk of SAB from 6–19 weeks' gestation was 14.1% (95% CI: 12.1, 16.1%). Using direct age standardization to the selected reference population, the age-standardized cumulative risk of SAB was 12.8% (95% CI: 10.8–14.8%). **Conclusions:** When compared to the expected range of SABs in recognized pregnancies, these data suggest receipt of an mRNA COVID-19 vaccine preconception or during pregnancy is not associated with an increased risk of SAB. These findings add to accumulating evidence that mRNA COVID-19 vaccines during pregnancy are safe.

11- Kachikis et al. (02 août 2021) Short-term Reactions Among Pregnant and Lactating Individuals in the First Wave of the COVID-19 Vaccine Rollout

Vaccin(s): Pfizer-BioNTech (n=4777 femmes enceintes, n=4156 femmes allaitantes), Moderna (n=2970 femmes enceintes, n=2596 femmes allaitantes), Janssen (n=23 femmes enceintes, n=23 femmes allaitantes). **Results:** Among all participants, 17 005 individuals (97.0%) reported any postvaccination reactions after the first dose, with the most common reactions being pain at injection site (16 019 individuals [91.4%]) and fatigue (5489 individuals [31.3%]). The frequency of reactions after the second dose was higher than after the first dose (eg, 10 399 individuals [69.2%] with fatigue after the second dose), but with similar distribution of symptoms (Figure). Odds of several reactions were statistically significantly decreased among individuals who were pregnant (eg, fever after BNT162b2 dose 2: OR, 0.44; 95% CI, 0.38-0.52; P < .001 and after mRNA-1273 dose 2: OR, 0.48; 95% CI, 0.40-0.57; P < .001) compared with individuals who were neither pregnant nor lactating (Figure). (…) Participants seeking medical care after vaccination included 100 individuals (0.6%) after dose 1 (including 50 pregnant individuals) and 221 individuals (1.5%) after dose 2 (including 156 pregnant individuals) (…) Among pregnant participants, any obstetrical symptoms were reported by 346 of 7809 individuals (4.4%) after the first dose and 484 of 6444 individuals (7.5%) after the second dose. **Conclusion:** This large prospective cohort study found that COVID-19 vaccines were well-tolerated among individuals who were pregnant, lactating, or planning pregnancy. A strength of this study was the ability to compare vaccine reactions and perceptions in pregnant and lactating individuals vs individuals of similar age and fertility intentions who were neither pregnant nor lactating. Vaccination reactions for day 1 were similar among groups and comparable with findings among pregnant individuals previously reported.[6] All groups reported increased reactions following dose 2 of BNT162b2 and mRNA-1273 vaccines.

12- Mendes-de-Almeida et al. (15 juillet 2021) Intracerebral hemorrhage associated with vaccine-induced thrombotic thrombocytopenia following ChAdOx1 nCOVID-19 vaccine in a pregnant woman

Vaccin(s): AstraZeneca (n=1 femme enceinte) **Results:** Herein we present a fatal case of a 35 years-old pregnant woman who developed intracerebral hemorrhage in the left temporal lobe associated with VITT twelve days after the off-label ChAdOx1nCOVID-19 vaccination and we show the characterization of hemostatic profile. A 35-years-old white pregnant woman at 23 weeks gestation was in prenatal follow-up with normal platelet counts and controlled

hypothyroidism due to Hashimoto's disease. She received the first dose of the ChAdOx1 nCov-19 vaccine in late April 2021 (day 0). The next day, she reported having minor symptoms (malaise, chills, tremors, and "cold feeling"). On day two, she presented a generalized skin rash on her legs, abdomen, and back with spontaneous resolution. Prenatal exams on day three identified urinary tract infection caused by Morganella morganii treated with trimethoprim-sulfamethoxazole and 148,000/mm3 platelets at the routine complete blood count. On day seven, she presented headache, nausea, nonspecific malaise, polaciuria, pain in the lower limbs and hips. Despite having 121,000 /mm3 platelets, she received analgesics and was discharged from the obstetric emergency room. On the following days, she maintained headache and bilateral leg pain, partially responsive to dipyrone. On day 11, she reported a severe headache located in the left maxillary region, and on day 12, she was admitted with 33,000 /mm3 platelets and an excruciating headache. During the computed tomography (CT) exam, she became comatose and underwent endotracheal intubation, which precluded the realization of CT cerebral venography, confirming the suspicion of central venous sinus thrombosis. Brain CT showed a large acute intraparenchymal hematoma in the temporal lobe, insula, and temporoparietal transition of the left cerebral hemisphere measuring approximately 10.1 x 5.4 x 5.5 cm. The hematoma was surrounded by vasogenic edema with midline shift to the right, herniation of the uncus, marked compressive effect on the midbrain, and subtotal collapse of the supratentorial ventricular system (Figure 1B). The patient received platelet concentrate transfusion and underwent urgent neurosurgery for hematoma drainage and decompressive craniectomy. After receiving critical care procedures, obstetric ultrasound detected fetal death. There were no platelet clumps, signs of erythrocyte fragmentation, or blast cells on blood film. She received 80 g (1g/Kg) immunoglobulin and 2g fibrinogen without success. The patient died on day seventeen (after vaccination) with refractory intracranial hypertension despite all pressure control measures (…). **Conclusion:** This case report draws attention to this possible severe vaccine side effect among pregnant women and the challenges related to an early diagnosis. When symptomatic, pregnant women experience difficulties diagnosing VITT due to avoidance of screening methods involving radiation and presenting features possibly related to pregnancy, such as thrombocytopenia. The presence of persistent headache and thrombocytopenia within 30 days of vaccination should raise the suspicion of VITT. D-dimer, fibrinogen, and image exams help to guide prompt treatment, preventing a rapidly progressive disease5. At least five countries had instituted limitations primarily based on age on which patients should receive the ChAdOx1 nCoV-19 vaccine2, and Brazil recently temporarily suspended the administration of this vaccine in pregnant women (…).

2- Shimabukuro et al. (17 juin 2021) Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons
Vaccin(s): Pfizer-BioNTech (n=19 252 femmes enceintes), Moderna (n=16 439 femmes enceintes). **Results:** Although not directly comparable, calculated proportions of adverse pregnancy and neonatal outcomes in persons vaccinated against Covid-19 who had a completed pregnancy were similar to incidences reported in studies involving pregnant women that were conducted before the Covid-19 pandemic. Among 221 pregnancy-related adverse events reported to the VAERS, the most frequently reported event was spontaneous abortion (46 cases). **Conclusion:** Preliminary findings did not show obvious safety signals among pregnant persons who received mRNA Covid-19 vaccines. However, more longitudinal follow-up, including follow-up of large numbers of women vaccinated earlier in pregnancy, is necessary to inform maternal, pregnancy, and infant outcomes.

13- Mattar et al. (25 mai 2021) Addressing anti-syncytin antibody levels, and fertility and breastfeeding concerns, following BNT162B2 COVID-19 mRNA vaccination
Vaccin(s): Pfizer-BioNTech (n=2 femmes enceintes et 5 femmes allaitantes) **Results:** Fifteen consented participants (mean age 40.4 years, various ethnicities) who received at least one dose of BNT162B2, including five breast-feeding women and two women who were inadvertently vaccinated in early pregnancy, were recruited (…) Vaccine recipients demonstrated strong SARS-CoV-2 neutralising activity by at least four weeks after the first dose (n=15), including the two pregnant women. None had placental anti-syncytin-1 binding antibodies at either time-point following vaccination. **Conclusion:** BNT162B2-vaccinated women did not transmit vaccine mRNA to breast milk, and did not produce a concurrent humoral response to syncytin-1, suggesting that cross-reactivity to syncytin-1 on the developing trophoblast, or other adverse effects in the breast-fed infant from vaccine mRNA ingestion, are unlikely.

14- Golan et al. (08 mars 2021) COVID-19 mRNA vaccine is not detected in human milk

Vaccin(s): Pfizer-BioNTech (n=5 femmes allaitantes), Moderna (n=1 femme allaitante) **Results:** Post-vaccine human milk samples were collected from six individuals 4-48 hours after administration, 5 vaccinated with BNT162b2 (Pfizer) and 1 individual with mRNA-1273 (Moderna) vaccine. We first optimized our RT-qPCR by isolating the residual vaccine mRNA from vials, showing that our assay is capable to detect up to 1.5 pico grams of the mRNA-1273 vaccine cDNA and up to 0.195 pico grams of the BNT162b2 vaccine. We next used pre-vaccine milk samples and spiked-in the mRNA-1273 vaccine (12 and 0.12ng/ul vaccine mRNA). RNA was extracted from the supernatant and fat layer of these spiked-in milk samples. We were able to detect the spiked-in vaccine mRNA in these samples, with higher levels of vaccine mRNA in fat layer fraction. We next analyzed 12 post-vaccine samples (4-48 hours post vaccine, Table 1) and found that none of the samples from vaccinated lactating mothers showed detectable levels of vaccine mRNA in milk fat layer or milk supernatant at any time point. **Conclusion:** We show here that the mRNA from anti-COVID vaccines is not detected in human breast milk samples collected 4-48 hours post-vaccine. These results strengthen the recommendation of ABM and WHO that lactating individuals who receive the anti-COVID-19 mRNA-based vaccine should continue to breastfeed their infants uninterrupted. Clinical data from larger populations need to be collected and analyzed to better estimate the effect of these vaccines on lactation outcomes.

15- FDA Briefing document Janssen Ad26.COV2.S Vaccine for the Prevention of COVID-19 (26 février 2021)

Vaccin(s): Janssen (n=4 femmes enceintes) **Résumé:** Eight pregnancies were reported through January 22, 2021 (4 vaccine, 4 placebo). In 7 participants (3 vaccine, 4 placebo) vaccination was within 30 days after last menstrual period (LMP) and in 1 vaccine recipient vaccination was prior to LMP. Unsolicited AEs related to pregnancy include spontaneous abortion (1 vaccine, 0 placebo), incomplete abortion (0 vaccine, 1 placebo), elective abortion (0 vaccine, 2 placebo) and ectopic pregnancy (1 vaccine, 0 placebo). Among participants in the vaccine group, two pregnancies are ongoing with outcomes unknown at this time. A combined developmental and perinatal/postnatal reproductive toxicity study of Ad26.COV2.S in rabbits was submitted to FDA on January 19, 2021. FDA review of this study concluded that Ad26.COV.S given prior to mating and during gestation periods at dose of 1x1011 vp (2 times the human dose) did not have any adverse effects on female reproduction, fetal/embryonal development, or postnatal development.

Revue de littérature

1- Rasmussen et al. Pregnancy, postpartum care, and COVID-19 vaccination in 2021
2- Malinowski et al. (14 mai 2021) Expecto Patronum! Leveraging the Positive Force of COVID-19 Vaccines for Pregnant and Lactating Individuals
3- Brillo et al. (20 avril 2021) COVID-19 vaccination in pregnancy and postpartum
4- Damayanti et al. (21 août 2021) A Literature Review on the Vaccination of COVID-1 in Pregnant and Breastfeeding Women: Effectiveness and Safety
5- Adhikari et al. (08 février 2021) COVID-19 Vaccination in Pregnant and Lactating Women
6- Stattford et al (mai 2021), The Coronavirus disease 2019 vaccine in pregnancy: Risks, benefits, and recommendations
7- Stattford et al (mai 2021), The Coronavirus disease 2019 vaccine in pregnancy: Risks, benefits, and recommendations
8- Rasmussen et al. (mars 2021) Coronavirus disease 2019 (COVID-19) vaccines and pregnancy.
9- Garg et al. (31 juillet 2021) COVID-19 Vaccine in Pregnant and Lactating Women: A Review of Existing Evidence and Practice Guidelines
10- Adhikari et al. (16 mars 2021) COVID-19 Vaccination in Pregnant and Lactating Women
11- Ciapponi et al. (24 septembre 2021) Safety of components and platforms of COVID-19 vaccines considered for use in pregnancy: A rapid review
12- Pramanik et al. (28 mai 2021) A reasoned approach towards administering COVID-19 vaccines to pregnant women
13- Wengian Wang et al. (mai 2021) SARS-CoV-2 Vaccination During Pregnancy: A Complex Decision
14- Sculli et al. (30 juin 2021) COVID-19 vaccination in pregnant and lactating diabetic women
15- Craig et al (10 décembre 2020) Coronavirus disease 2019 vaccines in pregnancy

Issues de grossesse suivies par les instances de santé publique

ASPC

Tableau 1. Nombre et taux de rapports (par 100,000 doses administrées) d'événements indésirables présentant un intérêt à particulier signalés par nom de vaccin (Total) en date du 10 septembre 2021 (n=2 879).

Issues de grossesse	Restriction de la croissance fœtale	5
	Avortement spontané	31
	Sous-total	**36**

ANSM

Pfizer-BioNTech, Moderna et AstraZeneca

Suivi spécifique des effets indésirables rapportés chez les femmes enceintes et allaitantes

Les fausses couches spontanées représentent la majorité des effets indésirables enregistrés dans la BNPV. Les données actuelles ne permettent pas de conclure que ces événements sont liés au vaccin, d'autant que des facteurs de risques étaient associés dans plusieurs cas et qu'il s'agit d'un évènement relativement fréquent en population générale (de 12 à 20% des grossesses selon les études).

Événements déjà sous surveillance

- Évènements thromboemboliques (Pfizer-BioNTech)
- Contractions utérines douloureuses (Pfizer-BioNTech)
- Morts in utero (Pfizer-BioNTech et Moderna)

Recommandations :

International Society of Infectious Disease in Obstetrics and Gynecology (ISIDOG)

- ISIDOG Consensus Guidelines on COVID-19 Vaccination for Women before, during and after Pregnancy (29 juin 2021)

The American College of Obstetricians and Gynecologists (ACOG)

- Vaccinating pregnant and lactating patients against COVID-19.
- Practice advisory; 2021. COVID-19 vaccination considerations for obstetric–gynecologic care.

Centers for Disease Control and Prevention (CDC)

- COVID-19 (coronavirus disease): people with certain medical conditions.
- Information about COVID-19 Vaccines for People who Are Pregnant or Breastfeeding.

Society for Maternal-Fetal Medicine (SMFM)

- Society for Maternal-Fetal Medicine (SMFM) Statement: SARS-Co-V-2 Vaccination in pregnancy.
- COVID-19 Vaccination if you are pregnant or breastfeeding
- COVID-19 Vaccination during pregnancy. Get the facts and get vaccinated
- SMFM: Provider Considerations for Engaging in COVID-19 Vaccine Counseling With Pregnant and Lactating Patients

The Society of Obstetricians and Gynaecologists of Canada

- SOGC Statement on COVID-19 Vaccination in Pregnancy

Royal College of Obstetricians and Gynaecologists (RCOG)

- Updated advice on COVID-19 vaccination in pregnancy and women who are breastfeeding.

Royal Australian and New Zealand College of Obstetricians and Gynaecologists

- COVID-19 Vaccination in Pregnant and Breastfeeding Women

Academy of Breastfeeding Medicine Considerations

- Academy of Breastfeeding Medicine Considerations for COVID-19 vaccination in lactation. ABM Statement.

The European Medicines Agency

- COVID-19 mRNA Vaccine (Nucleoside-modified)
- EU Regulator Says Pfizer Vaccine Should Be Considered Case by Case for Pregnant Women
- COVID-19 Vaccine Moderna.

John Hopkins University

- The COVID-19 Vaccine and Pregnancy: What You Need to Know?

UK's Joint Committee of Vaccination and Immunisation (JCVI)

- Advice on priority groups for COVID-19 vaccination, 30 December 2020

World Health organization (WHO)

- The Moderna COVID-19 (mRNA-1273) vaccine: what you need to know
- The Pfizer BioNTech (BNT162b2) COVID-19 vaccine: What you need to know
- Update on WHO Interim recommendations on COVID-19 vaccination of pregnant and lactating women

Table. Recommendations for Pregnant or Lactating Individuals Regarding Use of Pfizer-BioNTech and Moderna COVID-19 Vaccines[a]

Table. Recommendations for Pregnant or Lactating Individuals Regarding Use of Pfizer-BioNTech and Moderna COVID-19 Vaccines[a]

Pregnancy	Lactation
US Food and Drug Administration (FDA)	
• Available data on COVID-19 vaccine administered to pregnant individuals are insufficient to inform vaccine-associated risks in pregnancy	• Data are not available to assess the effects of COVID-19 vaccine on the breastfed infant or on milk production/excretion
Centers for Disease Control and Prevention (CDC)	
• People who are pregnant and part of a group recommended to receive COVID-19 vaccination, such as health care personnel, may choose to be vaccinated • A conversation between pregnant patients and their clinicians may help them decide whether to receive a vaccine that has been authorized for use under EUA • A conversation with a clinician may be helpful but is not required prior to vaccination • Routine testing for pregnancy before COVID-19 vaccination is not recommended • Persons who are trying to become pregnant do not need to avoid pregnancy after receiving an mRNA COVID-19 vaccine	• There are no data on the safety of COVID-19 vaccines in lactating mothers or on the effects of mRNA vaccines on the breastfed infant or on milk production/excretion • mRNA vaccines are not thought to be a risk to the breastfeeding infant • People who are breastfeeding and are part of a group recommended to receive a COVID-19 vaccine, such as health care personnel, may choose to be vaccinated
American College of Obstetricians and Gynecologists (ACOG)	
• ACOG recommends that COVID-19 vaccines should not be withheld from pregnant individuals who meet criteria for vaccination based on ACIP-recommended priority groups • While a conversation with a clinician may be helpful, it should not be required prior to vaccination because this may cause unnecessary barriers to access • Pregnancy testing should not be a requirement prior to receiving any EUA-approved COVID-19 vaccine • Pregnant patients who decline vaccination should be supported in their decision	• ACOG recommends COVID-19 vaccines be offered to lactating individuals similar to nonlactating individuals when they meet criteria for receipt of the vaccine based on prioritization groups outlined by the ACIP • While lactating mothers were not included in most clinical trials, COVID-19 vaccines should not be withheld from lactating individuals who otherwise meet criteria for vaccination • Theoretical concerns regarding the safety of vaccinating lactating individuals do not outweigh the potential benefits of receiving the vaccine; there is no need to avoid initiation or discontinue breastfeeding in patients who receive a COVID-19 vaccine
Society for Maternal-Fetal Medicine (SMFM)	
• SMFM strongly recommends that pregnant people have access to COVID-19 vaccines and that they discuss potential benefits and unknown risks with their clinicians regarding receipt of vaccine • Counseling should also include the theoretical risk of harm to the fetus; the risk from mRNA vaccines is thought to be low due to the expected degradation of mRNA in the circulation • Individual decision-making needs to balance theoretical risks with risks associated with delayed vaccination and possible maternal SARS-CoV-2 infection	• Vaccination is recommended for lactating persons • Counseling should balance the lack of data on vaccine safety and a person's individual risk for infection and severe disease • The theoretical risks regarding the safety of vaccinating lactating people do not outweigh the potential benefits of the vaccine

Abbreviations: ACIP, Advisory Committee on Immunization Practices; EUA, Emergency Use Authorization.

[a] Sources: FDA (Pfizer-BioNTech) (Moderna); CDC; ACOG; SMFM.

Source: Rasmussen et a. (08 février 2021). Pregnancy, Postpartum Care, and COVID-19 Vaccination in 2021

Table II Vaccine recommendations for women who are pregnant or breastfeeding.

	General population	Categories at risk of exposure/ infection	Comorbidities—Categories with clinical history of HIV (independent of pregnancy)	Comorbidities (any) and pregnancy	Contraindications	Recommended waiting time for pregnancy after vaccine administration (Months)	Breastfeeding women
WHO[1]	NR	MBC	MBC	–	History of severe allergic reaction/ hypersensitivity to vaccine components	NA	–
CDC[1]	NR	R	R	R	History of severe allergic reaction/ hypersensitivity to vaccine components	NA	MBC (no risk expected)
EMA	NR	MBC	MBC (immunocompromised)	–	History of severe allergic reaction/ hypersensitivity to vaccine components	NA	MBC (no risk expected)
JCVI	NR	MBC	MBC	MBC	History of severe allergic reaction/ hypersensitivity to vaccine components	NA	MBC
Pfizer	R	R	R	–	History of severe allergic reaction/ hypersensitivity to vaccine components	NA	R
Moderna	NR	MBC	MBC	–	History of severe allergic reaction/ hypersensitivity to vaccine components	NA	unknown
AstraZeneca	NR	MBC	MBC	–	History of severe allergic reaction/ hypersensitivity to vaccine components	NA	unknown

R, recommended; NR, not recommended; MBC, may be considered; NA, non-applicable; -, no advice given.
[1] Advice for mRNA vaccines only.

Source: Ory et al. (16 avril 2021) Joint IFFS/ESHRE statement on COVID-19 vaccination for pregnant women and those considering pregnancy

Conclusion

- Les données disponibles sur l'efficacité et la sécurité vaccinale sont actuellement insuffisantes et ne permettent pas une évaluation précise de l'ensemble des risques et bénéfices de la vaccination des femmes enceintes ou allaitantes.

- Actuellement, seules deux études ont rapporté des données sur l'efficacité vaccinale. Ces études suggèrent qu'un schéma vaccinal complet assurerait une haute protection contre les infections, les infections symptomatiques et diminuerait le risque d'hospitalisation. L'efficacité vaccinale serait comparable à celle de la population générale. Il est à noter que seule l'efficacité du vaccin de Pfizer-BioNTech a été rapportée dans ces deux études qui ont été menées dans la même région du monde (Israël). Des données supplémentaires incluant des données sur l'efficacité du vaccin de Moderna, d'AstraZeneca et de Janssen sont nécessaires. L'impact des nouveaux variants tel que le variant Delta sur l'efficacité vaccinale des femmes enceintes et allaitantes devra également être évalué. D'autres études sont également nécessaires afin de mieux caractériser la dynamique de l'efficacité du vaccin tout au long de la grossesse, la relation entre le moment de la vaccination et la protection du nourrisson après la naissance ainsi que les résultats de sécurité liés à la grossesse et non à la grossesse.

- Plusieurs études rapportent que les vaccins à ARNm (Pfizer-BioNTech et Moderna) induisent une forte immunité humorale contre le SRAS-CoV-2 et que cette immunité peut être transmise de la mère à l'enfant pendant la grossesse ou lors de l'allaitement.

- Sur la base d'information limitée, la vaccination des femmes enceintes ou allaitantes avec des vaccins à ARNm semblent sécuritaire et les taux de complications maternelles ou néonatales, incluant les avortements spontanés et les naissances prématurées, sont comparables à ceux de femmes enceintes non vaccinées. Un cas de thrombocytopénie immune a cependant été rapporté suite à l'administration du vaccin de Moderna chez une femme enceinte. L'administration du vaccin d'AstraZeneca chez les femmes enceintes ne semble cependant pas recommandé au Brésil après le décès d'une femme enceinte suite à la vaccination avec ce vaccin. Finalement, l'absence de détection d'ARNm dans le lait maternel de femmes vaccinées avec les vaccins de Pfizer-BioNTech ou de Moderna renforce les recommandations selon lesquelles les femmes qui allaitent et qui reçoivent un vaccin à ARNm anti-COVID-19, devraient continuer à allaiter leur nourrisson.

INSPQ
INSTITUT NATIONAL DE SANTÉ PUBLIQUE DU QUÉBEC
Centre d'expertise et de référence

Vaccination contre la COVID-19 et la grossesse

Chantal Sauvageau, MD, M.Sc, FRCP(C)
Gisèle Trudeau, MD, M.Sc

30 avril 2021

Révision 13 décembre 2021

www.inspq.qc.ca

Institut national de santé publique Québec

Déclarations

Chantal Sauvageau

Médecin spécialiste en santé publique et médecine préventive

- Institut national de santé publique du Québec (INSPQ) et
- Direction régionale de santé publique de la Capitale-Nationale

Professeure agrégée, Faculté de médecine, Université Laval

Chercheure, Centre de recherche du CHU de Québec-Université Laval

Membre actif du Comité sur l'Immunisation du Québec

Gisèle Trudeau

Médecin-conseil à l'Institut national de santé publique du Québec (INSPQ)

Geneviève Boily (mise à jour décembre 2021)

Conseillère scientifique à l'Institut national de santé publique du Québec (INSPQ)

Aucun lien avec les compagnies développant des vaccins

Institut national de santé publique Québec

Objectifs

Que les professionnels de la santé soient en mesure de:

- Répondre aux questions sur la vaccination contre la COVID-19 chez la femme enceinte, celle qui allaite ou qui désire devenir enceinte

Institut national de santé publique Québec

Plan de la présentation

- Épidémiologie et fardeau de la COVID-19 chez la femme enceinte
- Données disponibles sur la vaccination contre la COVID-19 chez la femme enceinte
- Recommandations du Comité sur l'immunisation du Québec
- Points à discuter avec la femme enceinte en vue d'une décision éclairée
- Outils d'information disponibles

Institut national de santé publique Québec

Historique des recommandations de vaccination de la femme enceinte

- **Début de pandémie**: femmes enceintes pas considérées à risque particulier
- **23 décembre 2020**: Avis du CIQ « la vaccination **peut être offerte** aux femmes enceintes, particulièrement en présence de facteurs de risque ou d'exposition élevée (ex. trav. de la santé)
- **Hiver 2021**: études montrent un risque accru pour la femme enceinte. La grossesse devient une condition qui augmente le risque de maladie grave
- **27 avril 2021**: MAJ avis du CIQ « la vaccination **devrait être offerte** à une femme enceinte »
- **Été 2021**: de plus en plus de données disponibles sur l'immunogénicité et l'innocuité des vaccins COVID-19 chez les femmes enceintes
- **3 septembre 2021**: MAJ avis du CIQ « **la vaccination devrait être recommandée à une femme enceinte ou qui allaite** »

Sources: INSPQ https://www.inspq.qc.ca/sites/default/files/publications/3093-utilisation-vaccin-arn-messager-covid-19.pdf
CCNI: https://www.canada.ca/fr/sante-publique/services/immunisation/comite-consultatif-national-immunisation-ccni/recommandations-utilisation-vaccins-covid-19.html#a6
INESSS: https://www.inesss.qc.ca/covid-19/traitements-specifiques-a-la-covid-19/grossesse-allaitement.html

Institut national de santé publique Québec

Épidémiologie et fardeau de la COVID-19 chez la femme enceinte

www.inspq.qc.ca

Institut national de santé publique Québec

Présentation clinique de la COVID-19 chez la femme enceinte

- Le plus souvent, symptômes légers ou modérés ou asymptomatique
  - Possible biais: représentation de l'état de la femme à l'accouchement et pas l'état de toutes les femmes à n'importe quel moment de la grossesse
- Infection plus fréquente aux 2e et 3e trimestres
  - Possible biais: dépistage non-systématique aux 1er et 2e trimestre versus dépistage systématique à l'accouchement
- Présentation sévère de l'infection (6 à 21%)
  - i.e. dyspnée, hypoxémie, détresse respiratoire progressive
  - Surtout plus tardivement durant la grossesse
  - Pourrait être plus fréquente avec le variant delta

Sources: Adhikari (2020; 2021); Lokken; Metz; Mullins, Villar; Vousden; Wei; Woodworth; Zambrano; Chmielewska; Mark; Money; INESSS, INSPQ, Karimi, Allotey, Delahoy, Figueiro-Filho, Knight

COVID-19 et grossesse

- Facteurs de risque d'une présentation sévère chez femme enceinte:
  - Obésité (IMC ≥30)
  - Âge ≥35 ans
  - Comorbidité avant la grossesse (hypertension artérielle, diabète)

Sources: CIQ; Allotey; Lokken; Chmielewska, Karimi, Ko, Metz, Villar, Vousden, Wei, Figuerio-Filho, Knight, Walter

Institut national de santé publique Québec

Comparaison avec la femme infectée mais non enceinte

- Risque accru de complications de la COVID-19 chez la femme enceinte infectée (vs femme non enceinte infectée):
  - Hospitalisation
  - Admission aux soins intensifs (2 à 7%)
  - Ventilation mécanique (1 à 5%)
  - Décès
- Parcours généralement plus favorable pour infection asymptomatique ou présentation légère/modérée

Sources: Allotey; Badr; Lokken; Martinez-Portilla; Zambrano, INESSS, Walter

Institut national de santé publique Québec

Comparaison avec la femme enceinte n'ayant pas la COVID-19

- Risque accru de complications périnatales chez la **femme** enceinte infectée (vs femme enceinte non infectée) :
  - Prééclampsie/éclampsie
  - Thromboembolie
  - Admission aux soins intensifs
  - Mortalité maternelle
  - Césarienne
  - Accouchement prématuré (< 37 sem.)
- Risque accru surtout pour les présentations sévères
  - Risque accru de prééclampsie même pour les infections asymptomatiques

Sources: Allotey; Badr; Lokken; Martinez-Portilla; Zambrano; Ko; Mark; Villar; Vousden; Metz; Wei; INESSS, Chmielewska, Knight, INSPQ, Walter

Institut national de santé publique Québec

Comparaison avec la femme enceinte n'ayant pas la COVID-19

- Risque de complications **néonatales** (femme enceinte infectée vs bébé femme enceinte non infectée)
  - Faible poids à la naissance
  - Admission aux soins intensifs néonataux
  - Mortinaissance
  - Risque accru surtout pour les présentations sévères chez la mère
- Risque de mortinaissance accru avec la présence du variant delta
- Transmission verticale rare (2 à 10%)
- Pas de risque accru de complications dans le futur pour le nouveau-né
- Allaitement maternel: pas associé à un risque accru d'infection

Sources: Allotey; Adhikari; Jering; Lokken; Metz; Mullins, Villar; Vousden; Walker; Woodworth; Mark; Money; Tolu; Fenizia; Flaherman; Knight; Kotlyar, Wei, Tolu, Salvatore, Raschetti, Centeno-Tablante, DeSisto

Institut national de santé publique Québec

Surveillance canadienne de la COVID-19 pendant la grossesse (CANCOVID-Preg)

Entre le 1er mars 2020 et le 31 mars 2021

- Taux de COVID-19 plus bas chez les femmes enceintes que chez toutes les femmes âgées de 20 à 49 ans dans la population générale
- Chez 1334 femmes enceintes canadiennes ayant la COVID-19 pour lesquelles l'information était disponible :
  - 7% (n=95) hospitalisées en raison de la COVID, 2,5% (n=38) admises aux SI
  - En comparaison, chez les femmes infectées non enceintes âgées de 18 à 45 ans: hospitalisation 1,5% et SI: 0,25%
- Naissances prématurées (12,9%), admission aux soins intensifs néonataux (15,2%)
- Taux de mortinaissance (10,6 pour 100 000) vs 5,4 pour 100 000 dans la population générale

Sources: Money, CANCOVID-Preg, Rapport no 4, 3 juin 2021

Institut national de santé publique Québec

Données préliminaires des femmes enceintes québécoises infectées par le SRAS-CoV-2

Sur 32 235 accouchements dans un des hôpitaux du Québec entre juin 2020 et avril 2021, 978 infections au SRAS-CoV-2 répertoriées

En comparaison des femmes enceintes non infectées, celles ayant eu une infection par le SRAS-CoV-2 avaient:

- Admissions aux soins intensifs et thromboses plus fréquentes
- Césariennes plus fréquentes si infection dans les 10 jours précédant l'accouchement
- Naissances prématurées (moins de 37 sem.) plus fréquentes pour les infections dans les 10 jours précédant l'accouchement
- Mortalité maternelle rare

Source: données partagées par Rachel McKay, INSPQ, 13 décembre 2021 (données de Méd-écho appariées avec le fichier des laboratoires et TSP)

Données disponibles sur la vaccination contre la COVID-19 chez la femme enceinte

www.inspq.qc.ca

Institut national de santé publique Québec

Données de vaccination contre la COVID-19 chez les femmes enceintes

- Au départ, peu de données disponibles sur l'immunogénicité, l'efficacité ou l'innocuité de ces vaccins, les femmes enceintes ayant été exclues des essais cliniques
- Pas de risque connu associé à l'utilisation d'un vaccin non vivant chez les femmes enceintes
  - Les vaccins contre la coqueluche et la grippe sont utilisés pendant la grossesse
  - Pas de raison de penser que ce soit différent avec les vaccins contre la COVID-19, mais pas de données spécifiques
- Études pré-cliniques avec les vaccins chez des animaux rassurantes (pas de tératogénicité) (vaccins COVID-19, Zika)
- Essais cliniques chez les femmes enceintes en cours (Pfizer, Moderna, Janssen)
  - Résultats préliminaires des études avec Pfizer/Moderna: pas de signal concernant la sécurité du vaccin chez les femmes enceintes

Sources: Moderna, monographie; Pfizer, monographie; Kalafat, Shimabukuro

Immunogénicité – femmes enceintes

- Immunité humorale élevée chez les femmes enceintes et allaitantes vaccinées (ARNm)
- Immunogénicité similaire aux femmes non enceintes
- Présence d'anticorps spécifiques au SRAS-Cov-2 dans le lait, sang de cordon ou placenta
- Suggère un transfert immunitaire de la mère à l'enfant pendant la grossesse et durant l'allaitement

Sources: Gray, Baird, Atyeo, Peretz, Charepe, Valcarce, Juncker, Collier, Perl, Douxfils, Beharier, Zdanowski, Gill, Prabhu, Low, Golan

Efficacité vaccinale – femmes enceintes

Deux études en Israël

- Réduit le risque d'infection (EV de 78% à 96%)
- Vaccin très efficace pour les variants circulant au moment de l'étude
  - Contre les infections, incluant les infections asymptomatiques et contre les hospitalisations
  - Efficacité comparable à la population générale

Sources: Goldshtein, Dagan

Données post commercialisation aux États-Unis : innocuité vaccination COVID-19 chez les femmes enceintes

- Étude de réactogénicité, aux États-Unis, vaccins à ARNm, 35 691 femmes enceintes
  - Plus douleur au site d'injection rapportée
  - Moins céphalée, myalgie, fièvre, frisson rapportés
- Sur 827 grossesses complétées
  - 9,4% accouchement prématuré
  - Pas de mortinaissance
- Complications périnatales et néonatales semblables entre les femmes enceintes vaccinées contre la COVID et les femmes enceintes avant la pandémie
- Données préliminaires ne montrent pas de préoccupation particulière quant à la sécurité des vaccins COVID ARNm chez les femmes enceintes

Institut national de santé publique Québec

Sources: CDC-V-safe , 18 oct 2021, Shimabukuro

Données du Québec sur la vaccination des femmes enceintes

En date du 13 décembre 2021, au Québec, environ:

- 29 000 doses administrées à des femmes ayant déclaré être enceintes au moment de la vaccination (certaine sous-estimation)
  - 16 000 1ère doses
  - 13 000 2e doses (incluant quelques 3e doses)

Rapport CV vigie, INSPQ, 14 décembre 2021

Institut national de santé publique Québec

Mise à jour de l'avis du CIQ sur la vaccination COVID-19 et grossesse, 3 septembre 2021

*Le CIQ **recommande la vaccination à une femme enceinte ou qui allaite***

Pour ces femmes, un vaccin à ARNm est à privilégier étant donné la disponibilité de plus de données de sécurité avec ce type de produit

7 décembre 2021: les femmes enceintes sont visées parmi les groupes prioritaires pour lesquels une dose de rappel (3e dose) est recommandée, 6 mois après la deuxième dose

Avis du CIQ sur l'utilisation des vaccins à ARN messager contre la COVID-19, 3 sept. 2021
https://www.inspq.qc.ca/publications/3093-utilisation-des-vaccins-arn-contre-la-covid19
Avis du CIQ sur la dose de rappel chez les adultes, 7 décembre 2021
https://www.inspq.qc.ca/publications/3184-dose-rappel-vaccin-covid19-adultes

Institut national de santé publique Québec

Avis du CIQ: vaccination COVID-19 et grossesse

Avant de se présenter au site de vaccination, la femme enceinte pourra, si elle le désire, choisir de parler avec un professionnel de la santé, par exemple avec son médecin traitant, pour discuter plus spécifiquement de:

- *Son risque personnel d'exposition (maison, travail, communauté)*
- *Son risque personnel de complications (facteurs de risque)*
- *Le risque augmenté de complications du fait d'être enceinte*
- *Avantages potentiels de la vaccination (vaccin très efficace et transfert d'anticorps au bébé)*
- *Données s'accumulant sur la sécurité de la vaccination chez la femme enceinte*

Source: Avis du CIQ sur l'utilisation des vaccins à ARN messager contre la COVID-19, 3 sept. 2021
https://www.inspq.qc.ca/publications/3093-utilisation-des-vaccins-arn-contre-la-covid19

Institut national de santé publique Québec

Avis du CIQ: vaccination COVID-19 et désir de grossesse

- De plus en plus de données observationnelles sont disponibles sur l'immunogénicité et l'innocuité des vaccins contre la COVID chez les femmes enceintes
- CCNI: les personnes qui tentent de devenir enceintes n'ont pas besoin d'éviter la grossesse après l'administration d'un vaccin à ARNm
- SOGC: recommande de procéder à la vaccination et encourage une discussion avec un professionnel de la santé sur les risques et les bénéfices de retarder la grossesse
- CIQ: propose de fournir l'information appropriée sur le peu de données disponibles, mais considère que les bénéfices attendus de la vaccination dépassent les risques potentiels chez les femmes planifiant une grossesse

Sources:
Avis du CIQ sur l'utilisation des vaccins à ARN messager contre la COVID-19 3 sept. 2021
https://www.inspq.qc.ca/publications/3093-utilisation-des-vaccins-arn-contre-la-covid19
CCNI: https://www.canada.ca/fr/sante-publique/services/immunisation/comite-consultatif-national-immunisation-ccni/recommandations-utilisation-vaccins-covid-19.html#ps

Institut national de santé publique Québec

Avis du CIQ Vaccination COVID-19 et allaitement

Vaccin et femmes qui allaitent:

- Ces femmes ont été exclues des essais cliniques initiaux sur les vaccins contre la COVID-19
- Les données sur l'excrétion des vaccins à ARNm dans le lait maternel et sur les risques associés pour le bébé allaité sont rassurantes
- Pas de risque connu associé à l'utilisation d'un vaccin non vivant chez les femmes qui allaitent

La vaccination contre la COVID-19 devrait être recommandée à une femme qui allaite

Source: Avis du CIQ sur l'utilisation des vaccins à ARN messager contre la COVID-19 3 sept. 2021
https://www.inspq.qc.ca/publications/3093-utilisation-des-vaccins-arn-contre-la-covid19

Institut national de santé publique Québec

Outils et documents supplémentaires

Protocole d'immunisation du Québec https://www.msss.gouv.qc.ca/professionnels/vaccination/piq-vaccins/#covid-19

Q/R sur les vaccins contre la COVID-19 à l'intention des vaccinateurs
https://publications.msss.gouv.qc.ca/msss/document-002830/

Capsule d'information Centre Image https://www.chusj.org/fr/soins-services/P/Pharmacie/Centre-IMAGe/Capsule-d-information

Avis du CIQ sur l'utilisation des vaccins à ARN messager contre la COVID-19, 3 septembre 2021
https://www.inspq.qc.ca/publications/3093-utilisation-des-vaccins-arn-contre-la-covid19

COVID-19 (SRAS-CoV-2) : Recommandations intérimaires sur les mesures de prévention en milieu de travail pour les travailleuses enceintes ou qui allaitent https://www.inspq.qc.ca/publications/2919-mesures-travailleuses-enceintes-allaitent-covid19

Institut national de santé publique Québec

Remerciements

- Dre Mylène Trottier, INSPQ
- Dre Agathe Croteau, INSPQ
- Mme Abigaelle Altenor, INSPQ

Mise à jour de décembre 2021:

- Mme Laurianne Padet, INSPQ
- Mme Gabrielle Asselin, INSPQ
- Dr Stéphane Caron, INSPQ
- Dre Nathalie Auger, INSPQ
- Dre Isabelle Boucoiran, Université de Montréal

Institut national de santé publique Québec

Références

Adhikari, JAMA 2020, doi:10.1001/jamanetworkopen.2020.29256

Adhikari, AJOG, 2021, https://www.ajog.org/article/S0002-9378(21)01005-X/fulltext

Allotey et al., BMJ, 2020, doi.org/10.1136/bmj.m3320

Atyeo et al., bioRxiv 2021 https://doi.org/10.1101/2021.04.04.438404

Badr, AJ of obst gyneco, nov 2020, https://www.ajog.org/article/S0002-9378(20)30776-6/pdf

Baird et al., medRxiv, 2021 https://doi.org/10.1101/2021.02.23.21252328

Beharier et al. J Clin Invest 2021 https://pubmed.ncbi.nlm.nih.gov/34014840/

CCNI, Recommandations sur l'utilisation des vaccins contre la COVID-19, 22 octobre 2021 https://www.canada.ca/fr/sante-publique/services/immunisation/comite-consultatif-national-immunisation-ccni/recommandations-utilisation-vaccins-covid-19.html#ps

Centeno-Tablante et al., Ann. N. Y. Acad Sci., 2021 DOI: 10.1111/nyas.14477

CDC, v-safe, 2021. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafe.html

Charepe et al, BMC Pregnancy Childbirth 2021 DOI: 10.1186/s12884-021-04051-6

Chmielewska et al., The Lancet, 2021. DOI:https://doi.org/10.1016/S2214-109X(21)00079-6

CIQ, INSPQ, Avis intérimaire sur l'utilisation des vaccins à ARN messager contre la COVID-19, 3 septembre 2021 https://www.inspq.qc.ca/publications/3093-utilisation-des-vaccins-arn-contre-la-covid19

CIQ, INSPQ, Pertinence d'une dose de rappel d'un vaccin contre la COVID-19 pour les différentes catégories d'adultes au Québec, 7 décembre 2021 https://www.inspq.qc.ca/publications/3184-dose-rappel-vaccin-covid19-adultes

Collier et al. JAMA 2021 https://jamanetwork.com/journals/jama/fullarticle/2780202

DeSisto et al, CDC, 2021 https://www.cdc.gov/mmwr/volumes/70/wr/mm7047e1.htm?s_cid=mm7047e1_w

Dagan et al. Nat Med 2021 DOI: 10.1038/s41591-021-01490-8

Delahoy et al., MMWR, 2020. DOI: 10.15585/mmwr.mm6938e1

Douxfils et al., Vaccines (Basel) 2021 https://pubmed.ncbi.nlm.nih.gov/34427487/

Institut national de santé publique Québec

Références

Fenizia et al., Nat Commun, 2020 https://www.nature.com/articles/s41467-020-18933-4

Figueiro-Filho et al. J Perinat Med, 2020. DOI: 10.1515/jpm-2020-0364

Flaherman et al., Clin Infect Dis, 2021. DOI: 10.1093/cid/ciaa1411

Gill & Jones, Obst & Gynecol 2021 doi: 10.1097/AOG.0000000000004367

Golan et al., MedRxiv, 2021 doi: https://doi.org/10.1101/2021.03.05.21252998

Goldshtein et al. JAMA 2021 https://jamanetwork.com/journals/jama/fullarticle/2782047

Gray et al. medRxiv, 2021 https://doi.org/10.1101/2021.03.07.21253094

INESSS, COVID et grossesse, 6 juillet 2021. https://www.inesss.qc.ca/covid-19/traitements-specifiques-a-la-covid-19/grossesse-allaitement.html

INSPQ, données de vigie non publiées, communication écrite Rachel McKay

Jering et al., JAMA 2021, https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2775396

Juncker et al. J Hum Lact. 2021 https://pubmed.ncbi.nlm.nih.gov/34176363/

Kalafat et al., Obst & Gyn 2021 https://doi.org/10.1002/uog.23631

Karimi et al., J Pregnancy, 2021 DOI: 10.1155/2021/8870129

Knight et al., BMJ, 2020 doi: https://doi.org/10.1136/bmj.m2107

Ko et al., Clin Infect Dis, 2021 DOI: 10.1093/cid/ciab344

Kotlyar et al., Am J Obstet Gynecol, 2021 DOI: 10.1016/j.ajog.2020.07.049

Lokken et al, Am J obstetric gyneco, 2021 https://doi.org/10.1016/j.ajog.2020.12.1221

Institut national de santé publique Québec

Références

Low et al. medRxiv, 2021 https://doi.org/10.1101/2021.09.20.21263808

Mark et al. Pediatr Infect Dis J 2021 https://pubmed.ncbi.nlm.nih.gov/33847297/

Martinez-Portilla et al., COV19Mx, 2021, Mexique DOI: 10.1002/uog.23575

Metz et al., Obstet Gynecol 2021 DOI: 10.1097/AOG.0000000000004339

Moderna, Monographie. https://www.modernacovid19global.com/ca/fr/product-monograph-french.pdf

Money, CANCOVID-Preg 2021 https://ridprogram.med.ubc.ca/cancovid-preg/

Mullins et al., Pan-Covid et AAP SONPM 2021, https://doi.org/10.1002/uog.23619

Peretz et al., Ultrasound Obstet Gynecol 2021 https://doi.org/10.1002/uog.23729

Perl et al. JAMA 2021 https://jamanetwork.com/journals/jama/fullarticle/2778766

Pfizer, Monographie. https://www.pfizer.ca/pfizer-biontech-covid-19-vaccine-covid-19-mrna-vaccine

Prabhu et al. bioRxiv, 2021 https://doi.org/10.1101/2021.04.05.438524

Raschetti et al., Nat Commun 2020 https://www.nature.com/articles/s41467-020-18982-9

Salvatore et al., Lancet Child Adolesc Health 2020 DOI:https://doi.org/10.1016/S2352-4642(20)30235-2

Shimabukuro, NEJM, 2021 DOI: 10.1056/NEJMoa2104983

Tolu et al. PLoS One 2021 DOI: 10.1371/journal.pone.0250196

Valcarce et al. Breastfeed Med 2021 https://pubmed.ncbi.nlm.nih.gov/34427487/

Villar et al. JAMA Pediatr. 2021 doi:10.1001/jamapediatrics.2021.1050

Institut national de santé publique Québec

Références

Vousden et al., UKOSS, PLoS One 2021 https://www.medrxiv.org/content/10.1101/2021.01.04.21249195v1

Walker et al. BJOG 2020 https://doi.org/10.1111/1471-0528.16362

Walter, JAMA Network, 2021 doi:10.1001/jama.2021.22679

Wei et al. CMAJ 2021 https://www.cmaj.ca/content/193/16/E540

Woodworth et al., MMWR, 2020 https://www.cdc.gov/mmwr/volumes/69/wr/mm6944e2.htm

Zambrano et al., MMWR, 2020, https://www.ncbi.nlm.nih.gov/pubmed/33151921

Zdanowski & Wasniewski, Vaccines (Basel) 2021 https://pubmed.ncbi.nlm.nih.gov/34205434/

Institut national de santé publique Québec

Éric Bédard

De: Paule Clément
Envoyé: 12 janvier 2022 12:11
À: Nicholas Brousseau; Vladimir Gilca - boite partagée; Julie Bestman-Smith; Yen Bui (CISSSMC16); Gaston De Serres; Philippe De Wals; Rodica Gilca; maryse.guay.agence16; Marilou Kiely; Chantal Sauvageau; Ève Dubé; Marc Brisson; France Bouchard (CIUSSSCN-Coordonnatrice); Élise Fortin; Isabelle Rouleau; Dominique Grenier; Marie-Claude Gariépy; Fannie Defay; Lauriane Padet; Gabrielle Asselin; Geneviève Deceuninck; Caroline Quach-Thanh
Objet: TR : Recommandation 3e dose vaccin contre COVID-19
Pièces jointes: Version diffusion_Recommandations_3e_dose.pdf

Catégories: Demande d'accès Information

PVI.

De : MSSS - Protection
Envoyé : 12 janvier 2022 11:12
Objet : Recommandation 3e dose vaccin contre COVID-19

ATTENTION: L'origine de cette communication est de source externe. Veuillez vous assurer que l'expéditeur et le contenu, incluant les pièces jointes, sont légitimes avant même de les ouvrir ou de les télécharger.

Aux responsables en immunisation

cc aux coordonnateurs MI, DCPMI, DAPM

Bonjour,

Vous trouverez ci-joint la recommandation de Dr Arruda portant sur la dose de rappel. **Cette recommandation s'applique uniquement aux personnes pour qui une dose de rappel est recommandée dans le Protocole d'immunisation du Québec (PIQ),** soit :

- aux personnes âgées de 18 ans ou plus
- aux travailleurs de la santé, peu importe l'âge
- aux femmes enceintes, peu importe l'âge

Cordialement,

Santé et Services sociaux Québec

Dominique Fortier, inf. M.A.P.
Infirmière-conseil en maladies infectieuses
Direction de la prévention et du contrôle des maladies infectieuses
Direction générale adjointe de la protection de la santé publique
Ministère de la Santé et des Services sociaux
1075, chemin Sainte-Foy, 12e étage
Québec (Québec) G1S 2M1
Téléphone: 418 266-8946
En télétravail – Merci d'utiliser TEAMS ou le courriel pour me contacter

IMPORTANT : Considérant le volume élevé de courriels que je reçois actuellement, n'hésitez pas à me contacter via Teams pour tout suivi urgent ou à me relancer par courriel si vous n'avez pas eu de retour dans un délai raisonnable.

AVIS DE CONFIDENTIALITÉ

Ce message peut renfermer des renseignements protégés ou des informations confidentielles. Si vous l'avez reçu par erreur, ou s'il ne vous est pas destiné, veuillez en prévenir immédiatement l'expéditeur et effacer ce courriel. Par respect pour l'environnement, imprimer ce courriel seulement si nécessaire.

Coronavirus (COVID-19)

DIRECTION GÉNÉRALE DE LA SANTÉ PUBLIQUE

Date : Le 10 janvier 2022

Nature : ☒ **Recommandations** ☐ **Propositions** ☐ **Présentation** ☐ **Avis**

Sujet : Recommandations en lien avec la 3e dose de vaccin contre la COVID-19

Considérant :

- La recommandation du Comité consultatif national en immunisation du Canada (CCNI) ;
- La position du Comité d'immunisation du Québec (CIQ), qui n'élimine pas cette option ;
- La position des CDC américains ;
- La non-disponibilité des tests PCR ;
- La capacité limitée des laboratoires ;

Nous recommandons :

- Que toute personne qui le désire puisse obtenir une 3e dose de vaccin contre la COVID-19 ;
- Que cette pratique s'applique également aux personnes qui ont contracté une COVID-19 récemment. Ainsi, dès que leur maladie aura été résolue, ces personnes pourront se prévaloir d'une 3e dose en respectant un intervalle minimal de trois (3) mois après la dernière dose de vaccin reçue.

Approuvé par le directeur national de santé publique, M. Horacio Arruda, le 10 janvier 2022.

Signature : _____

N/Réf. : 22-SP-00002-03

Risk Monitor: Wave 27

Preliminary Report

January 26, 2022

Methodology

- This study was conducted online using EKOS' probability-based research panel, Prob*it*
- The field dates for this survey are January 18-24, 2022
- In total, a random sample of 1,223 Canadian adults aged 18+ responded to the survey
- The margin of error associated with the total sample is ± 2.8 percentage points, 19 times out of 20
- All the data have been statistically weighted by age, gender, and region

Copyright 2022
No reproduction without permission

1) General Outlook
2) Vaccine Acceptance
3) Approval of Government Response
4) Attitudes to Public Health Measures and Vaccine Mandates
5) Disinformation
6) Conclusions

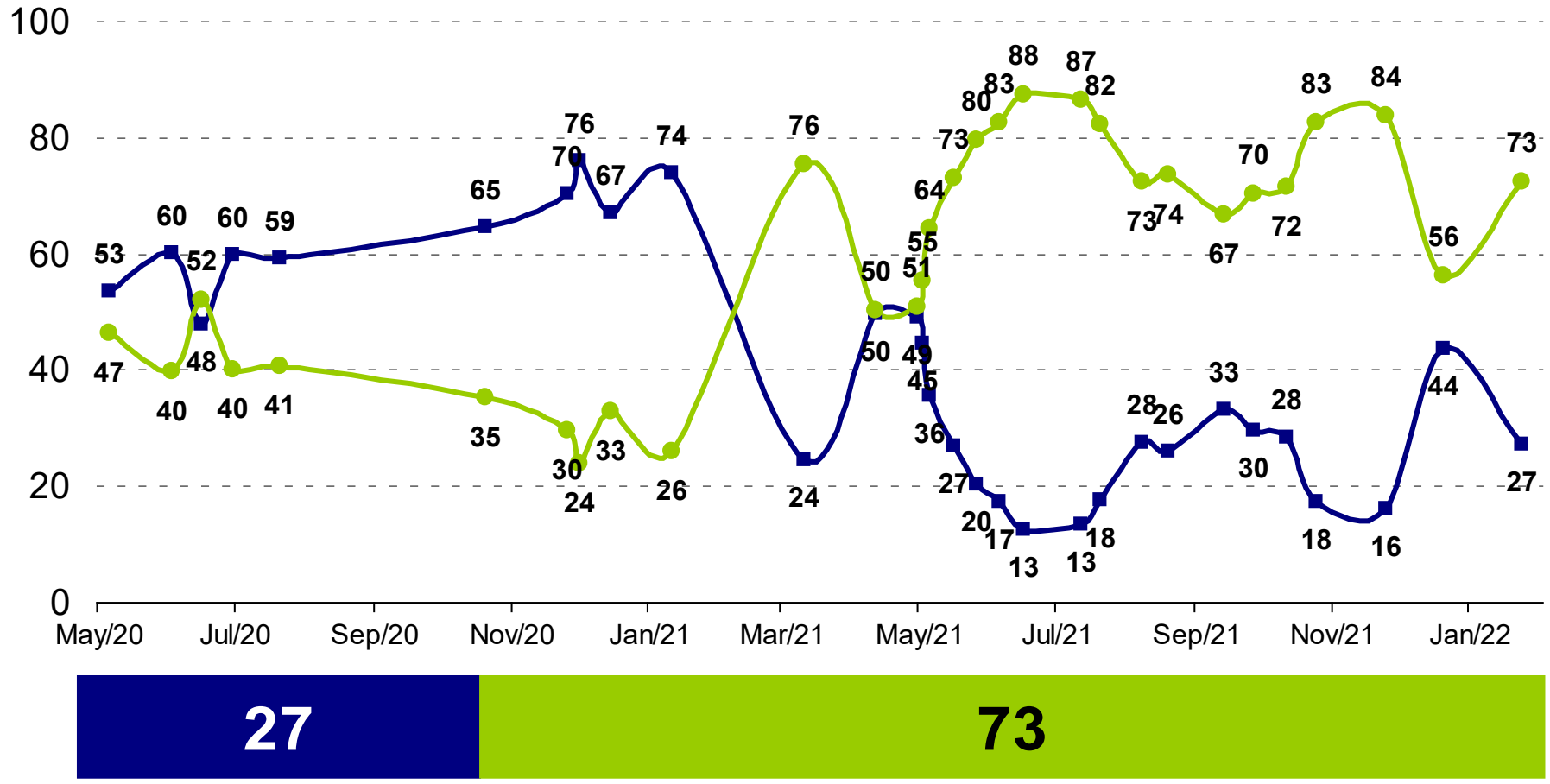
Outlook on the pandemic

- The public remain extremely stressed by the seemingly endless pandemic which has now produced a huge rise in cases and hospitalizations and a round of restrictions in most parts of the country
- However, for the first time since the onset of Omicron, we have seen a very recent but very clear elevation of a belief that the worst is now behind us
  - Seven in ten Canadians (73%) say the worst is over, a 16-point rise from just a month ago

Copyright 2022
No reproduction without permission

Outlook on COVID-19 pandemic

Q. *Which of the following best describes your outlook on the COVID-19 outbreak?*



Note: Figures adjusted to exclude those who skipped the question.

BASE: *Canadians; January 18-24, 2022, n=1,223, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

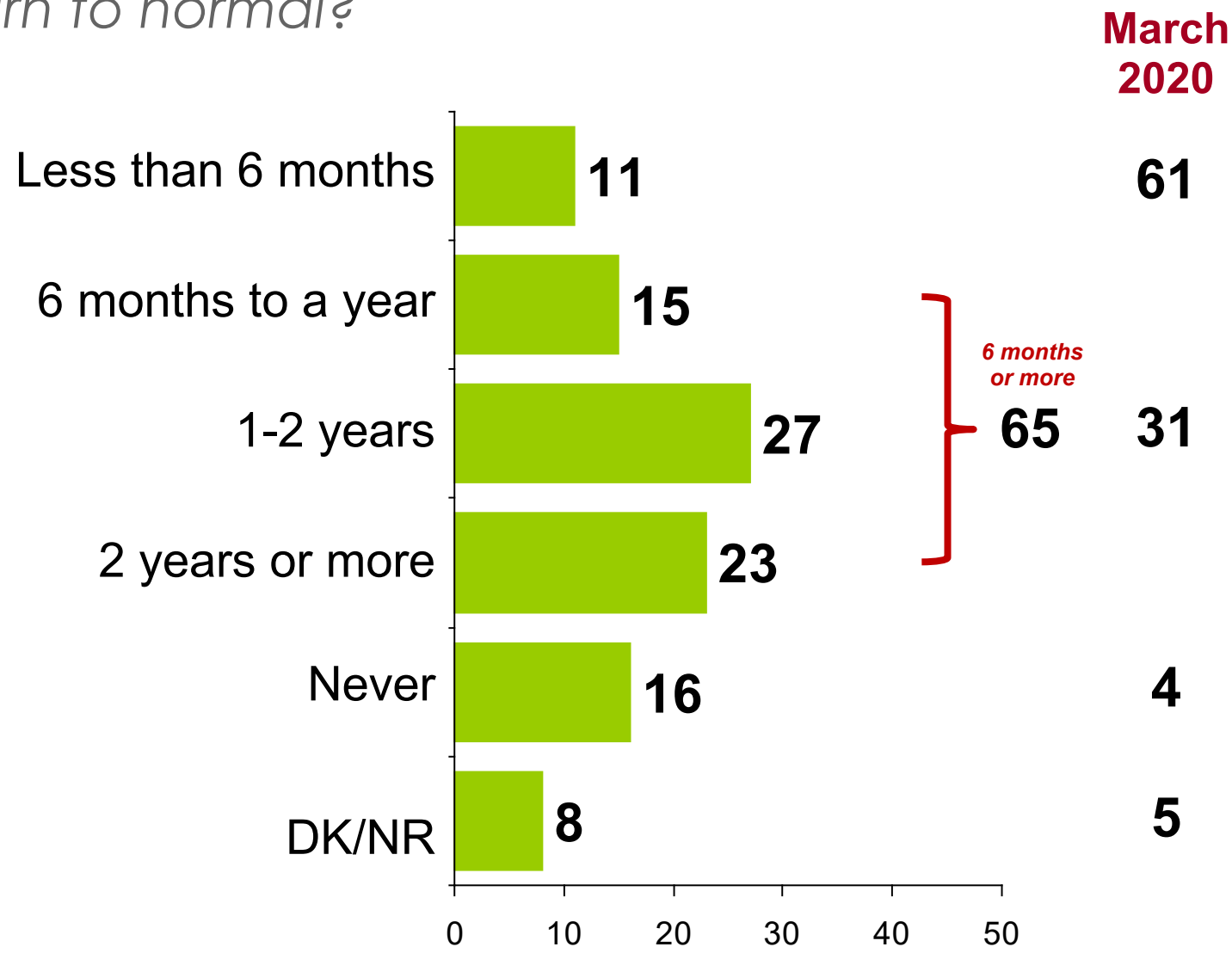
Anticipated duration of pandemic

- The improved outlook is also evident in a narrowing of the time frame for the resumption of 'normalcy'
  - The incidence of those who think normalcy is at least two years away – or worse, never – has dropped by nine points (39%, down from 48% in December 2021)

Copyright 2022
No reproduction without permission

Anticipated duration of pandemic

Q. *How long do you expect it will take until things to return to normal?*

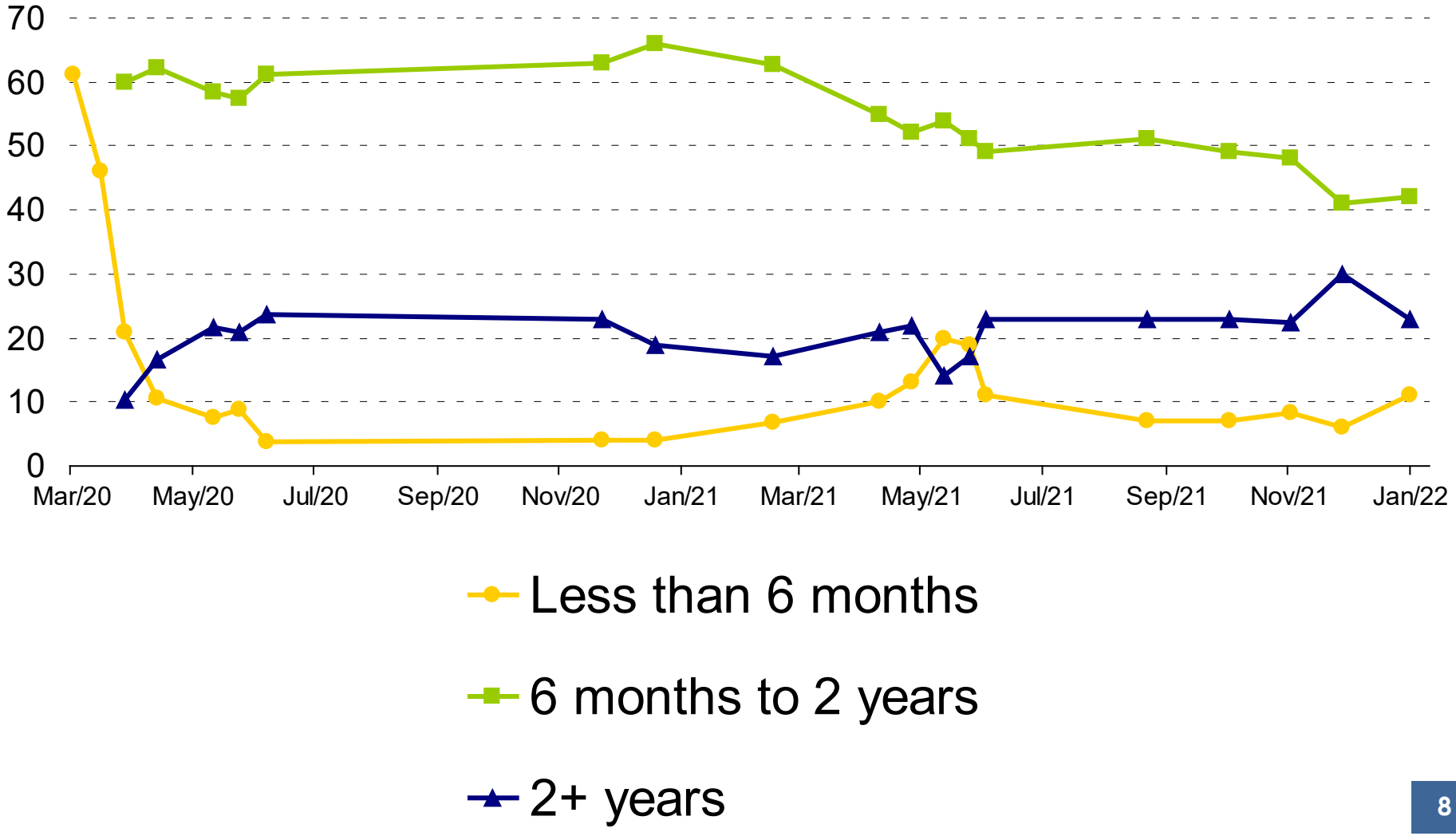


BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Tracking anticipated duration of pandemic

Q. *How long do you expect it will take until things to return to normal?*



BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

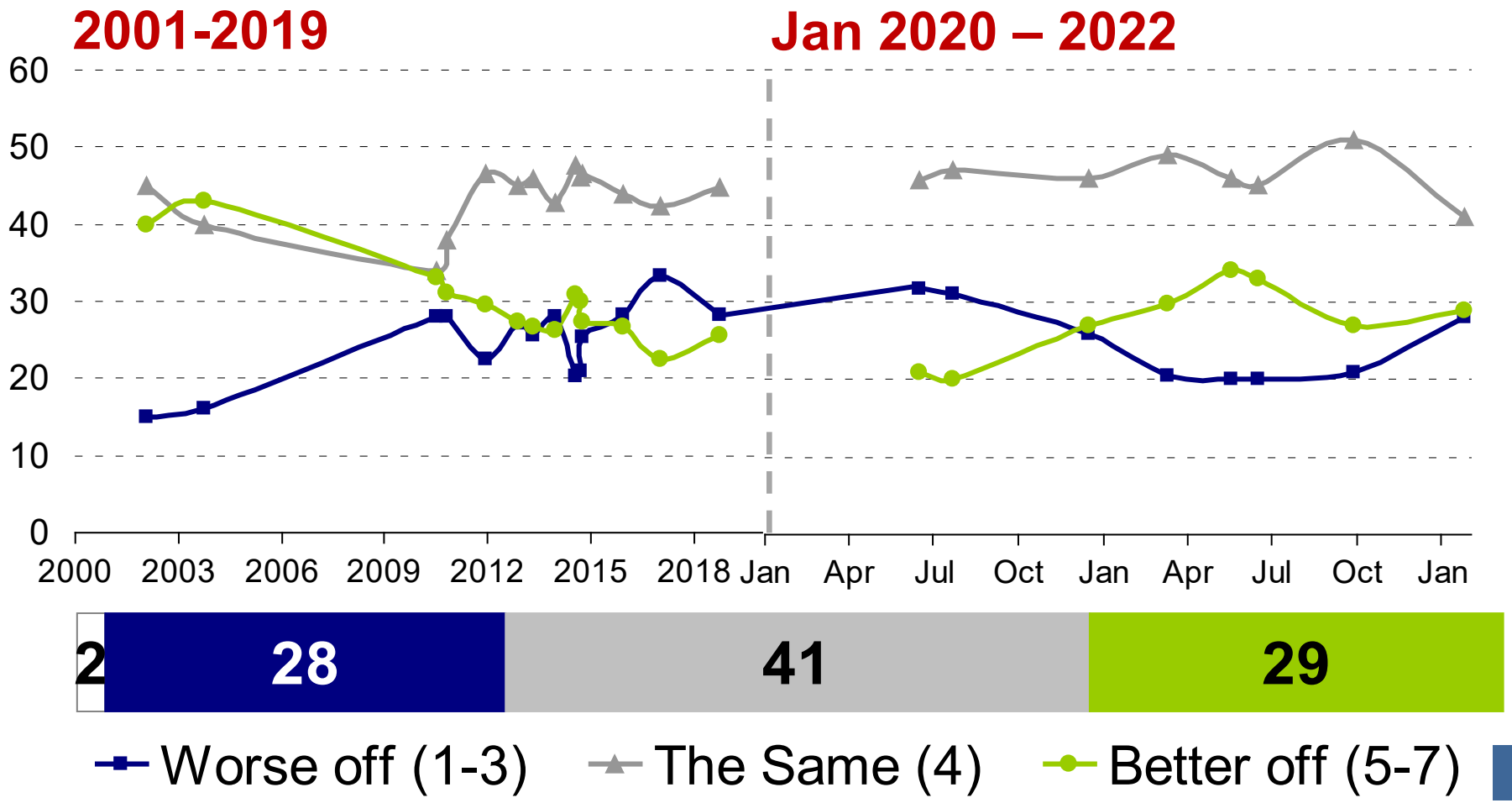
Financial outlook

- The improved outlook on the pandemic is bolstered by a stable and generally positive outlook on the economy
  - A plurality of Canadians (41%) say their personal financial situation will remain unchanged for the coming year, but a similar proportion (42%) believe their situation will improve over the next five years
- In terms of outlook on both the economy and the pandemic itself, the improvements are not seen evenly by the Canadian public
  - Outlook is strongly correlated with ethnicity and social class, with much more negative outlooks among the more vulnerable members of society

Copyright 2022
No reproduction without permission

Short-term financial outlook

Q. *Thinking ahead over the NEXT YEAR or so, do you think your personal financial situation will be better or worse than it is today?*

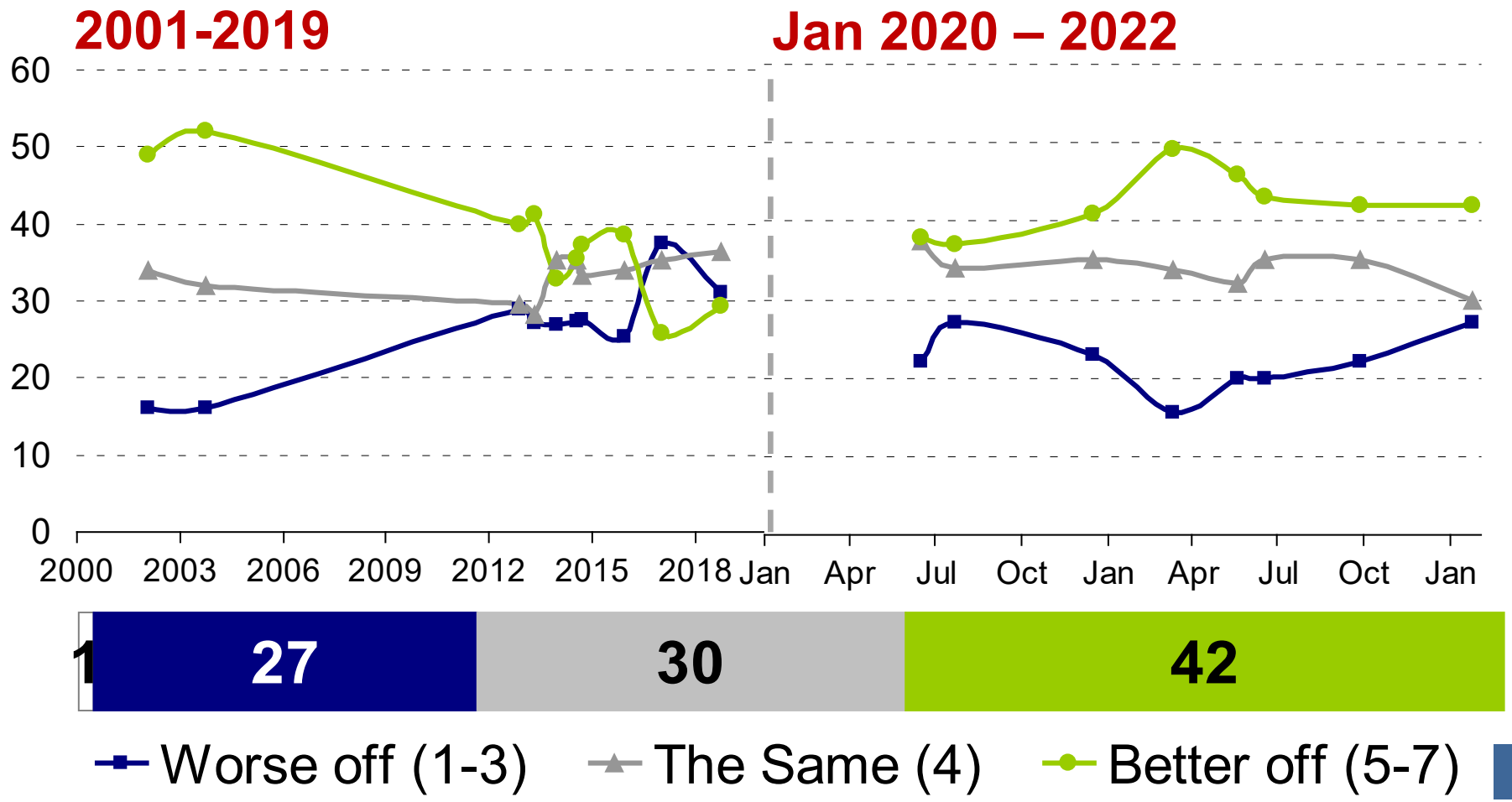


BASE: *Canadians (half-sample); January 18-24, 2022, n=603, MOE +/- 4.0%,19 times out of 20*

Copyright 2022
No reproduction without permission

Medium-term financial outlook

Q. *Thinking ahead over the NEXT FIVE YEARS or so, do you think your personal financial situation will be better or worse than it is today?*

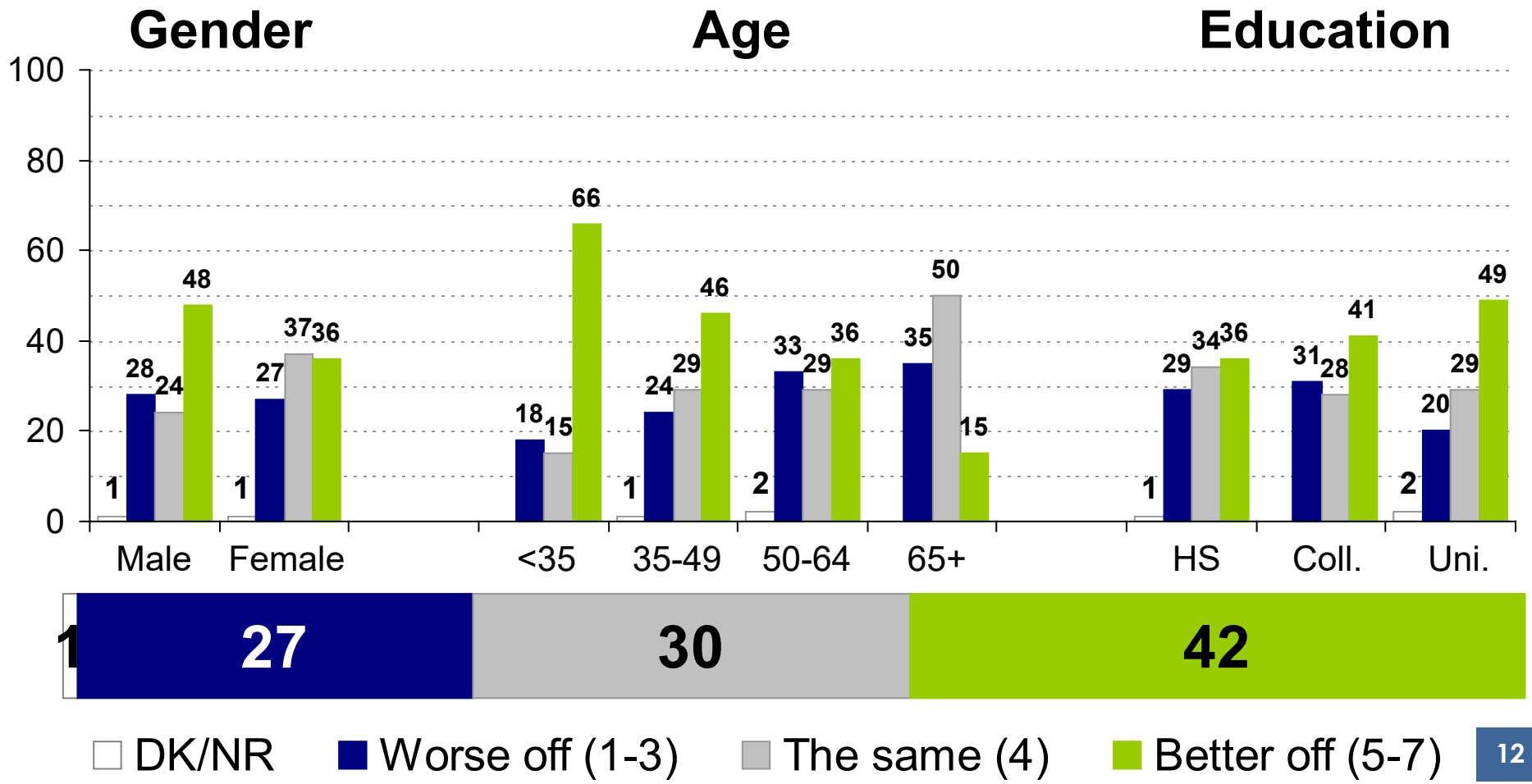


BASE: *Canadians (half-sample); January 18-24, 2022, n=620, MOE +/- 3.9%,19 times out of 20*

Copyright 2022
No reproduction without permission

Medium-term outlook by demographics

Q. *Thinking ahead over the NEXT FIVE YEARS or so, do you think your personal financial situation will be better or worse than it is today?*



BASE: *Canadians (half-sample); January 18-24, 2022, n=620, MOE +/- 3.9%,19 times out of 20*

Copyright 2022
No reproduction without permission

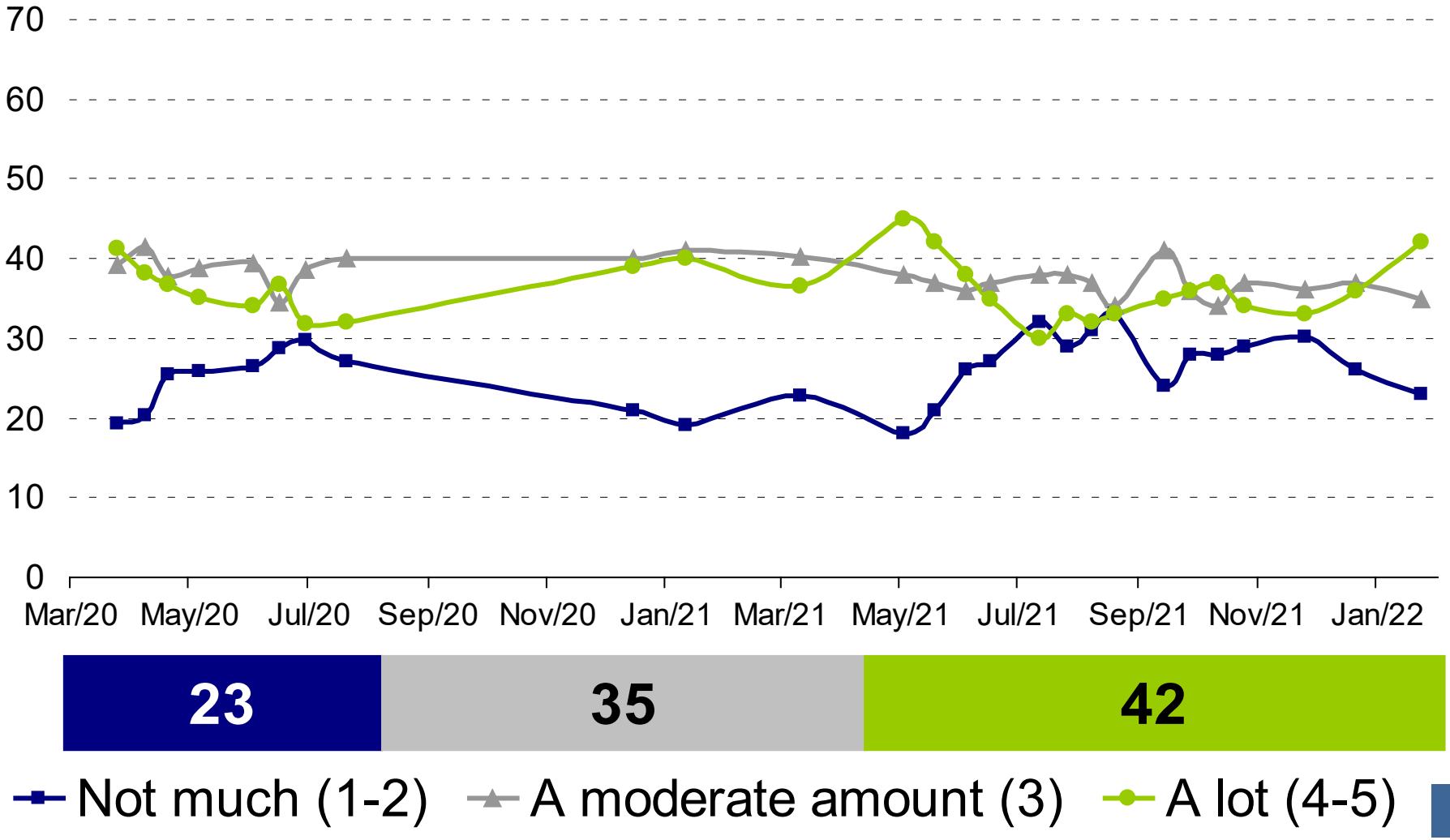
Financial outlook

- Despite an improved outlook on the pandemic, however, stress levels have not gone down – in fact, they have risen somewhat
  - Four in ten Canadians (42%) report experiencing a high degree of stress, up from 36% in December 2021
  - Curiously, self-reported stress is substantially higher among those who identify as 2SLGBTQ+ (61% of these respondents ay they are experiencing high levels of stress)
  - Stress levels are also higher among those with disabilities, working-class Canadians, and those aged 35 to 49

Copyright 2022
No reproduction without permission

Incidence of stress related to COVID-19

Q. *How much stress would you say you are experiencing as a result of the COVID-19 pandemic?*



BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

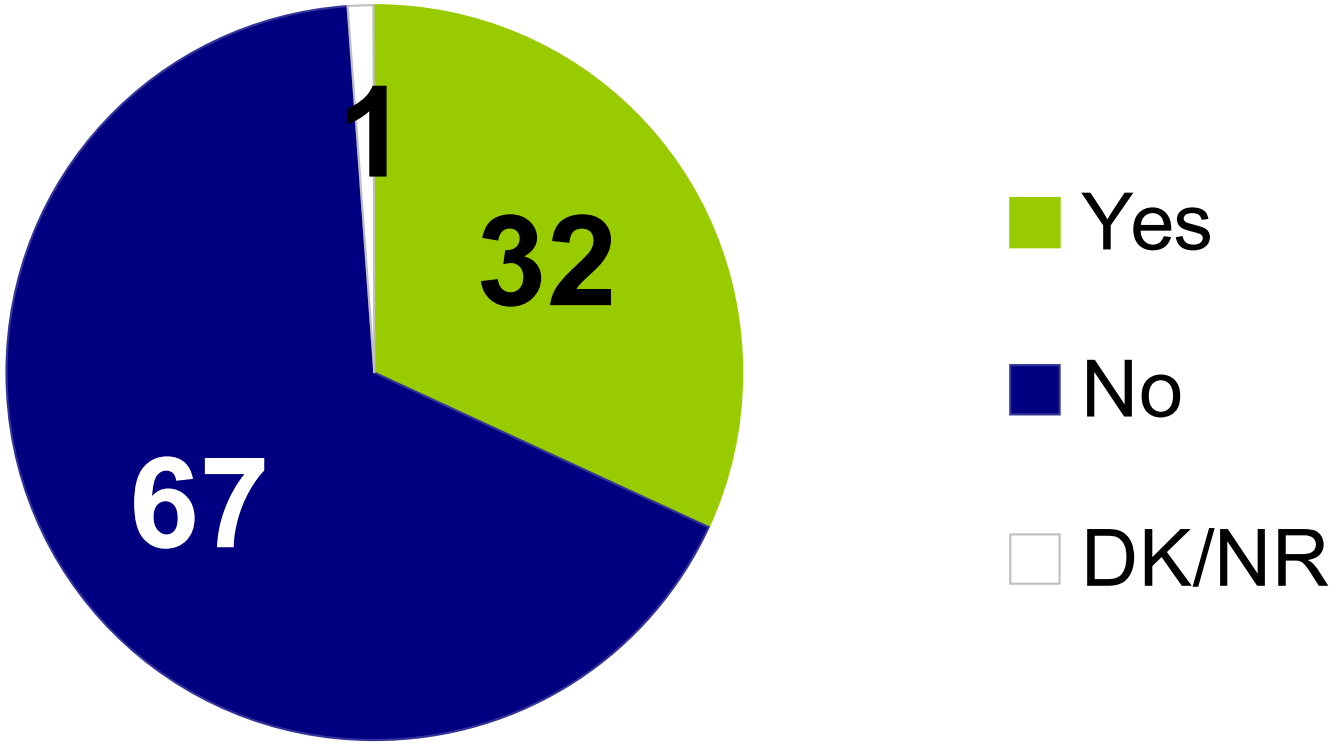
Experience with COVID-19 (i)

- As testing has become more difficult to obtain and process, our knowledge of the true levels of infection have been weakened
  - Many tests are now being done at home and not reported and many 'mild' cases are simply not being tested
- We asked Canadians if they personally know someone who has been hospitalized as a result of COVID-19 and one-third (32%) responded in the affirmative

Copyright 2022
No reproduction without permission

Knowledge of someone who has been hospitalized as a result of COVID-19

Q. *Do you personally know anyone who has been hospitalized as a result of COVID-19?*



BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%, 19 times out of 20*

Copyright 2022
No reproduction without permission

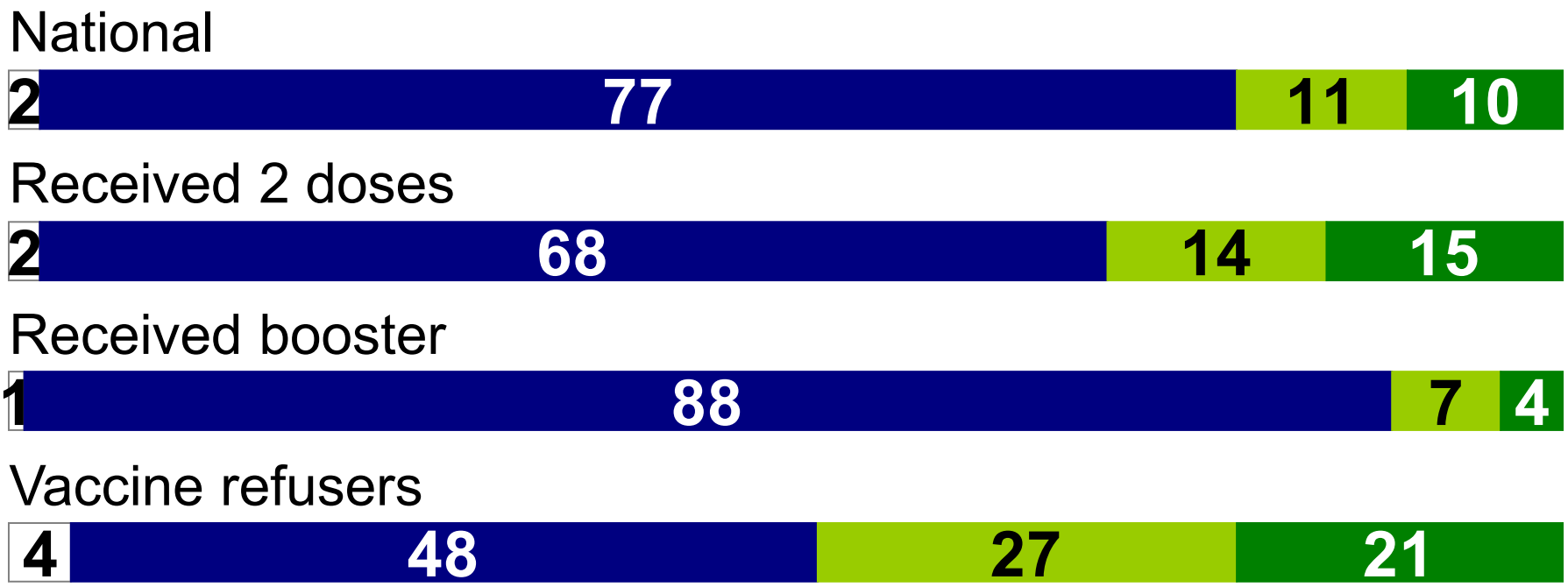
Experience with COVID-19 (ii)

- We also asked respondents if they had personally contracted COVID-19
  - 21% either had tested positive or were pretty certain they had contracted COVID-19 based on their symptoms
  - Applying this figure to Canada's adult population would yield a total of approximately seven million cases among those aged 18 and over
  - Naturally, the number of reported infections is higher in the areas that have had more cases (for instance, 31% of Albertans report having been infected, compared to just 8% of Atlantic Canada residents)
  - It is also notable that reported infections are lowest among those who have received three or more doses (11%) and highest among those who refuse to be vaccinated (48%)

Copyright 2022
No reproduction without permission

Incidence of COVID-19 infections

Q. *Have you contracted COVID-19 at any point since February 2020?*

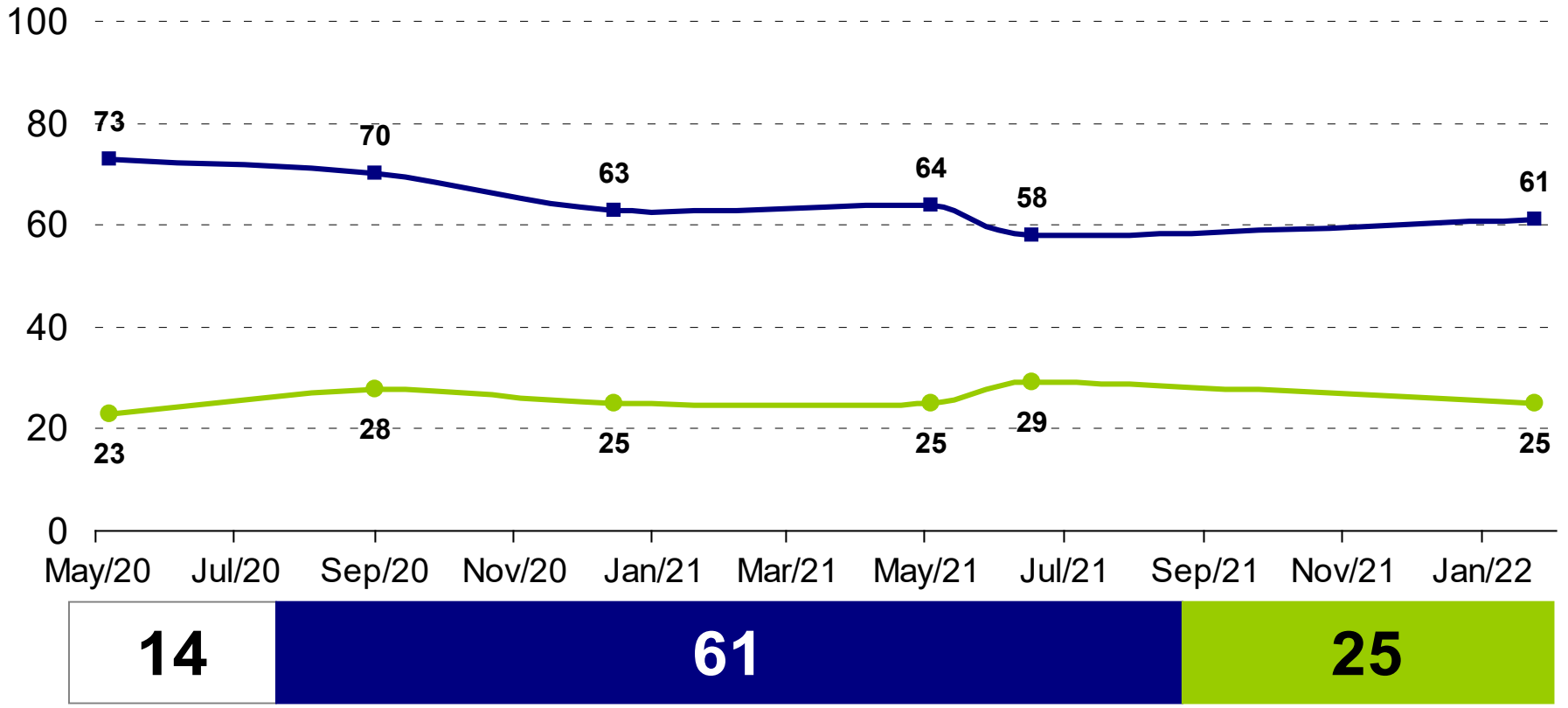


BASE: *Canadians; January 18-24, 2022, n=1,225, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Outlook on post-COVID-19 world

Q. *When the COVID-19 crisis ends, do you expect Canadian society to return to the status quo or do you expect a broad transformation of our society?*



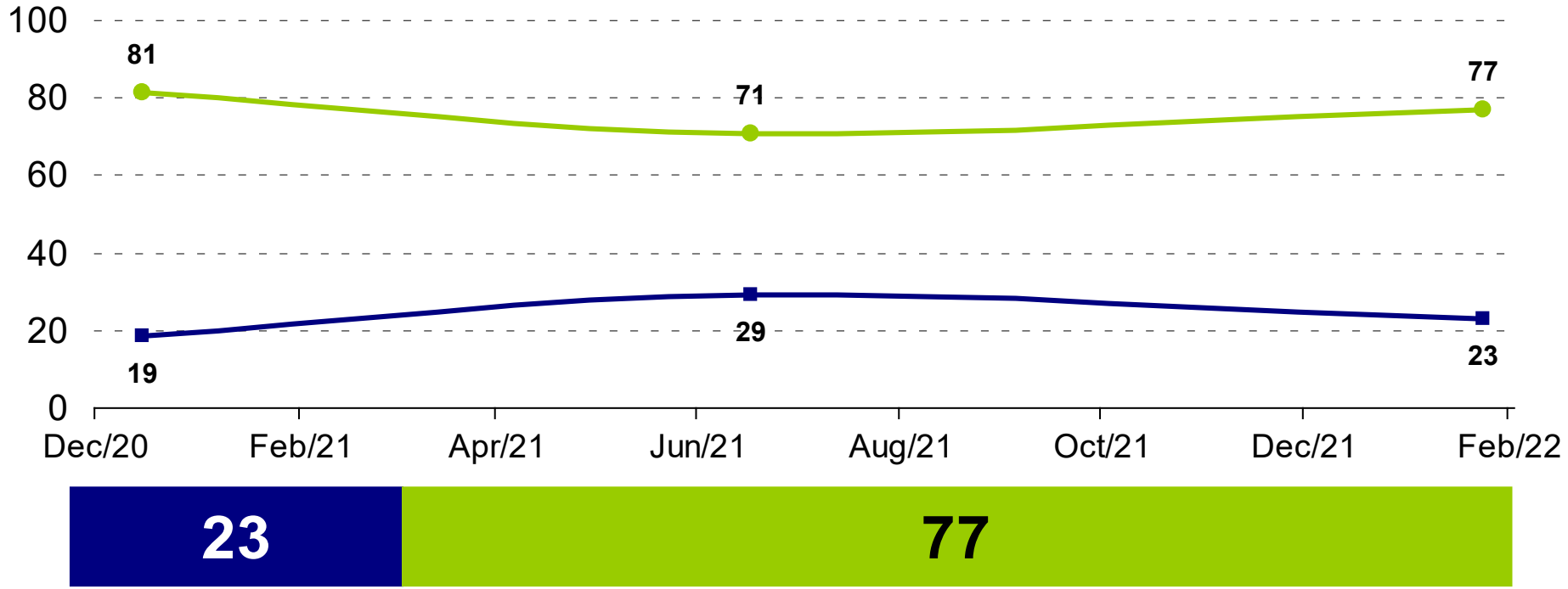
Note: Figures adjusted to exclude those who skipped the question.

BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Anticipated focus of post-pandemic world

Q. *[IF BROAD TRANSFORMATION OF OUR SOCIETY] Which of the following best describes how you think Canadian society will change as a result of this crisis?*



Note: Figures adjusted to exclude those who skipped the question.

BASE: *Foresees broad societal transformation; January 18-24, 2022, n=741, MOE +/- 3.6%,19 times out of 20*

Copyright 2022
No reproduction without permission

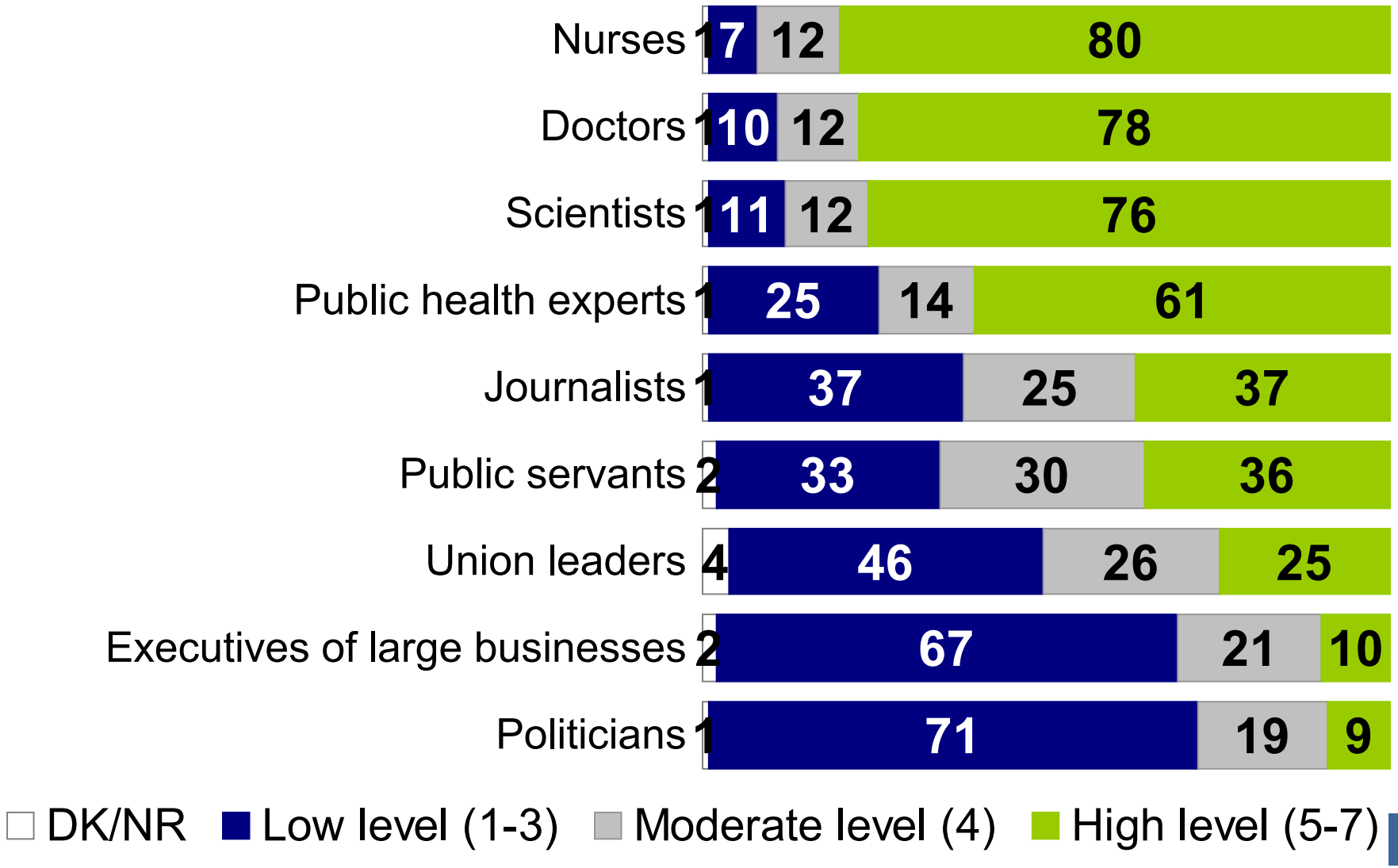
Trust in occupations

- Trust remains the strongest predictor of vaccine acceptance and safe behaviour
  - It is therefore concerning that trust in science and the medical community appears to be declining
  - Trust in science and public institutions is dramatically lower among vaccine refusers and it is directly linked to disinformation
  - Trust in mainstream media has declined and the refusers are turning to social media for what is often spurious information and advice

Copyright 2022
No reproduction without permission

Trust in occupations

Q. *How much trust do you have in each of the following?*

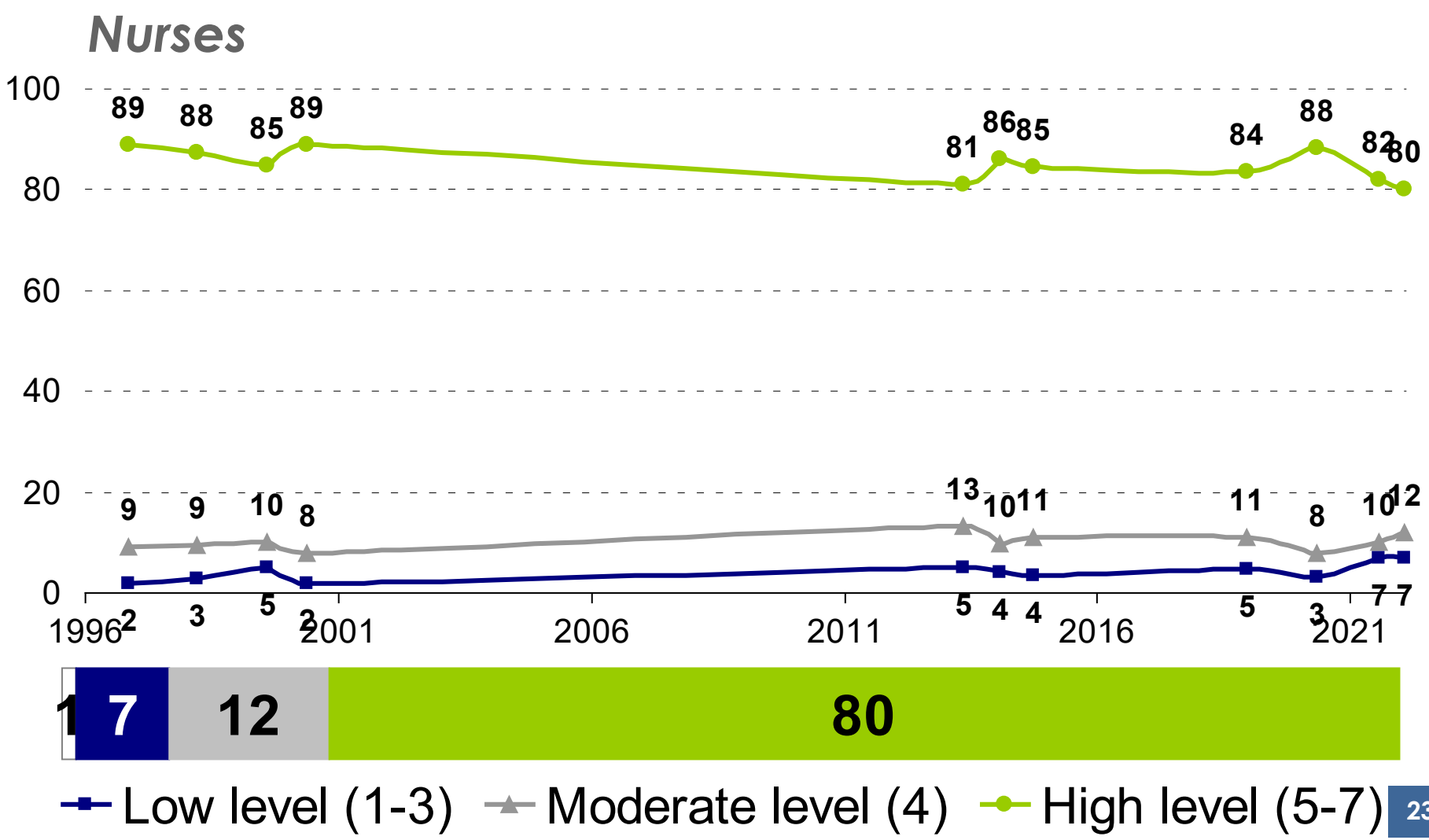


BASE: *Canadians; January 18-24, 2022, n=1,223, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Trust in occupations:
Nurses

Q. *How much trust do you have in each of the following?*

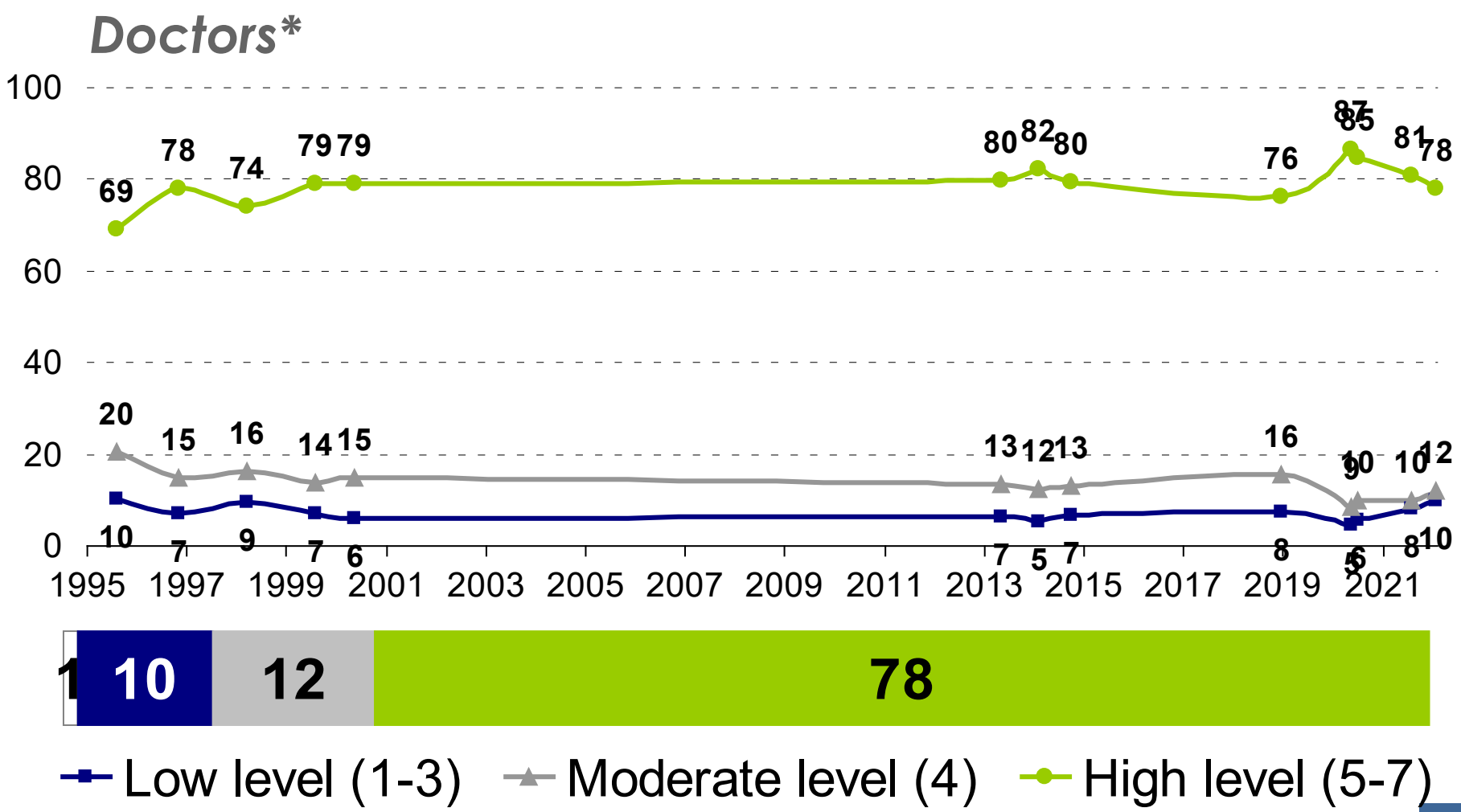


BASE: *Canadians; January 18-24, 2022, n=1,223, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Trust in occupations:
Doctors

Q. *How much trust do you have in each of the following?*



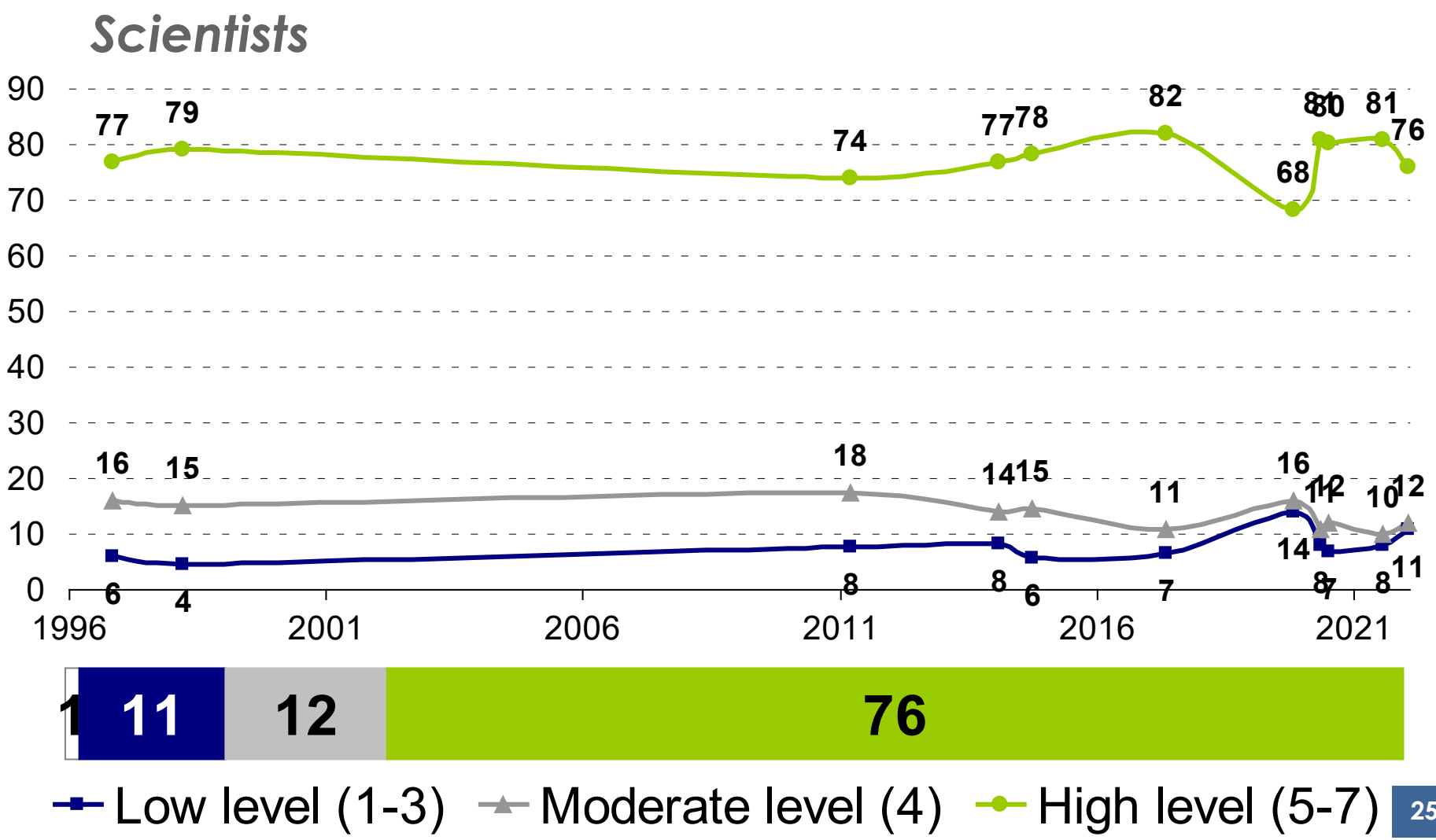
**Prior to 2010, "Medical doctors" was used*

BASE: *Canadians; January 18-24, 2022, n=1,223, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Trust in occupations:
Scientists

Q. *How much trust do you have in each of the following?*



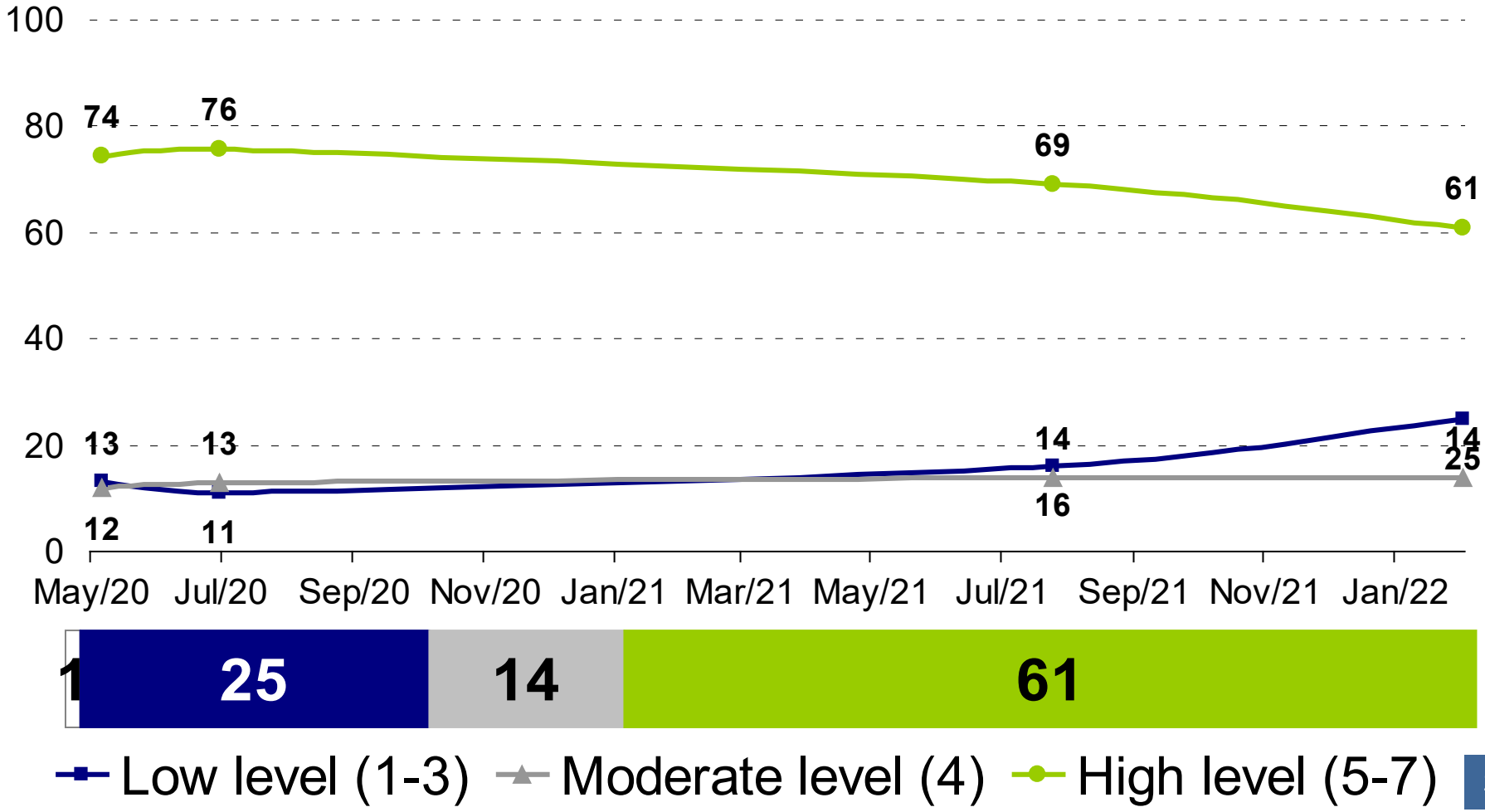
BASE: *Canadians; January 18-24, 2022, n=1,223, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Trust in occupations:
Public health experts

Q. *How much trust do you have in each of the following?*

Public health experts



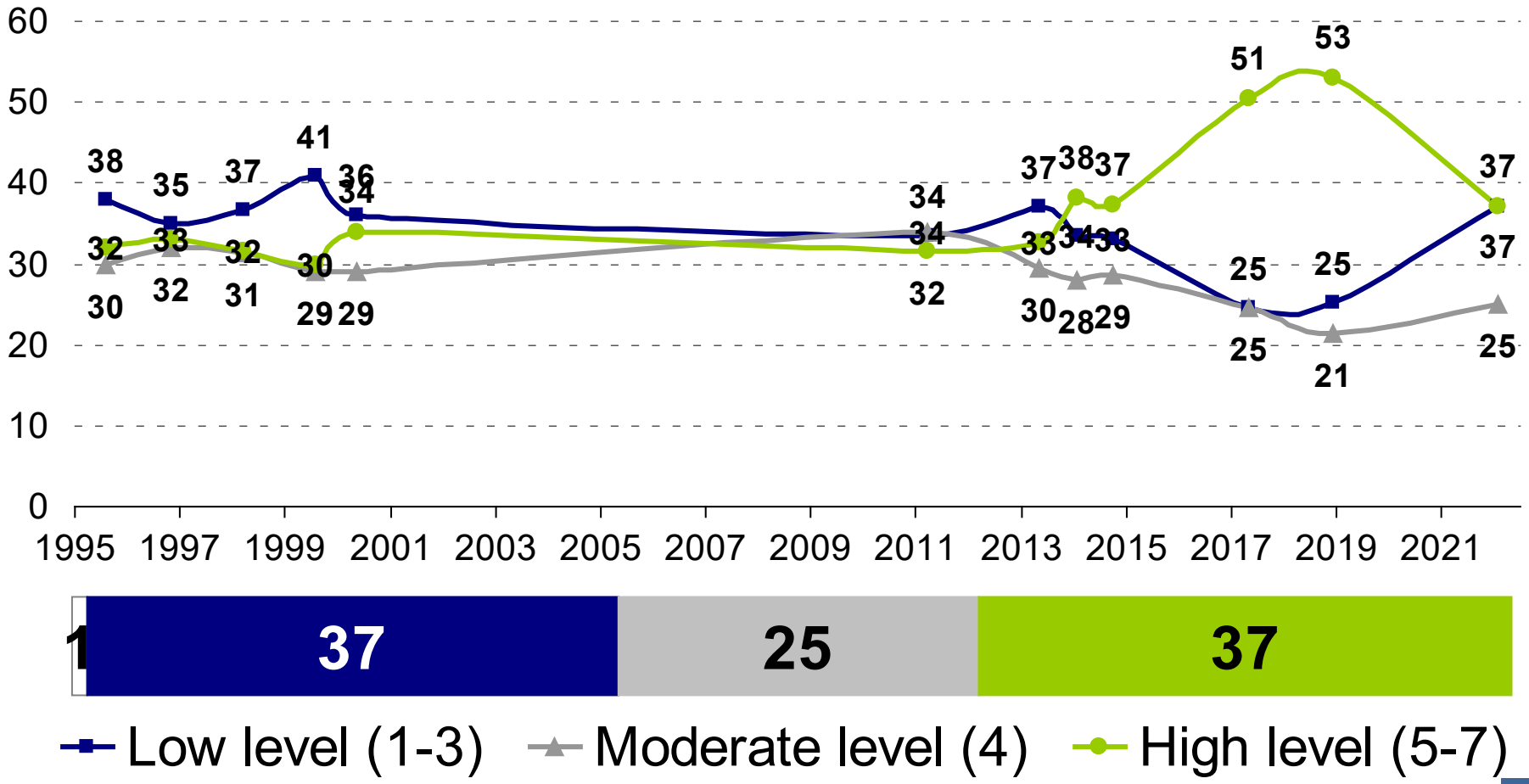
BASE: *Canadians; January 18-24, 2022, n=1,223, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Trust in occupations:
Journalists

Q. *How much trust do you have in each of the following?*

Journalists*



**Prior to 2010, "Journalists and reporters" was used*

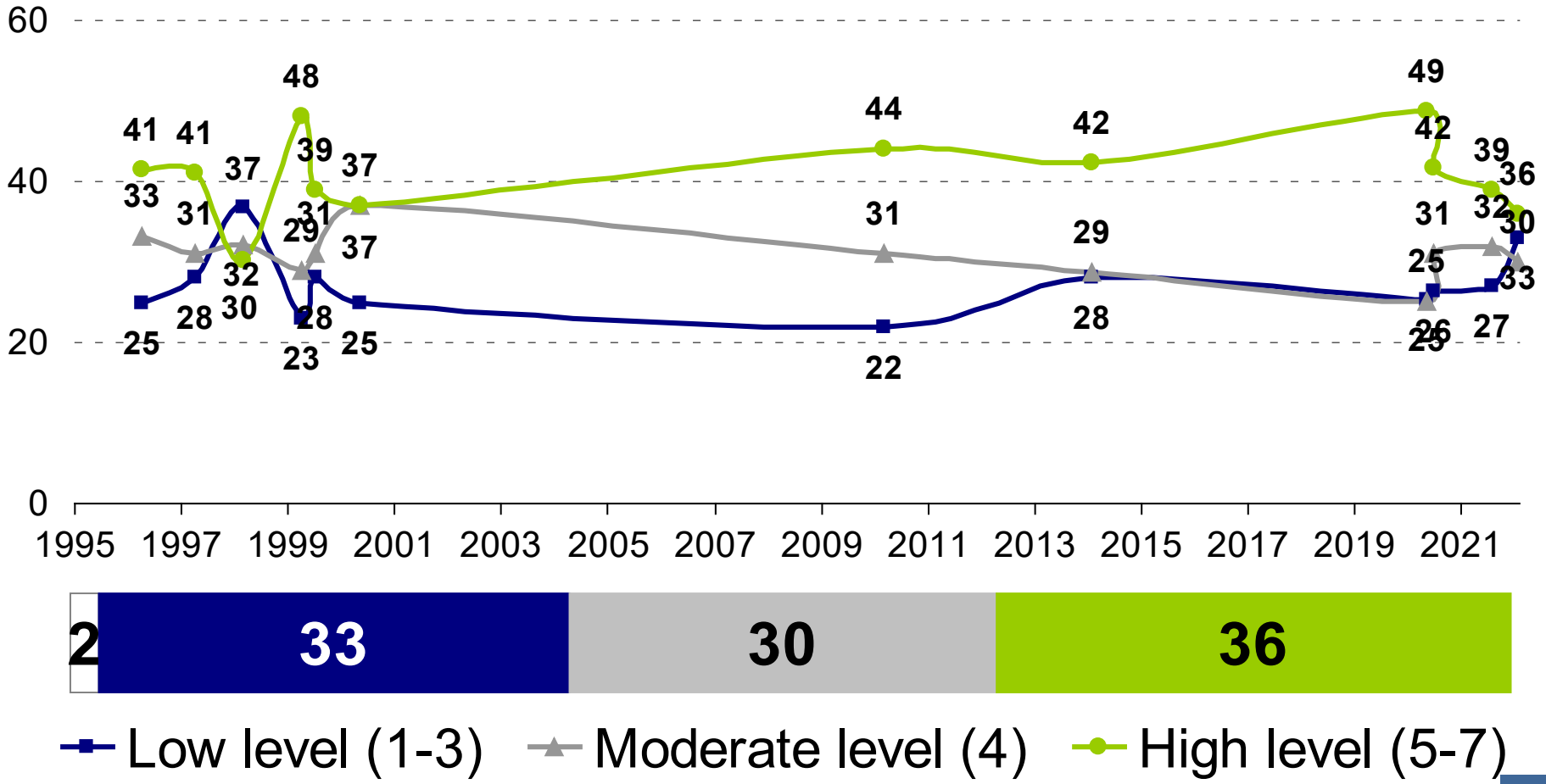
BASE: *Canadians; January 18-24, 2022, n=1,223, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Trust in occupations:
Public servants

Q. *How much trust do you have in each of the following?*

Public servants*



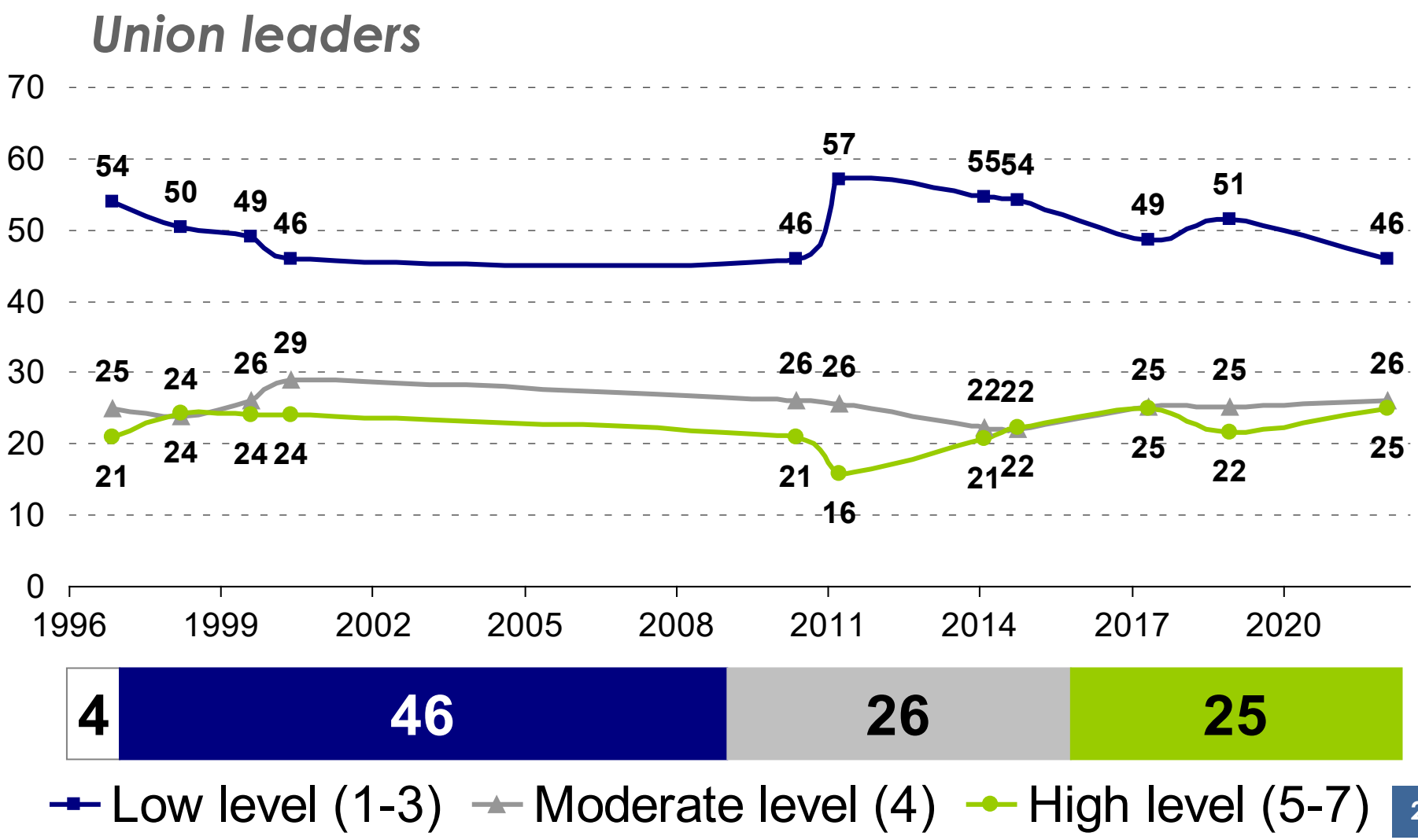
**Prior to 2010, "Federal public servants" was used*

BASE: *Canadians; January 18-24, 2022, n=1,223, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Trust in occupations:
Union leaders

Q. *How much trust do you have in each of the following?*



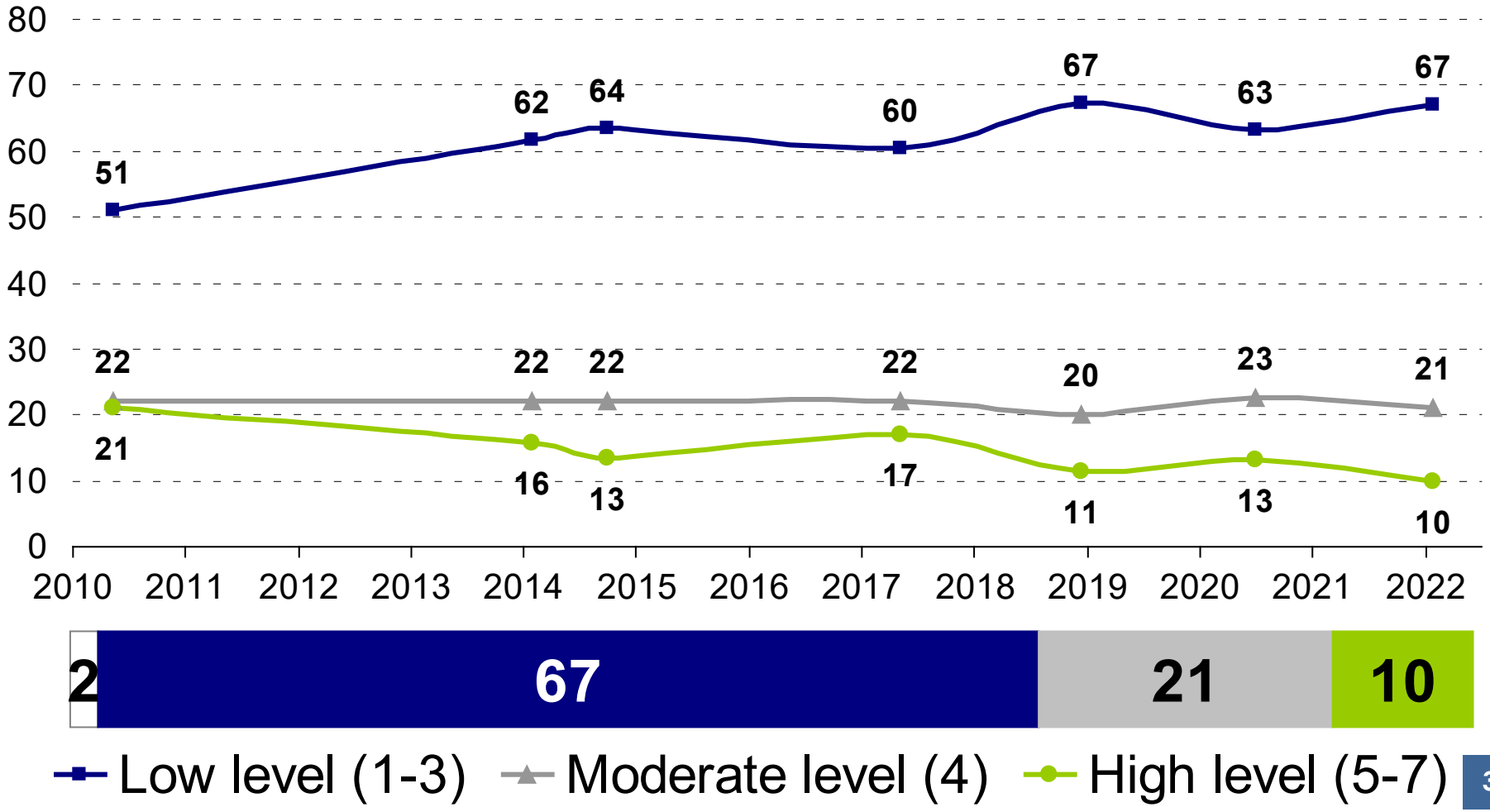
BASE: *Canadians; January 18-24, 2022, n=1,223, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Trust in occupations:
Executives of large businesses

Q. *How much trust do you have in each of the following?*

Executives of large businesses

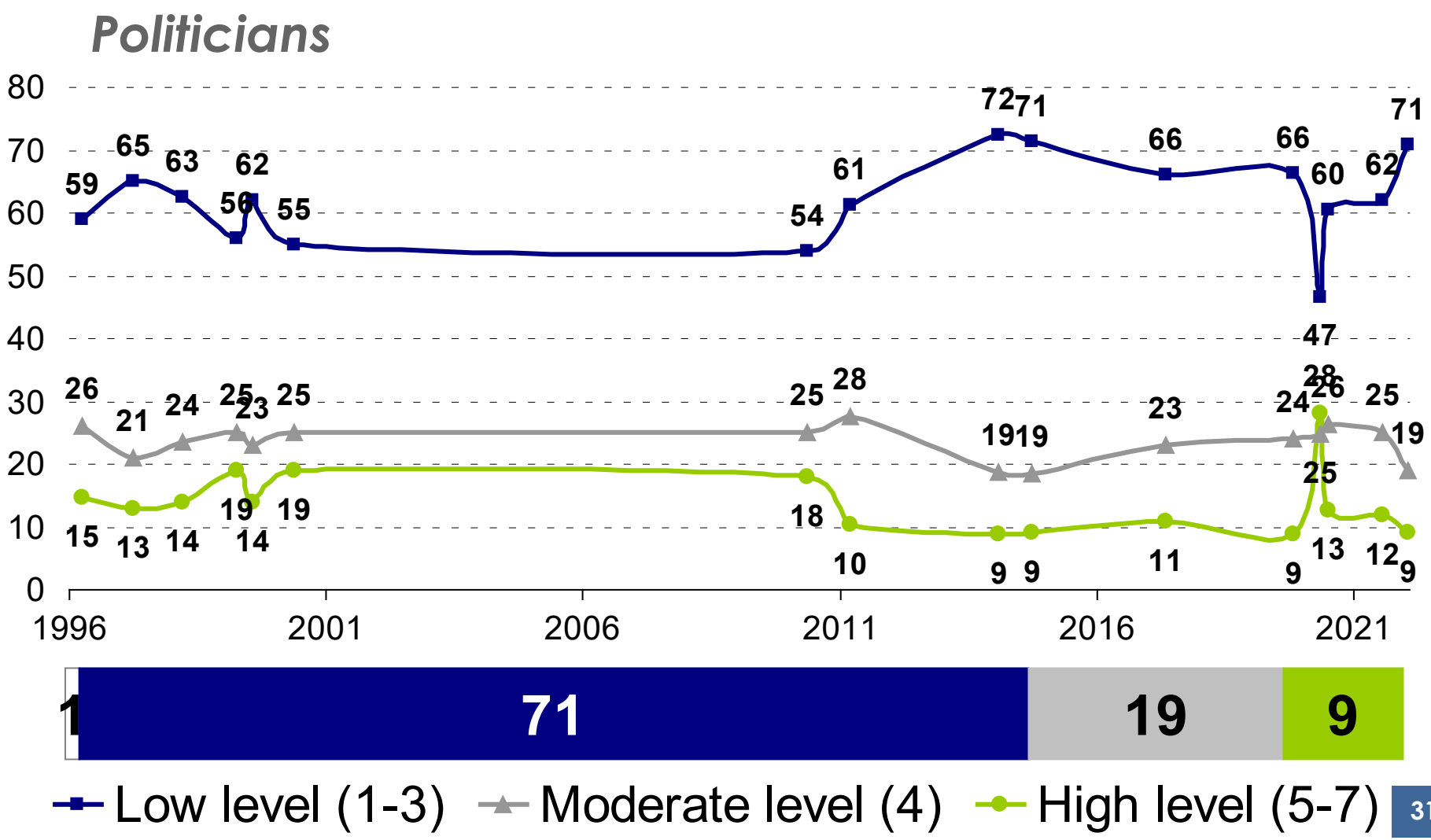


BASE: *Canadians; January 18-24, 2022, n=1,223, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Trust in occupations:
Politicians

Q. *How much trust do you have in each of the following?*



BASE: *Canadians; January 18-24, 2022, n=1,223, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

1) General Outlook
2) Vaccine Acceptance
3) Approval of Government Response
4) Attitudes to Public Health Measures and Vaccine Mandates
5) Disinformation
6) Conclusions

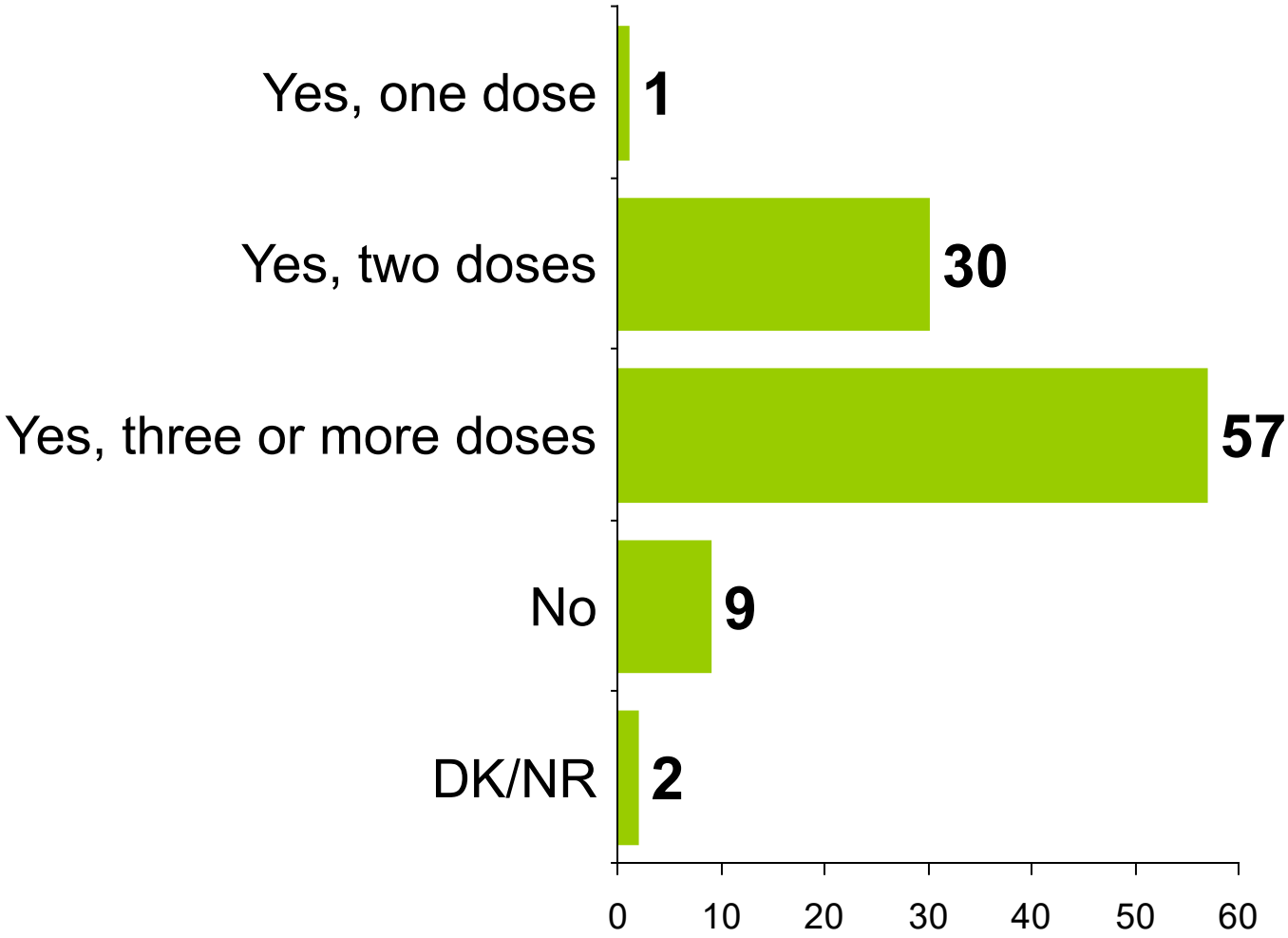
Vaccine acceptance

- Vaccine acceptance remains unchanged, though more than half of Canadians (57%) have now received a booster
- Vaccine refusal is higher among those under 50, non-university educated, and those who reside in the Prairies and rural settings
- Vaccine refusers are also much more distrustful of governments and public institutions and they are more likely to express authoritarian outlooks
- Social class is also a predictor of vaccine acceptance, with poor and working-class Canadians somewhat more likely to have not vaccinated

Copyright 2022
No reproduction without permission

Vaccine acceptance

Q. *Have you received at least one dose of a COVID-19 vaccine?*

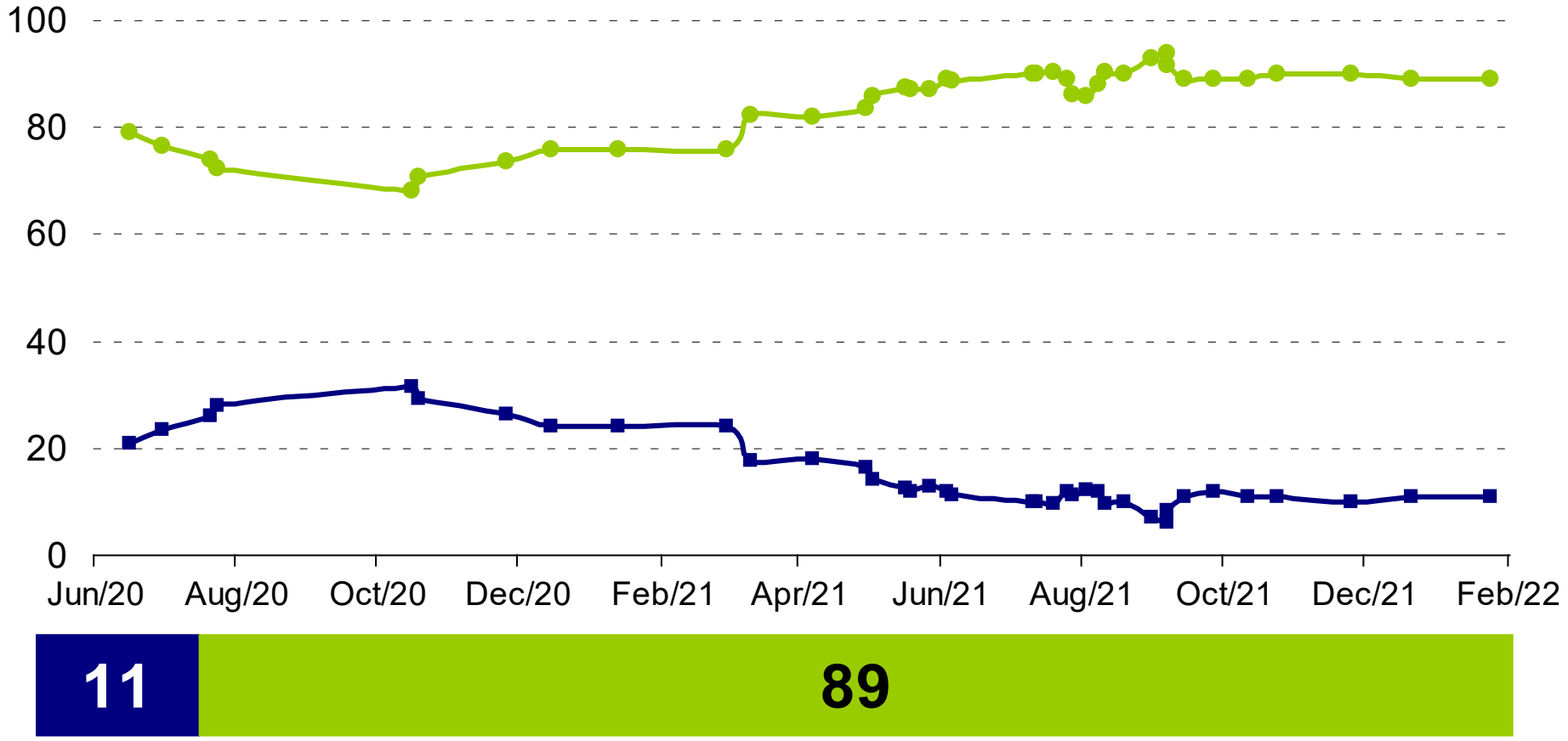


BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Vaccine acceptance

Q. *Have you received at least one dose of a COVID-19 vaccine? / Would you be willing to receive a COVID-19 vaccine if one were available?*

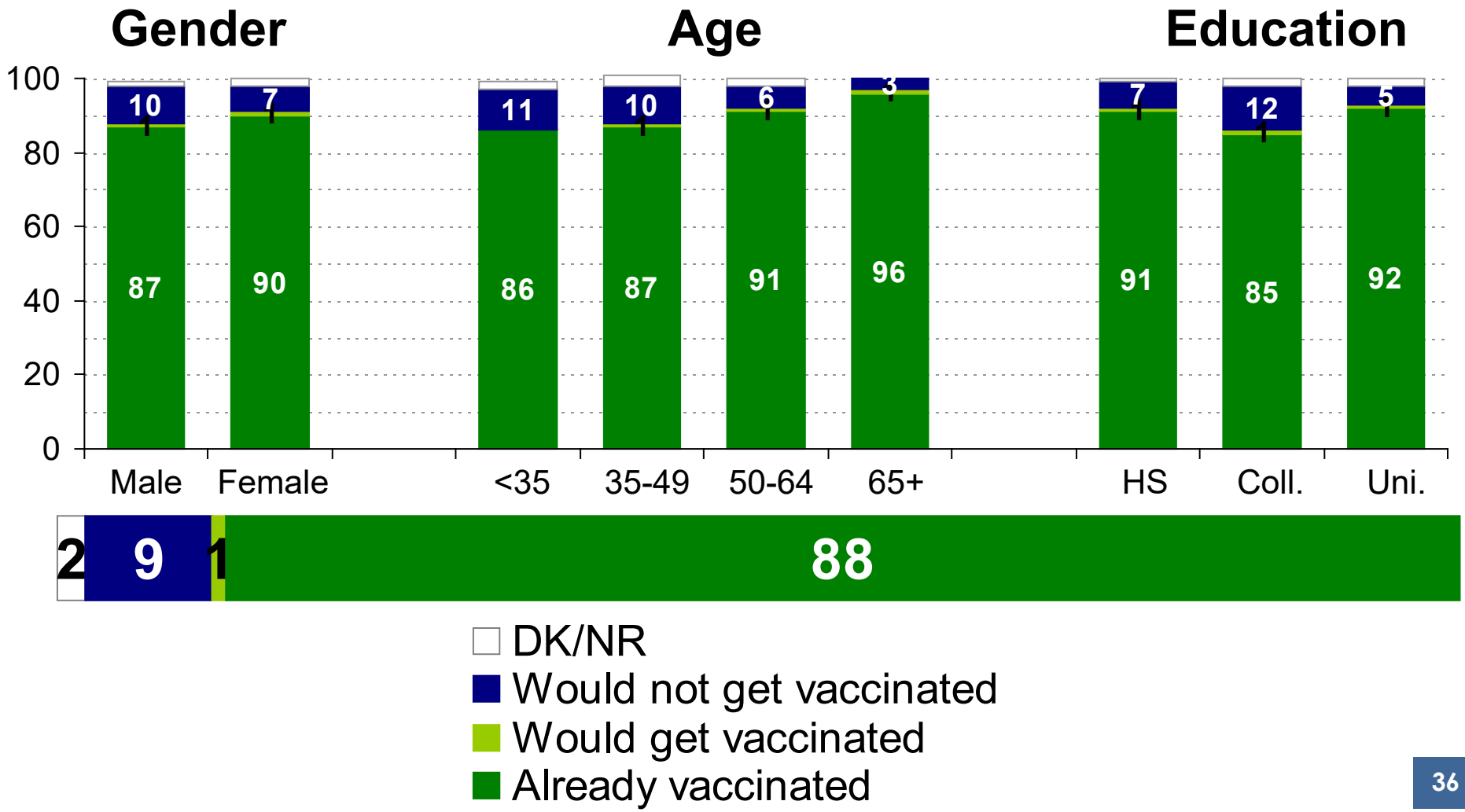


BASE: *Canadians; January 18-24, 2022, n=1,225, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Vaccine acceptance by demographics (i)

Q. *Have you received at least one dose of a COVID-19 vaccine? / Would you be willing to receive a COVID-19 vaccine?*

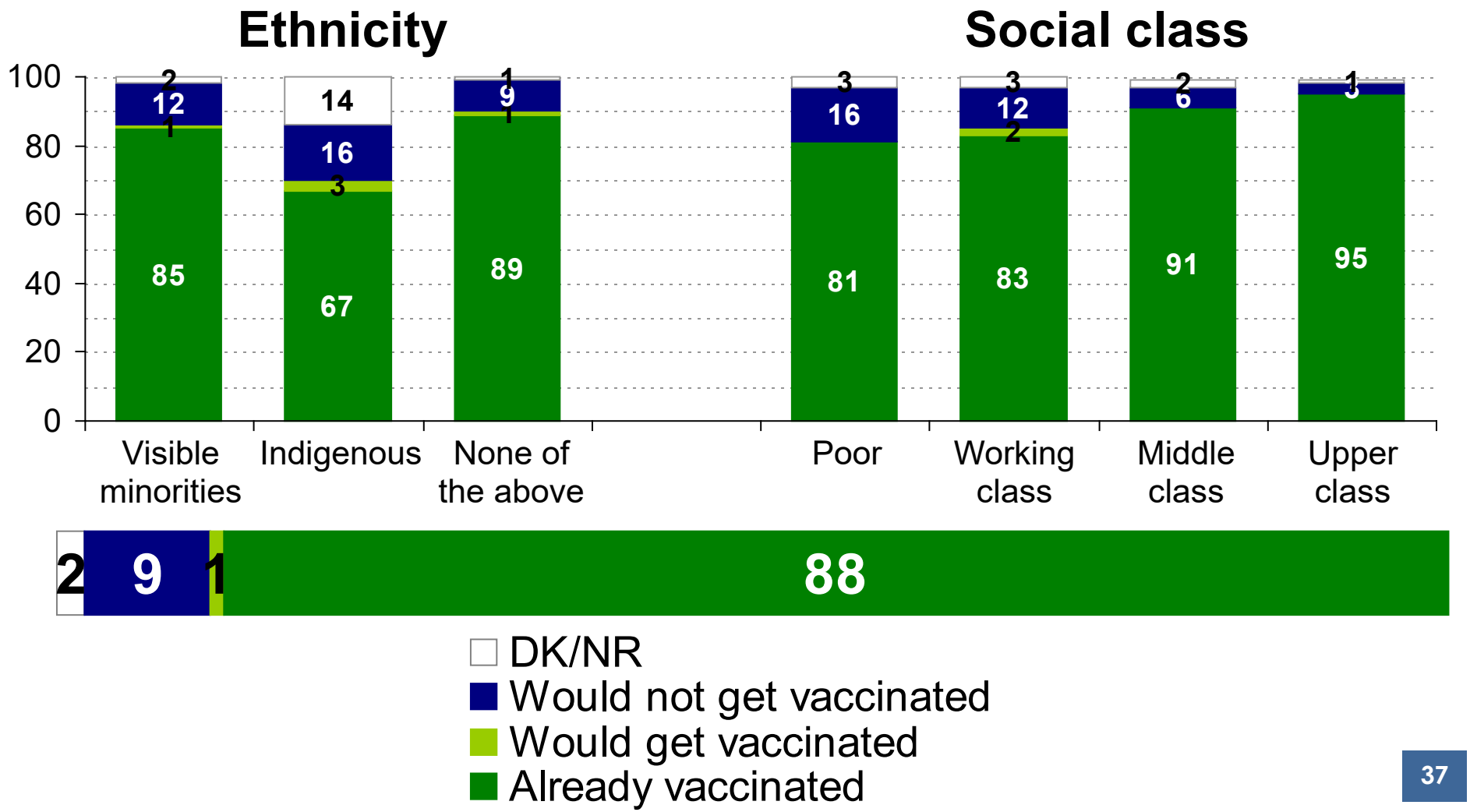


BASE: *Canadians; January 18-24, 2022, n=1,225, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Vaccine acceptance by demographics (ii)

Q. *Have you received at least one dose of a COVID-19 vaccine? / Would you be willing to receive a COVID-19 vaccine?*

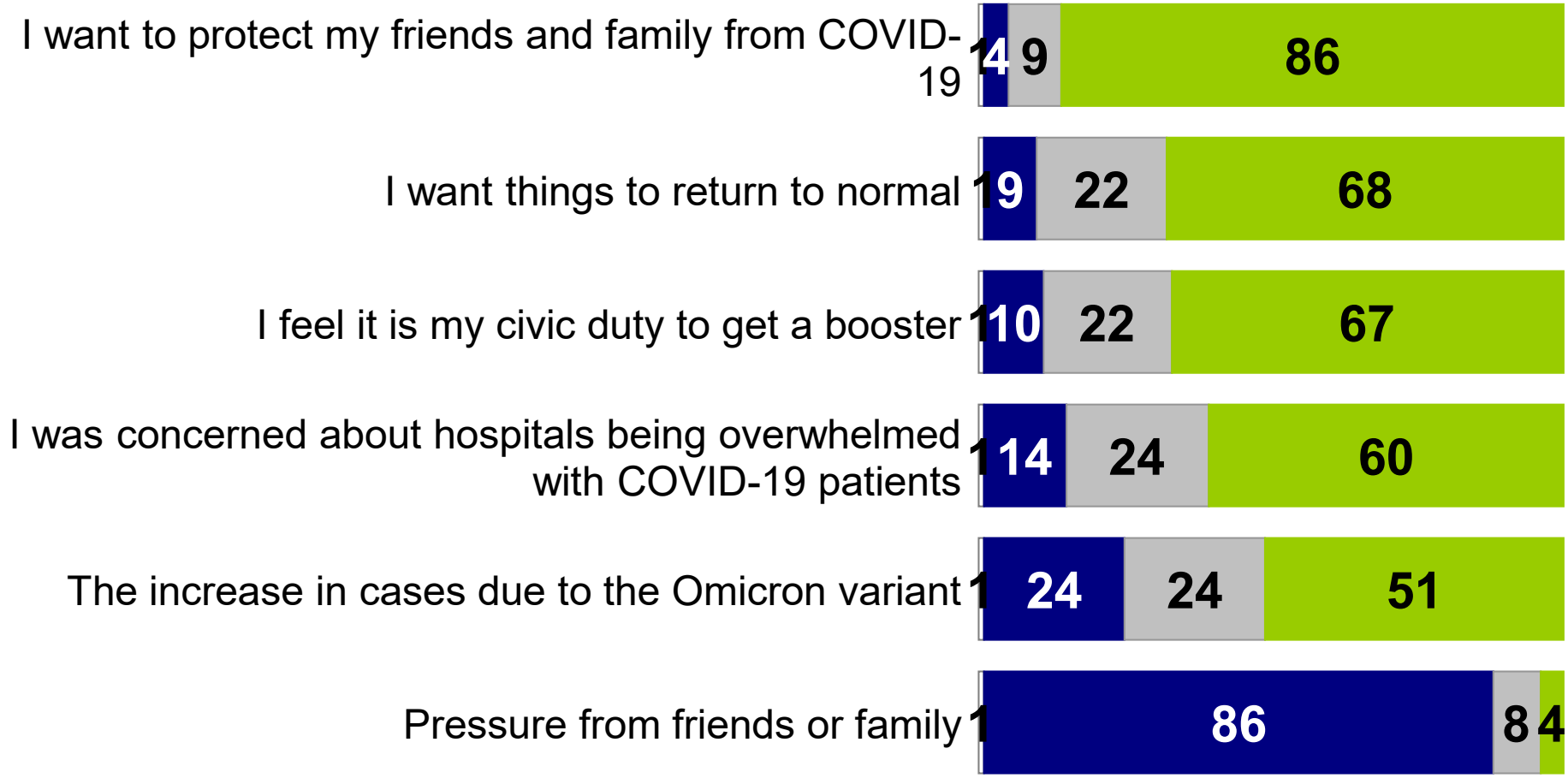


BASE: *Canadians; January 18-24, 2022, n=1,225, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Major reasons for seeking booster

Q. *[IF 3+ DOSES] Would you say each of the following was a major reason, minor reason, or not a reason for why you decided to receive a COVID-19 booster?*

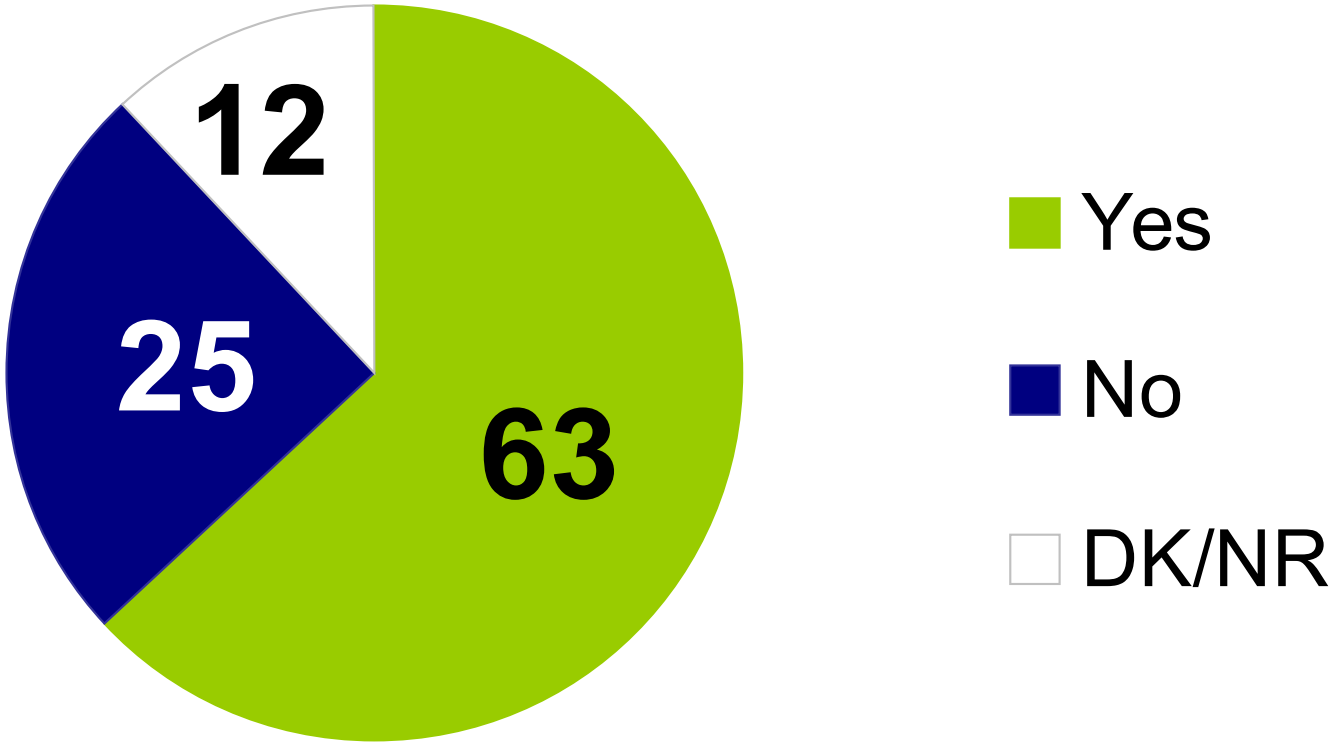


BASE: *If 3+ doses; January 18-24, 2022, n=728, MOE +/- 3.6%,19 times out of 20*

Copyright 2022
No reproduction without permission

Openness to boosters

Q. *[IF RECEIVED TWO DOSES] Would you be willing to receive a third dose of a COVID-19 vaccine?*

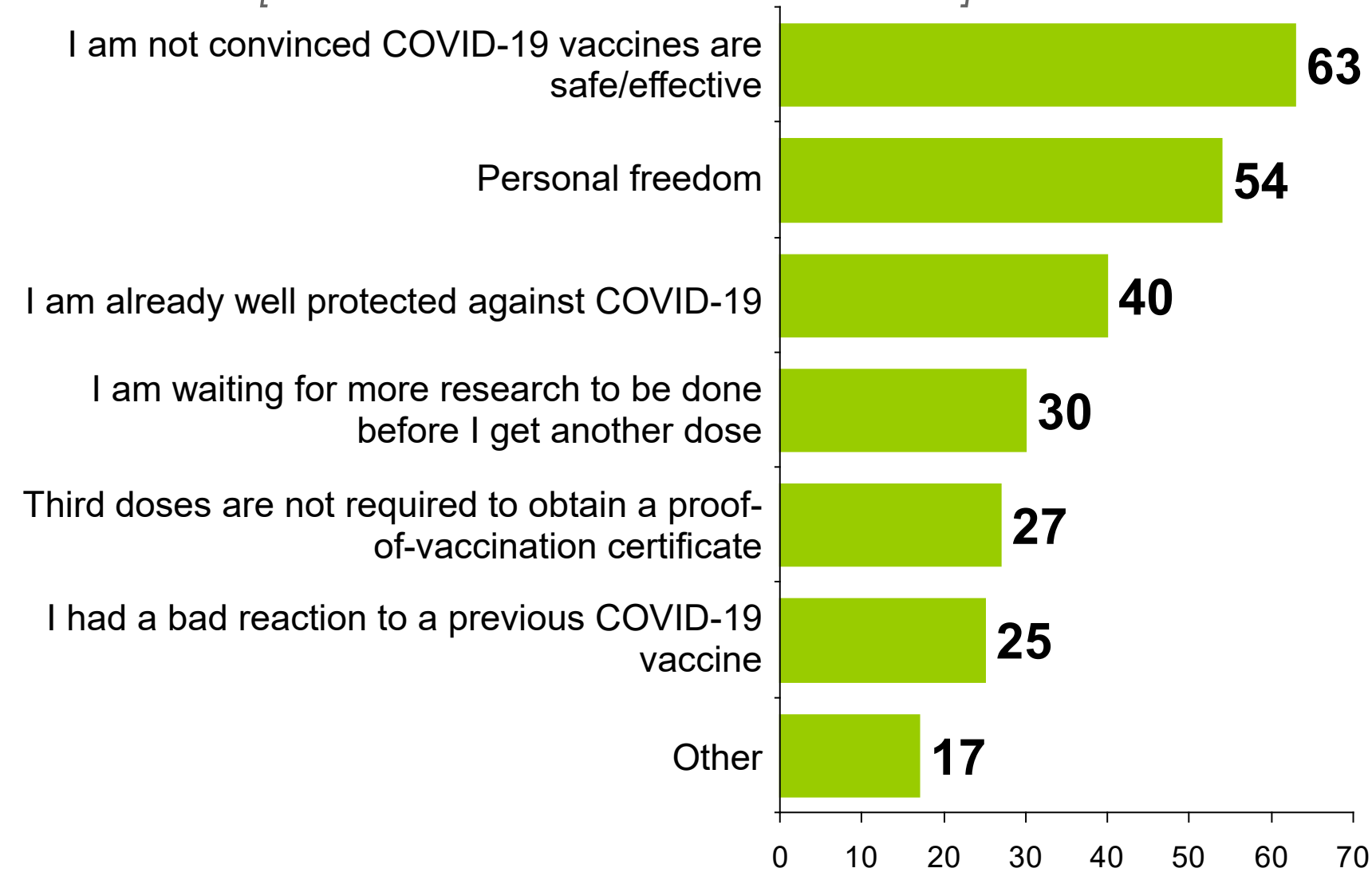


BASE: *Received two doses; January 18-24, 2022 , n=347, MOE +/- 5.3%, 19 times out of 20*

Copyright 2022
No reproduction without permission

Reasons for not getting booster

Q. *[IF NOT WILLING TO RECEIVE A THIRD DOSE] Why do you say that? [MULTIPLE RESPONSES ACCEPTED]*



BASE: *If not wiling to receive a third dose; January 18-24, 2022, n=86, MOE +/- 10.6%, 19 times out of 20*

Copyright 2022
No reproduction without permission

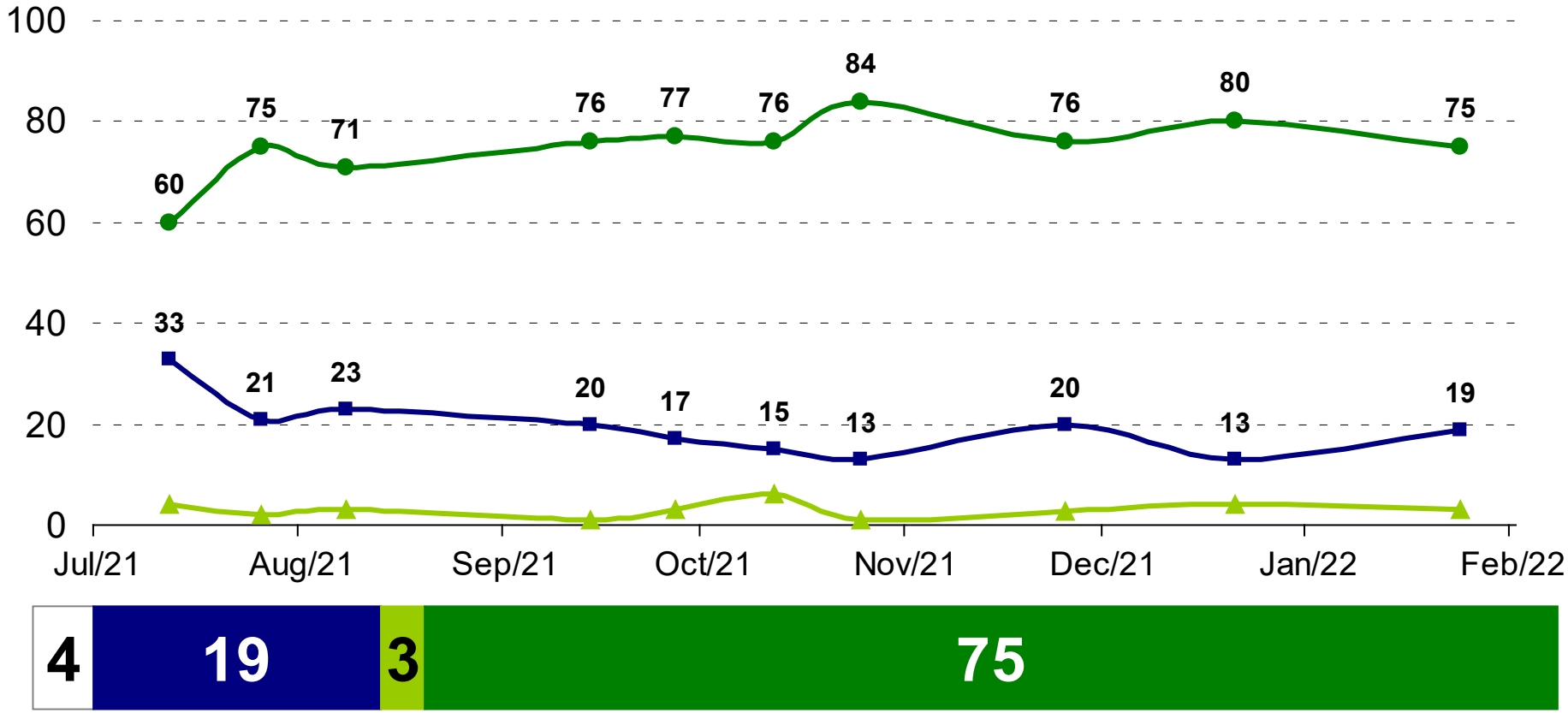
Vaccine acceptance among children

- Results suggest that approximately three-quarters of teenagers aged 12-17 have received a COVID-19 vaccine
  - Among families that have not yet had their eligible teenagers vaccinated, 95% have no intention of doing so
- Paediatric vaccinations are stuck on a path that will fall short of the required levels to achieve herd immunity
  - We would project about two-thirds of children will ultimately be vaccinated without some form of intervention

Copyright 2022
No reproduction without permission

Incidence of COVID-19 vaccines in teens

Q. *[IF 1 CHILD OR 2+ CHILDREN 12-17] Thinking of your [CHILD/CHILDREN] aged 12-17, have they received at least one dose of a COVID-19 vaccine?*

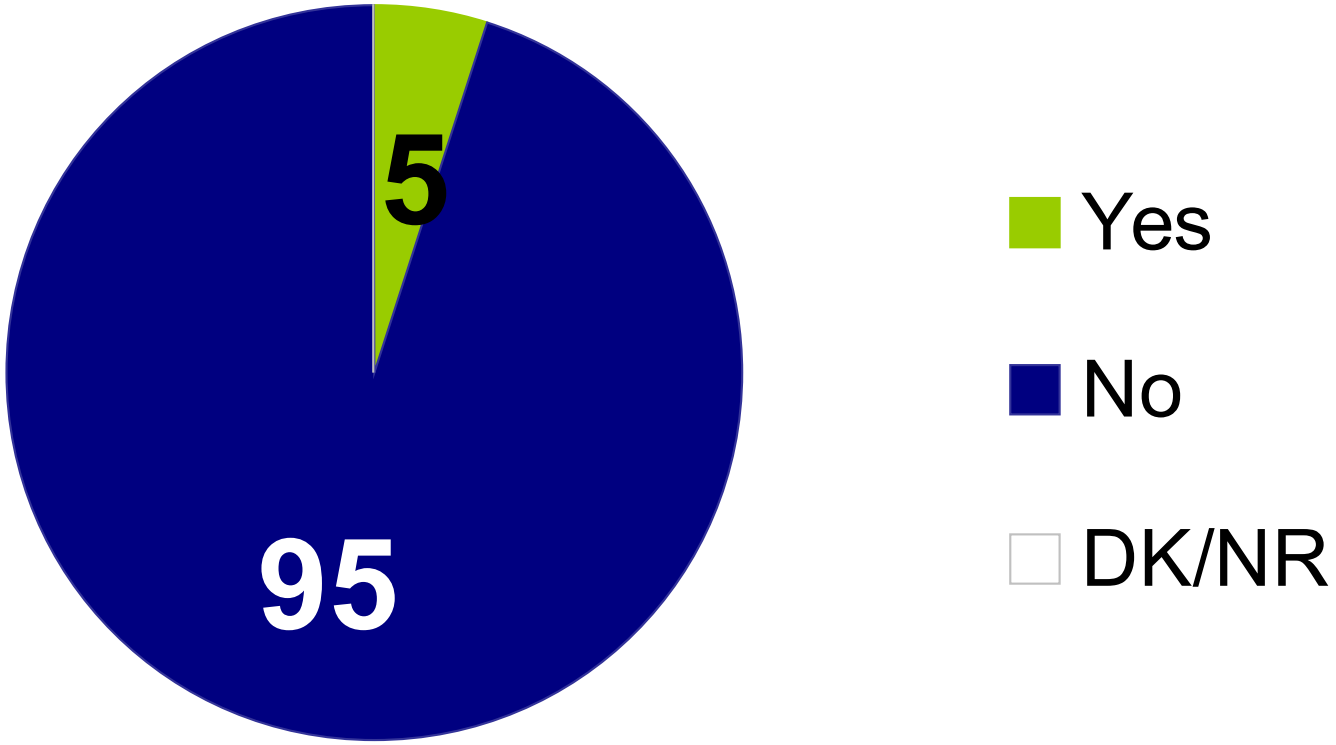


BASE: *If 1 child or 2+ children 12-17; January 18-24, 2022, n=139, MOE +/- 8.3%,19 times out of 20*

Copyright 2022
No reproduction without permission

Willingness to vaccinate remaining teens

Q. *[IF CHILD/CHILDREN HAVEN'T RECEIVED AT LEAST ONE DOSE] Thinking of your [CHILD/CHILDREN] aged 12-17, would you be willing to have them receive a COVID-19 vaccine?*

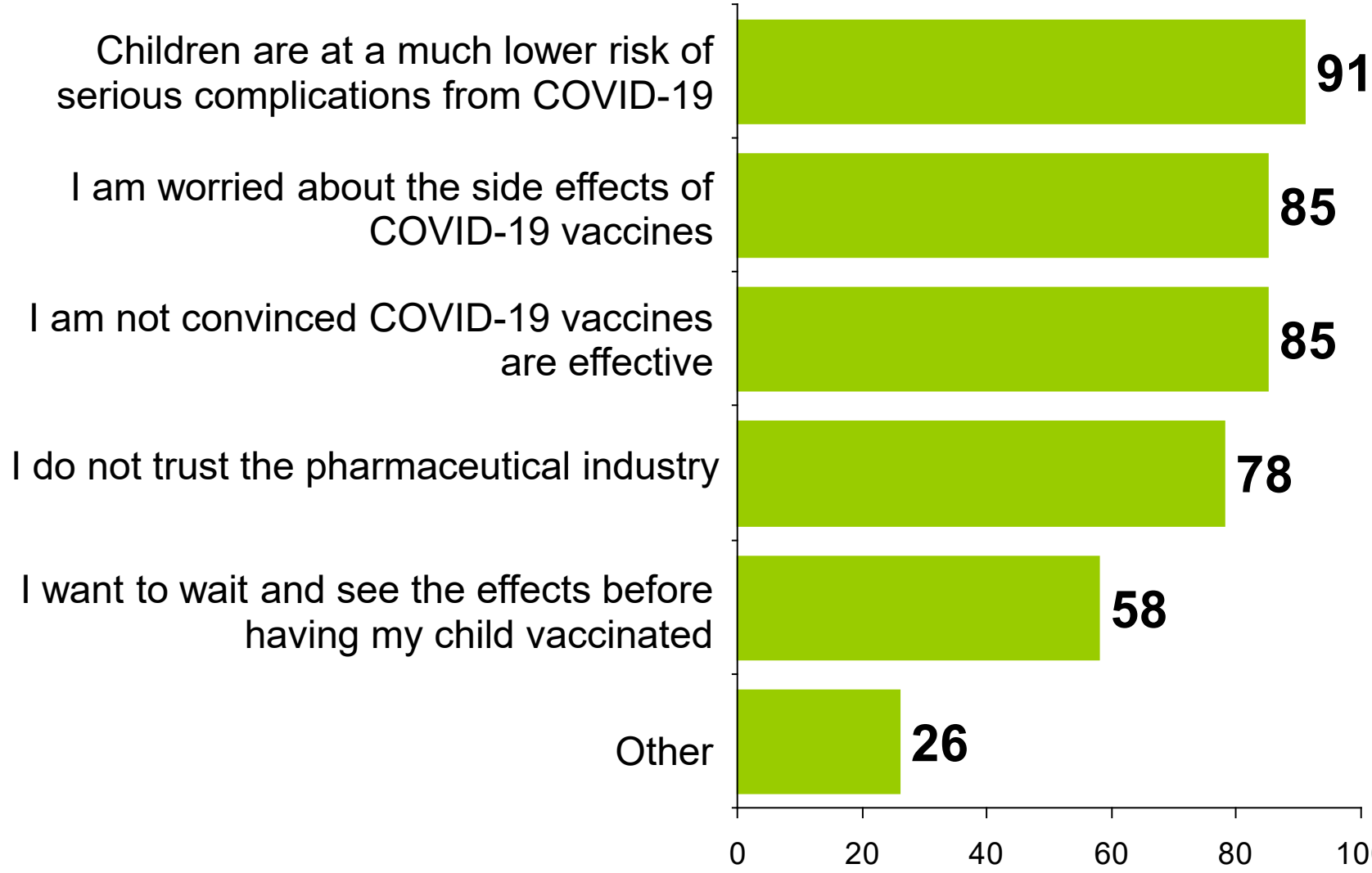


BASE: *If child haven't received at least one dose; January 18-24, 2022, n=26, MOE +/- 19.2%, 19 times out of 20*

Copyright 2022
No reproduction without permission

Reasons for not getting teens vaccinated

Q. *[IF NOT WILLING TO HAVE CHILD/CHILDREN VACCINATED] Why do you say that? [MULTIPLE RESPONSES ACCEPTED]*

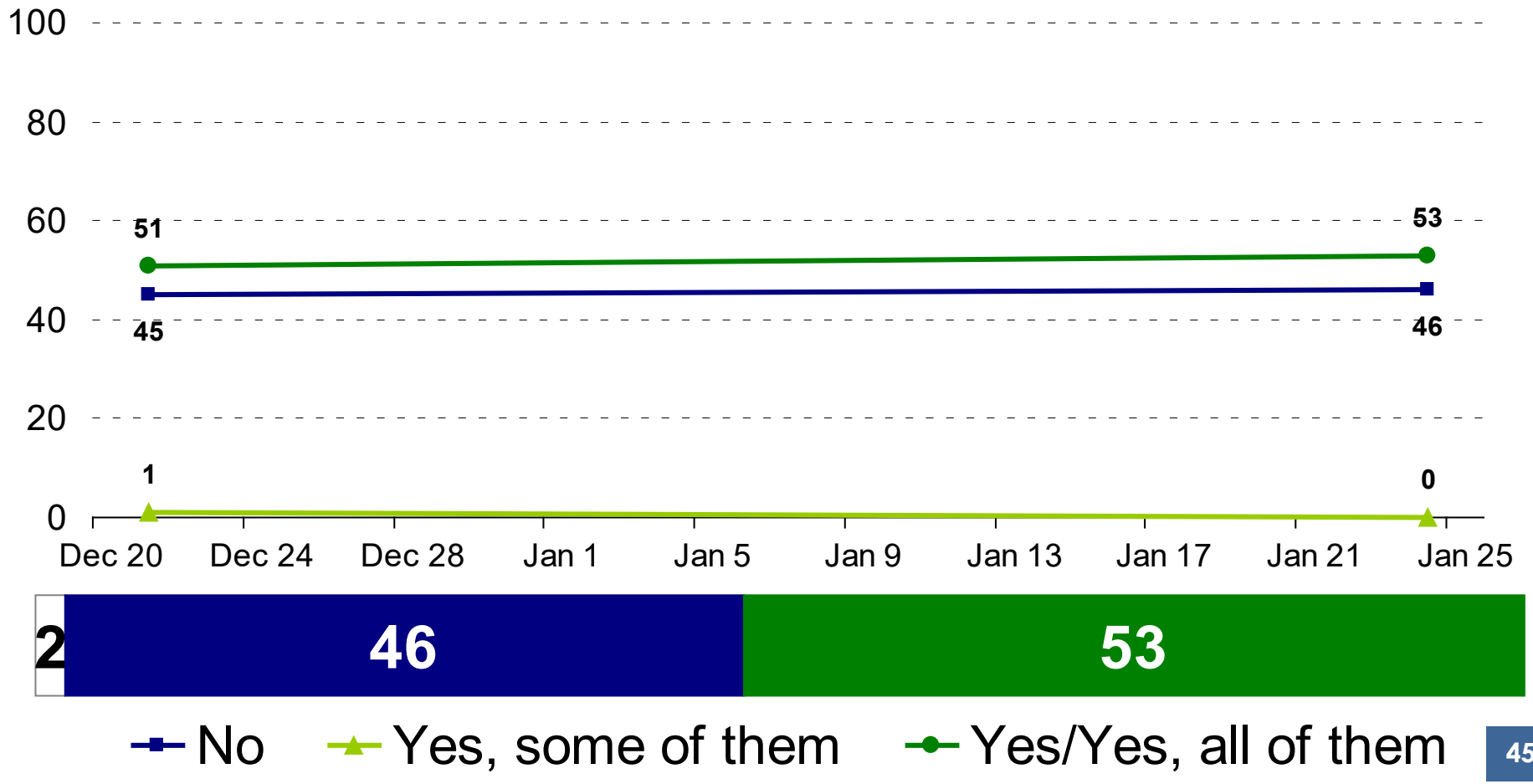


BASE: *If not wiling to have children vaccinated; January 18-24, 2022, n=24, MOE +/- 20.0%, 19 times out of 20*

Copyright 2022
No reproduction without permission

Incidence of COVID-19 vaccines in children

Q. *[IF 1 CHILD OR 2+ CHILDREN 12-17] Thinking of your [CHILD/CHILDREN] aged 12-17, have they received at least one dose of a COVID-19 vaccine?*

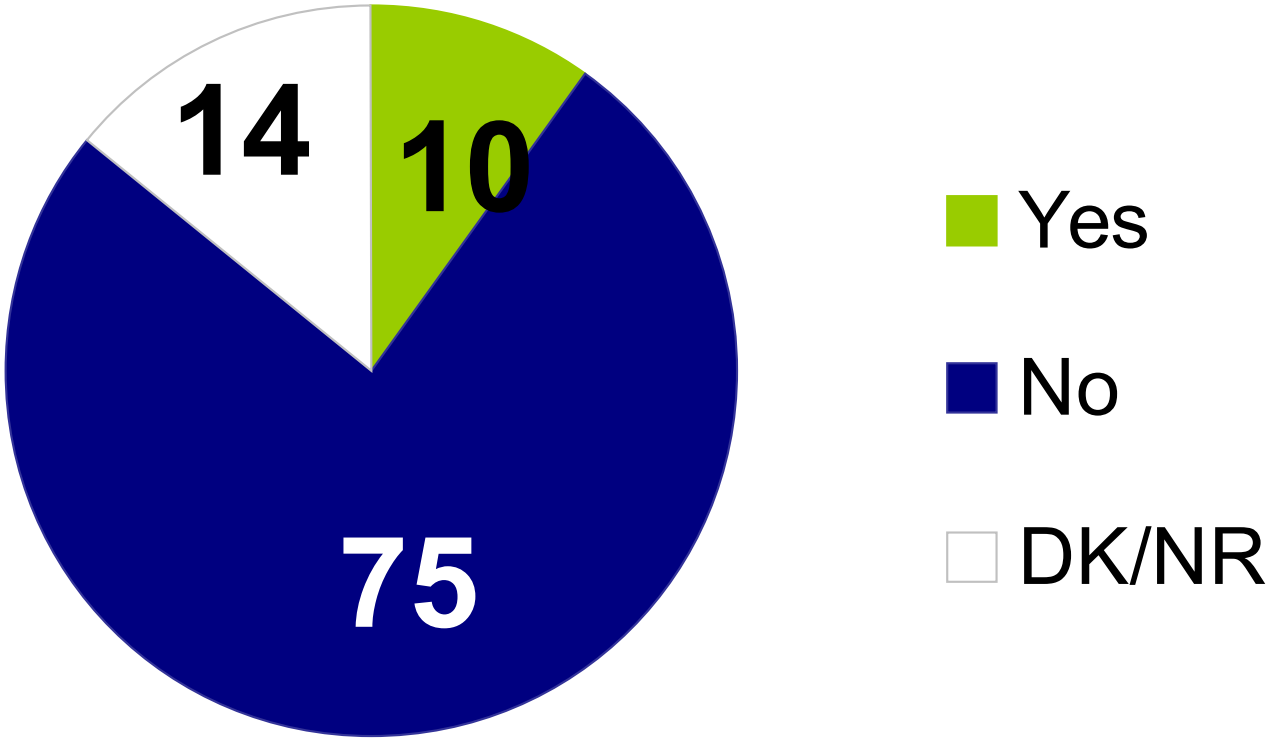


BASE: *If 1 child or 2+ children 12-17; January 18-24, 2022, n=139, MOE +/- 8.3%,19 times out of 20*

Copyright 2022
No reproduction without permission

Willingness to vaccinate remaining children

Q. *[IF CHILD/CHILDREN HAVEN'T RECEIVED AT LEAST ONE DOSE] Thinking of your [CHILD/CHILDREN] aged 5-11, would you be willing to have them receive a COVID-19 vaccine?*

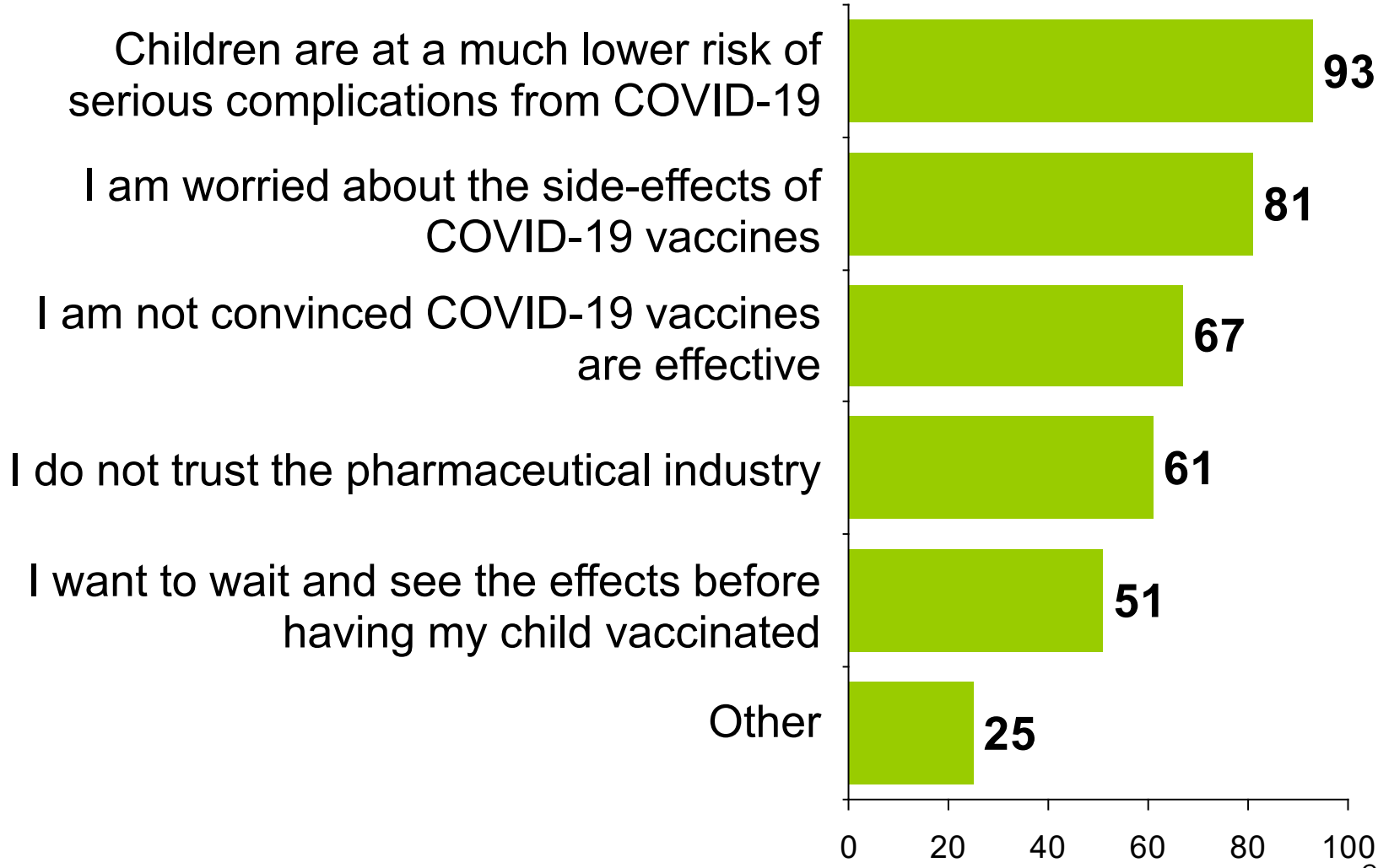


BASE: *If child haven't received at least one dose; January 18-24, 2022, n=75, MOE +/- 11.3%, 19 times out of 20*

Copyright 2022
No reproduction without permission

Reasons for not willing to get children vaccinated

Q. *[IF NOT WILLING TO HAVE CHILD/CHILDREN VACCINATED] Why do you say that?*



BASE: *Not willing to have children vaccinated; January 18-24, 2022, n=54, MOE +/- 13.3%,19 times out of 20*

Copyright 2022
No reproduction without permission

1) General Outlook
2) Vaccine Acceptance
3) **Approval of Government Response**
4) Attitudes to Public Health Measures and Vaccine Mandates
5) Disinformation
6) Conclusions

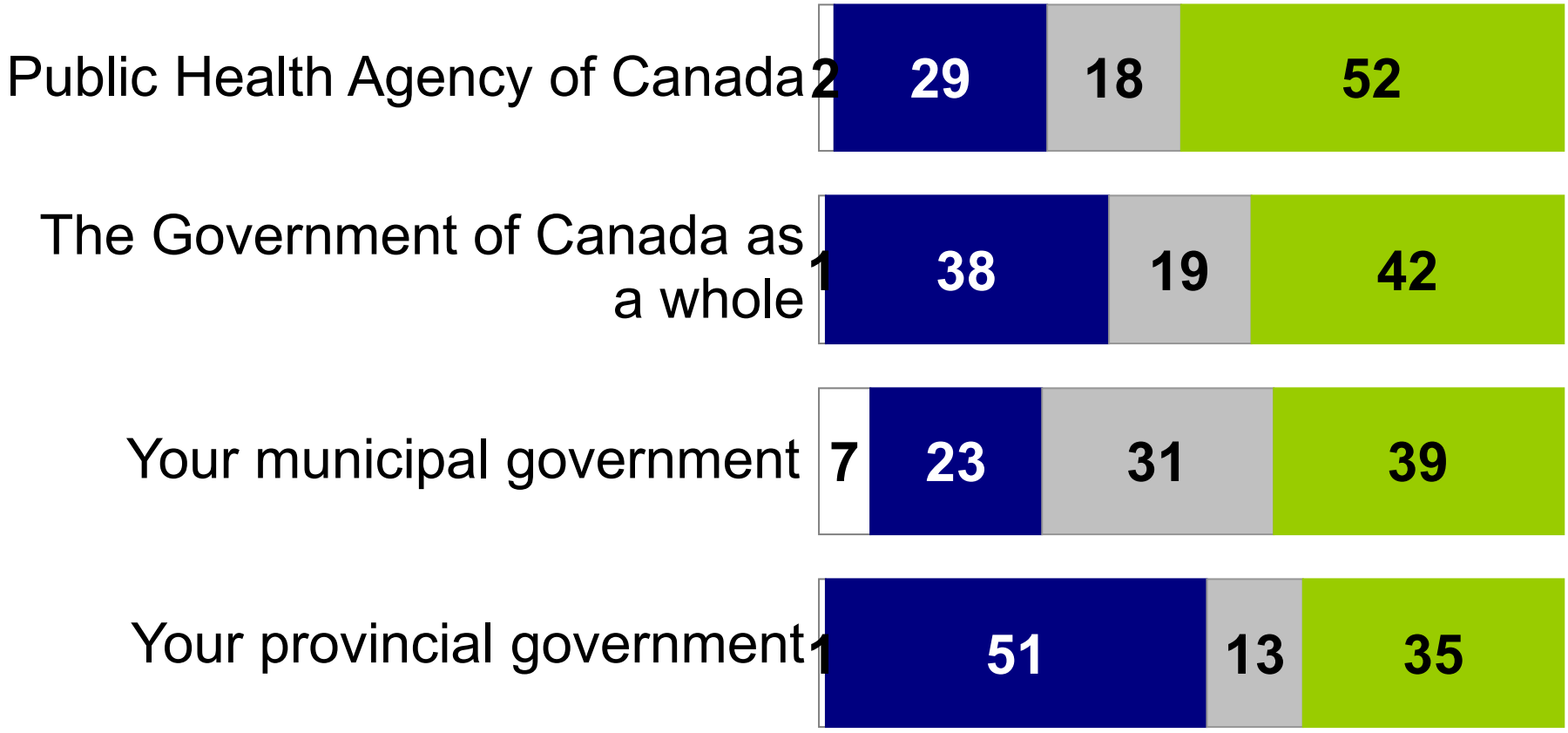
Approval of government response

- There is some evidence that the protracted pandemic has had a corrosive impact on trust and approval of governments
  - Four in ten Canadians (42%) approve of how the Government of Canada has handled the pandemic, down from 47% in October 2021
  - Provincial approval is also down slightly (35%, down from 39%), though this decline is driven primarily by a 19-point erosion in Quebec (42%, down from 61%)
  - In the case of provincial governments, public approval is lowest in the Prairies (particularly Alberta) and Ontario
  - Approval is strongly correlated with compliance and vaccine acceptance, with vaccine refusers giving the harshest ratings

Copyright 2022
No reproduction without permission

Approval of government response to COVID-19

Q. *All things considered, how strongly do you approve or disapprove of how each of the following is handling the COVID-19 pandemic?*

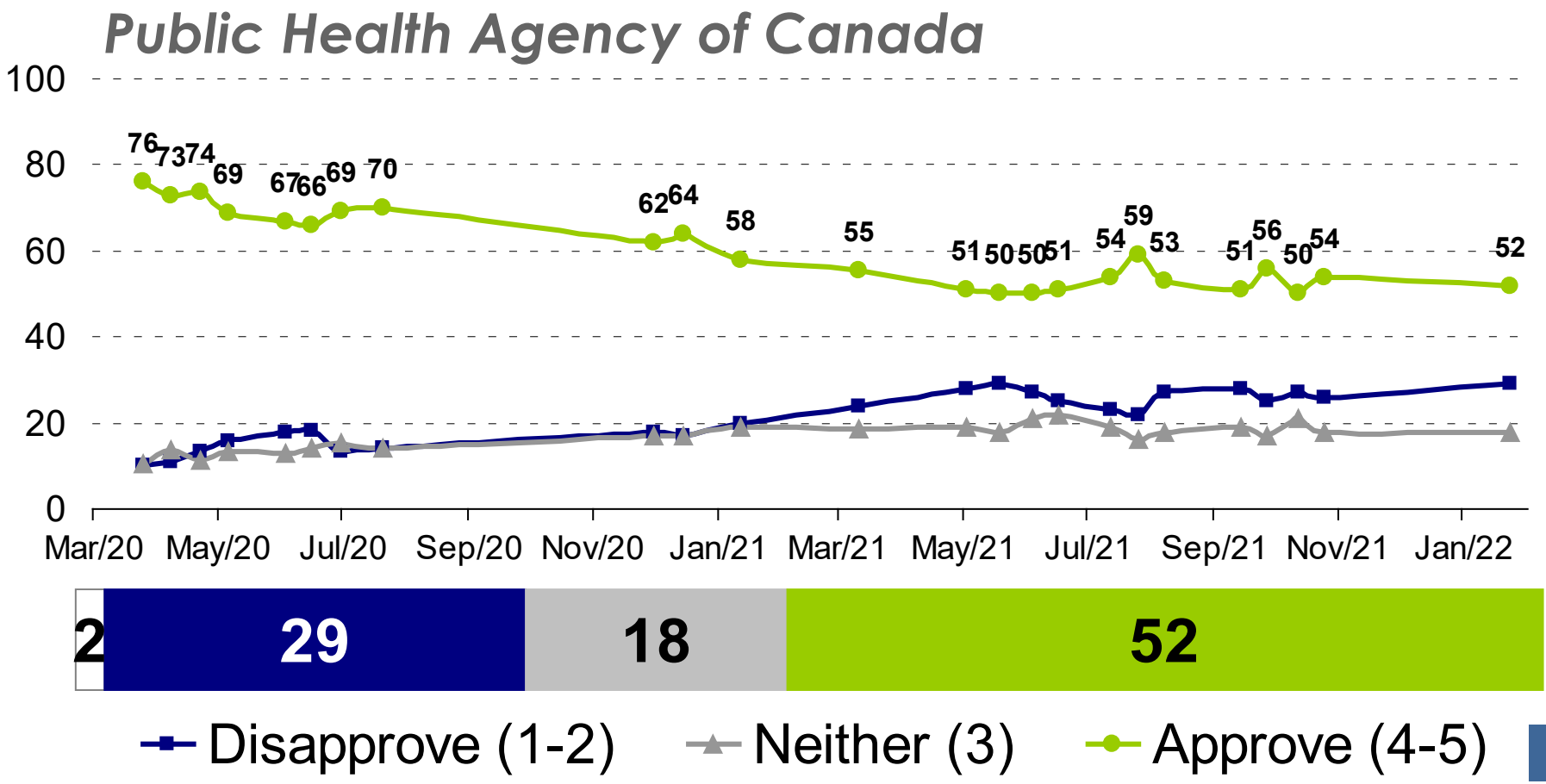


BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Approval of government response to COVID-19:
Public Health Agency of Canada

Q. *All things considered, how strongly do you approve or disapprove of how each of the following is handling the COVID-19 pandemic?*



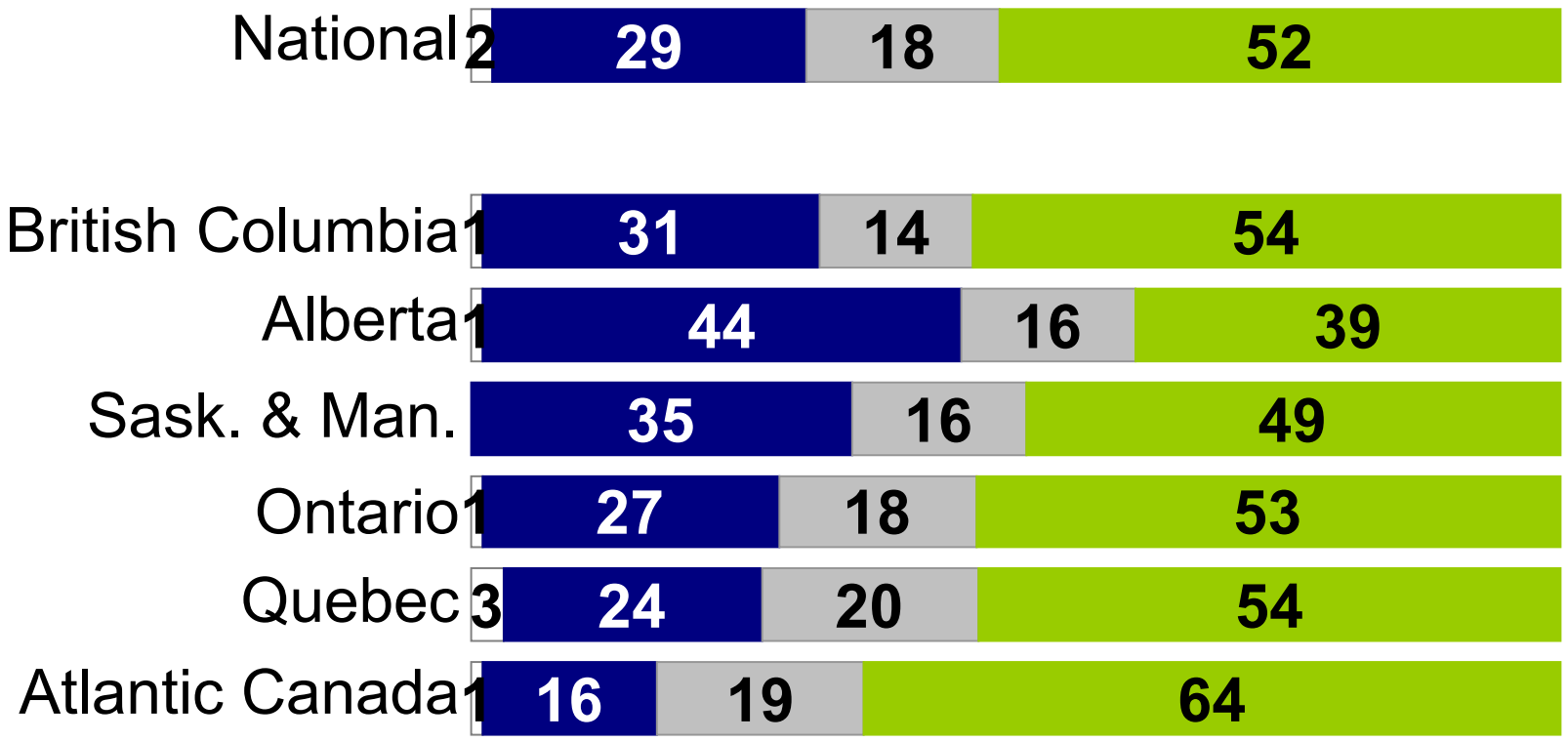
BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Approval of PHAC's response to COVID-19

Q. *All things considered, how strongly do you approve or disapprove of how each of the following is handling the COVID-19 pandemic?*

Public Health Agency of Canada



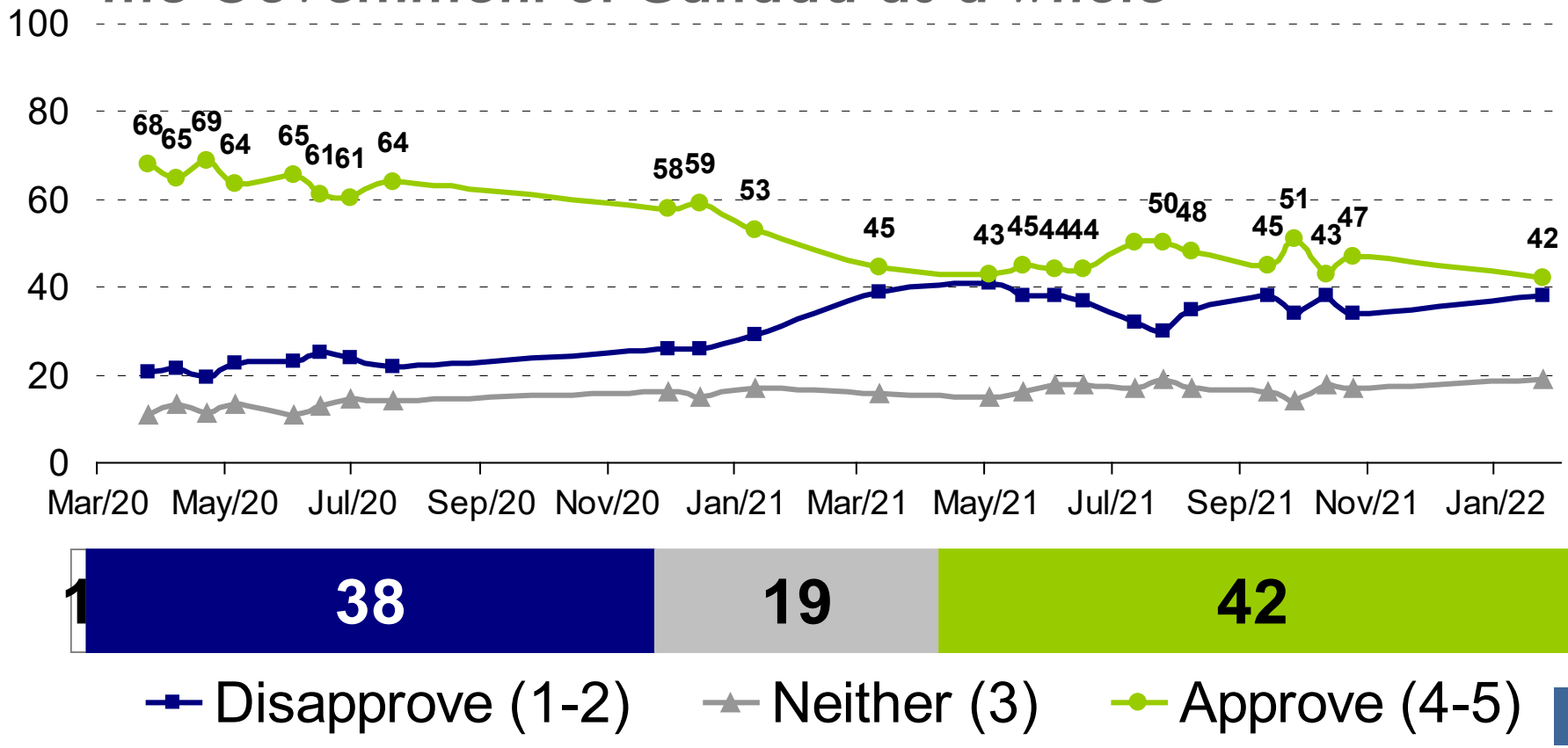
BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Approval of government response to COVID-19:
Government of Canada as a whole

Q. *All things considered, how strongly do you approve or disapprove of how each of the following is handling the COVID-19 pandemic?*

The Government of Canada as a whole



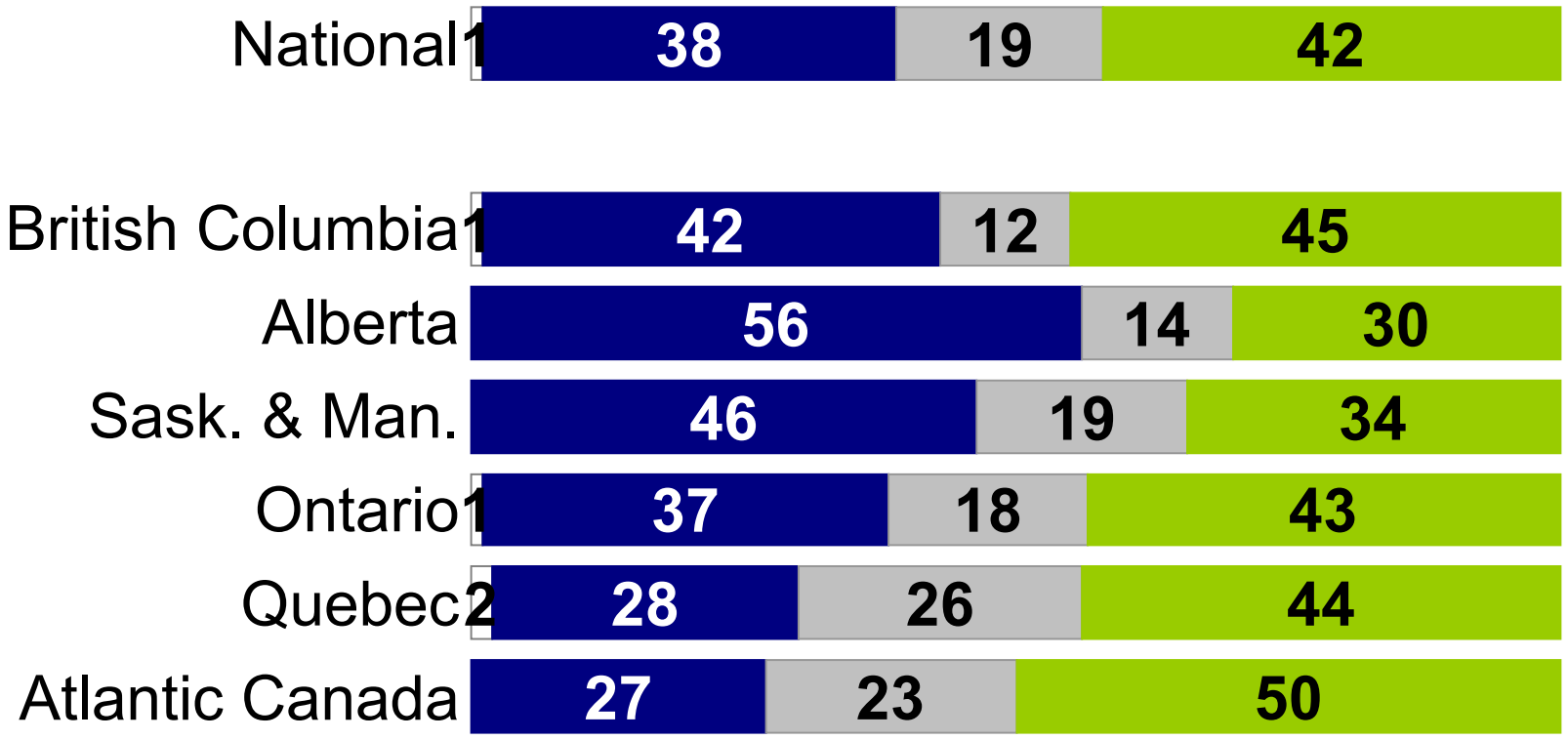
BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Approval of federal response to COVID-19

Q. *All things considered, how strongly do you approve or disapprove of how each of the following is handling the COVID-19 pandemic?*

The Government of Canada as a whole



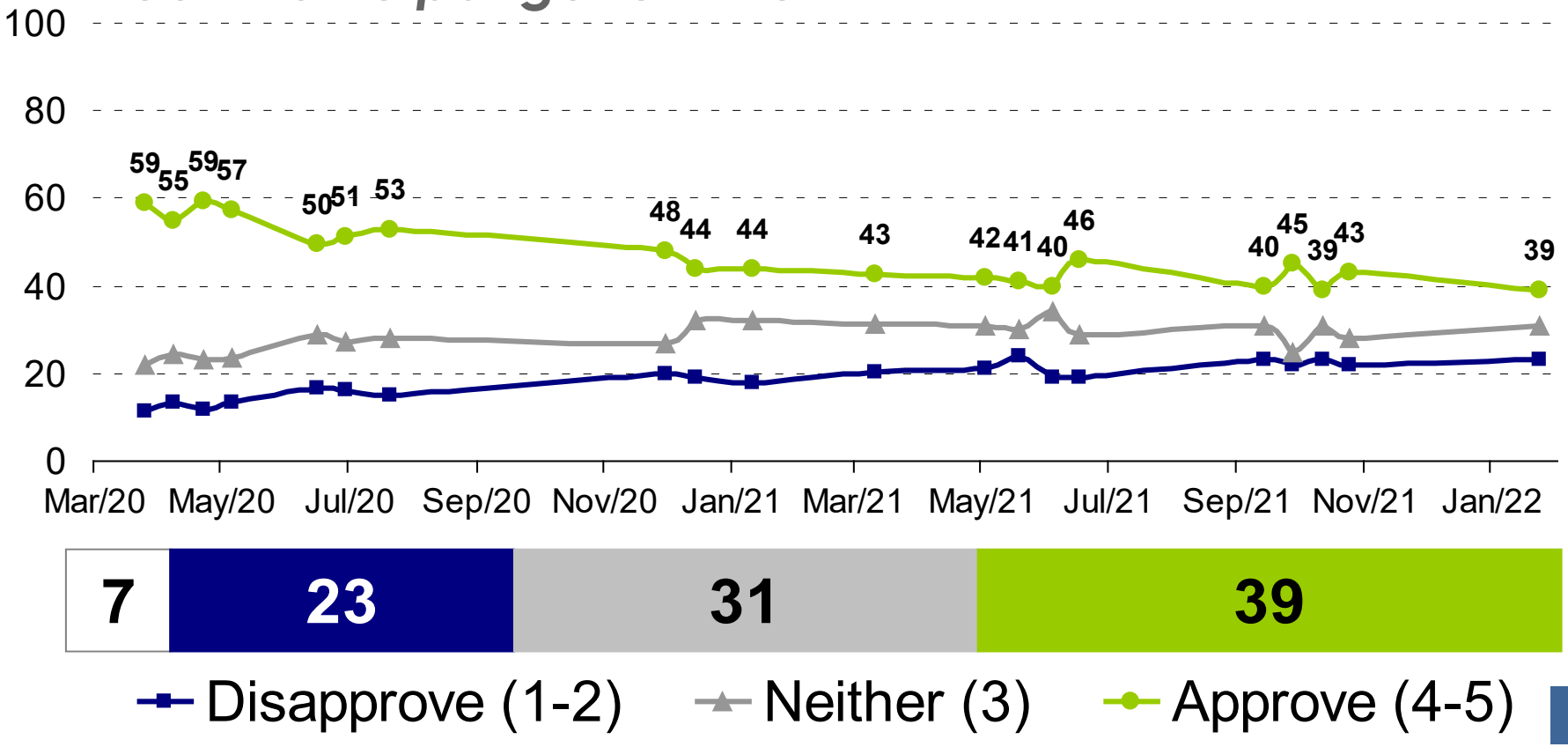
BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Approval of government response to COVID-19:
Municipal governments

Q. *All things considered, how strongly do you approve or disapprove of how each of the following is handling the COVID-19 pandemic?*

Your municipal government



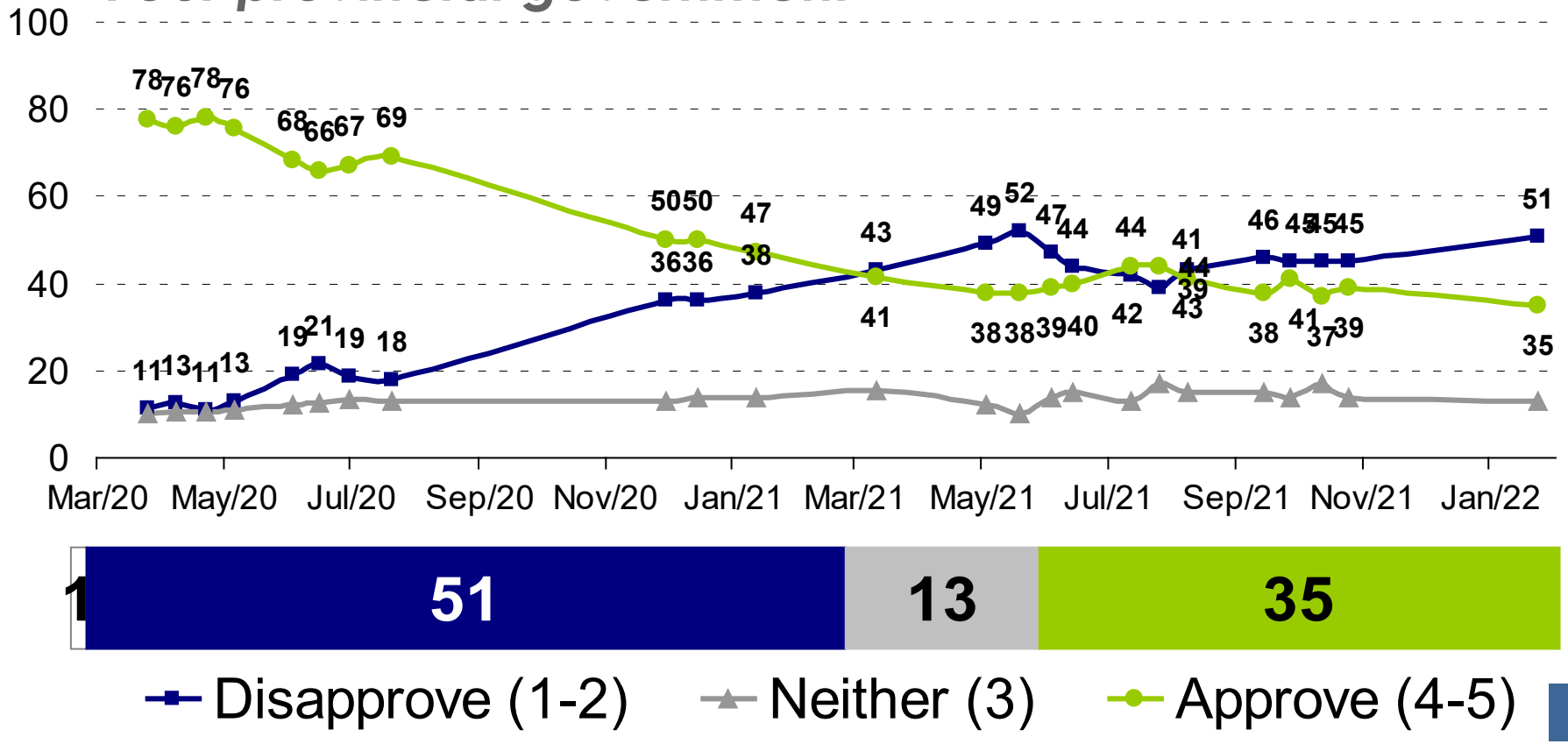
BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Approval of government response to COVID-19: Provincial governments

Q. *All things considered, how strongly do you approve or disapprove of how each of the following is handling the COVID-19 pandemic?*

Your provincial government



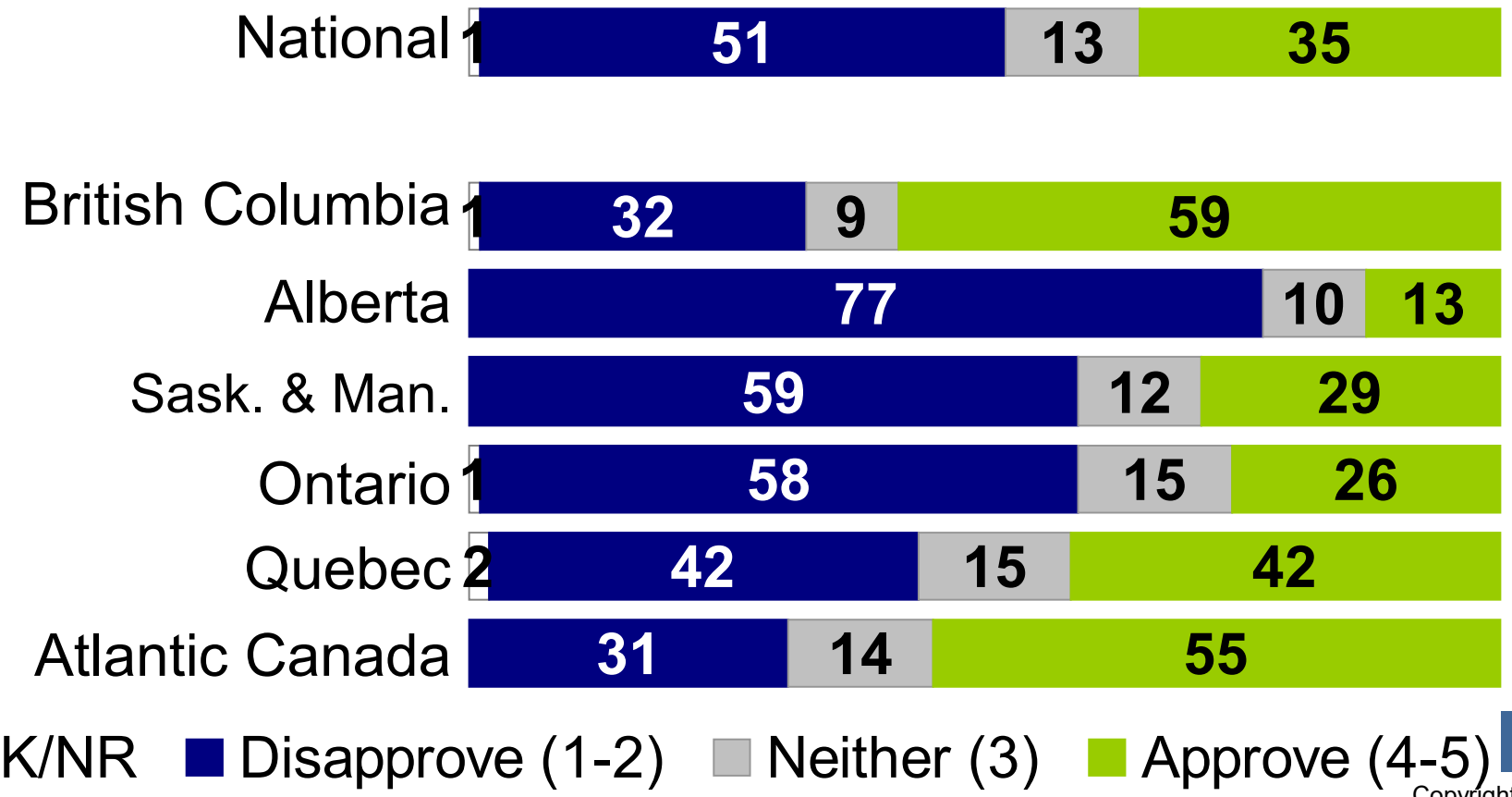
BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Approval of provincial response to COVID-19

Q. *All things considered, how strongly do you approve or disapprove of how each of the following is handling the COVID-19 pandemic?*

Your provincial government

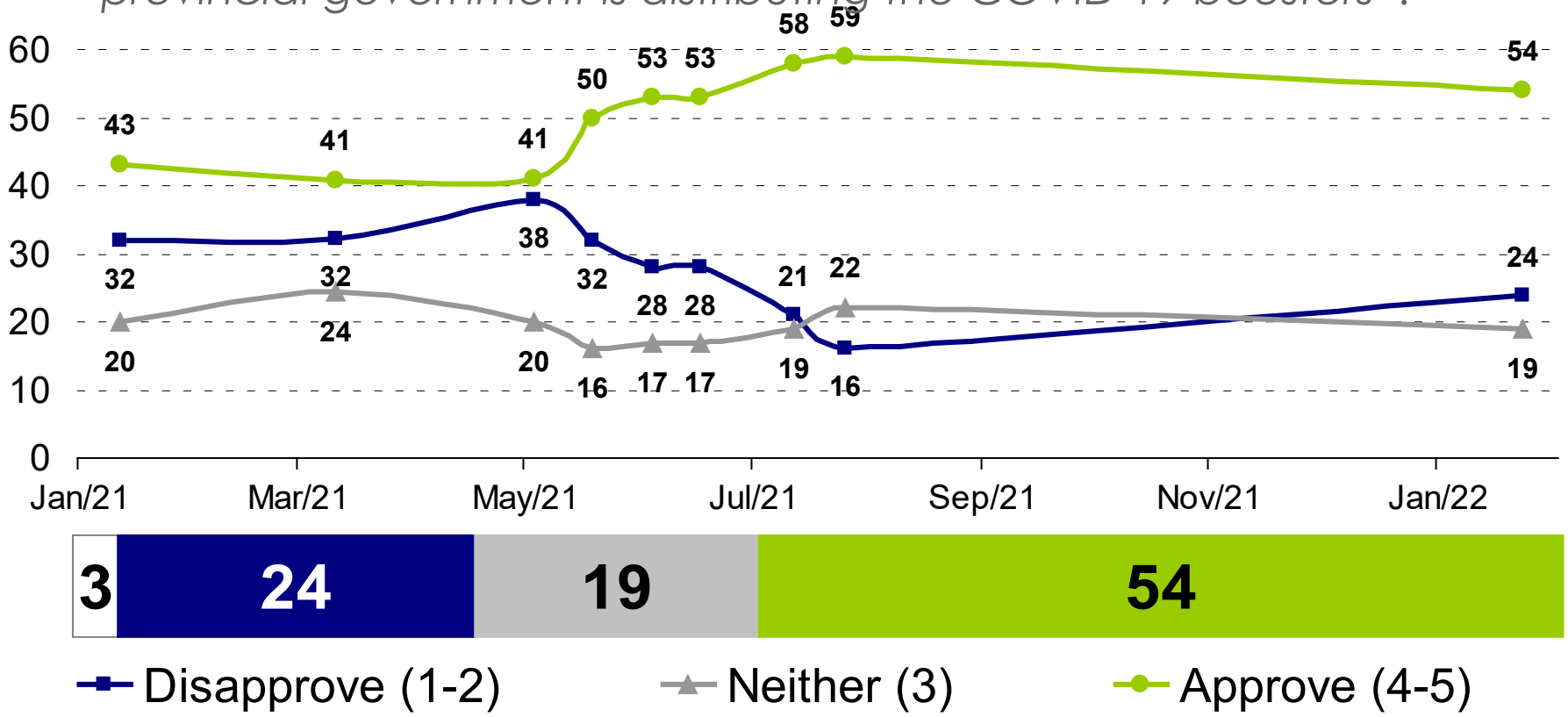


BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Approval of boosters distribution

Q. *As you may know, provinces and territories are mostly responsible for administering the COVID-19 vaccines and determining who receives them. How strongly do you approve or disapprove of how your provincial government is distributing the COVID-19 boosters*?*



**Prior to January 2022, respondents were asked about the distribution of vaccines in general, not specifically boosters*

BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

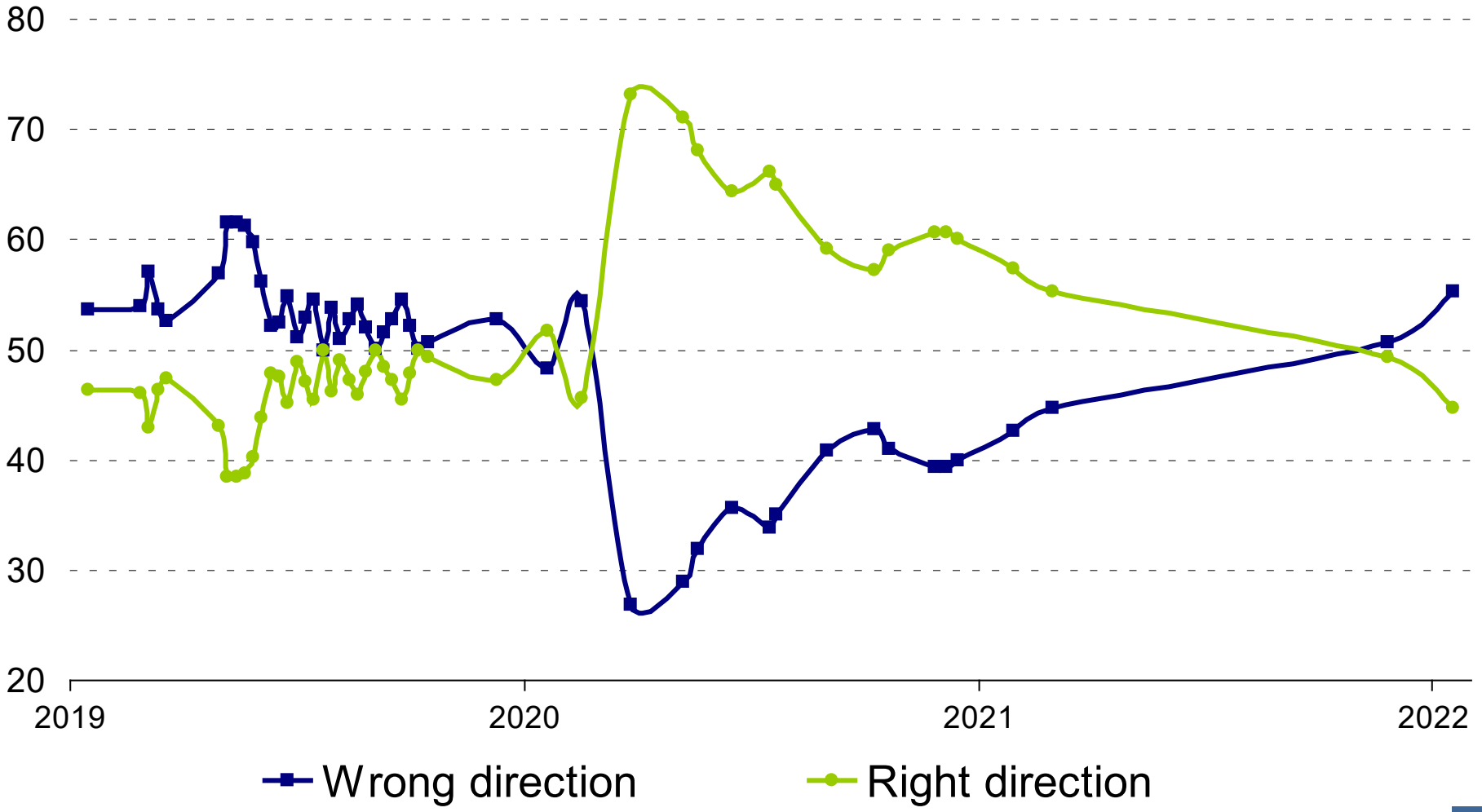
National direction

- We have seen a similar erosion in outlook on national direction and most Canadians now believe both the country and its government are headed in the wrong direction
  - Albertans, those under 50, and working-class Canadians are particularly unhappy
- This finding is problematic given the link between trust in government and vaccine acceptance
  - Among those who are fully vaccinated, the slimmest of majorities (51%) approve of federal direction
  - Among vaccine refusers, however, virtually everyone (98%) believes the federal government is moving in the wrong direction

Copyright 2022
No reproduction without permission

Direction of country

Q. *All things considered, would you say the country is moving in the right direction or the wrong direction?*



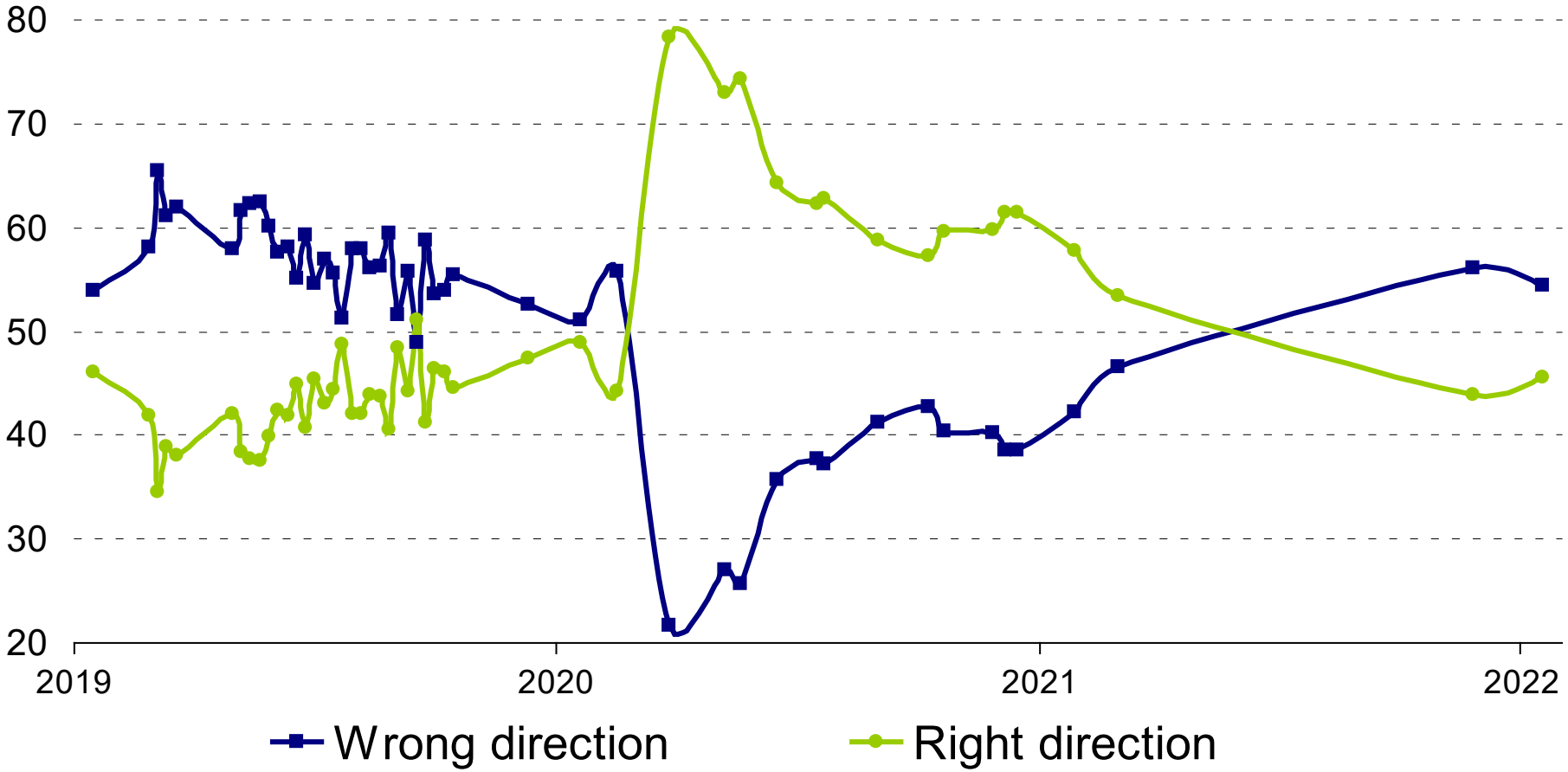
Note: Figures adjusted to exclude those who skipped the question.

BASE: *Canadians (half-sample); January 7-17, 2022, n=1,257, MOE +/- 2.8%, 19 times out of 20*

Copyright 2022
No reproduction without permission

Direction of government

Q. *All things considered, would you say the Government of Canada is moving in the right direction or the wrong direction?*



Note: Figures adjusted to exclude those who skipped the question.

BASE: *Canadians (half-sample); January 7-17, 2022, n=1,355, MOE +/- 2.7%, 19 times out of 20*

Copyright 2022
No reproduction without permission

Direction by vaccine acceptance

Q. *All things considered, would you say the country / the Government of Canada is moving in the right direction or the wrong direction?*

The country



The Government of Canada



Wrong direction Right direction

Note: Figures adjusted to exclude those who indicated 'Don't know/No response'.

BASE: *Canadians (half-sample); January 7-17, 2022, n=1,257-1,355, MOE +/- 2.7-2.8%, 19 times out of 20*

Copyright 2022
No reproduction without permission

1) General Outlook
2) Vaccine Acceptance
3) Approval of Government Response
4) **Attitudes to Public Health Measures and Vaccine Mandates**
5) Disinformation
6) Conclusions

Attitudes to public health measures

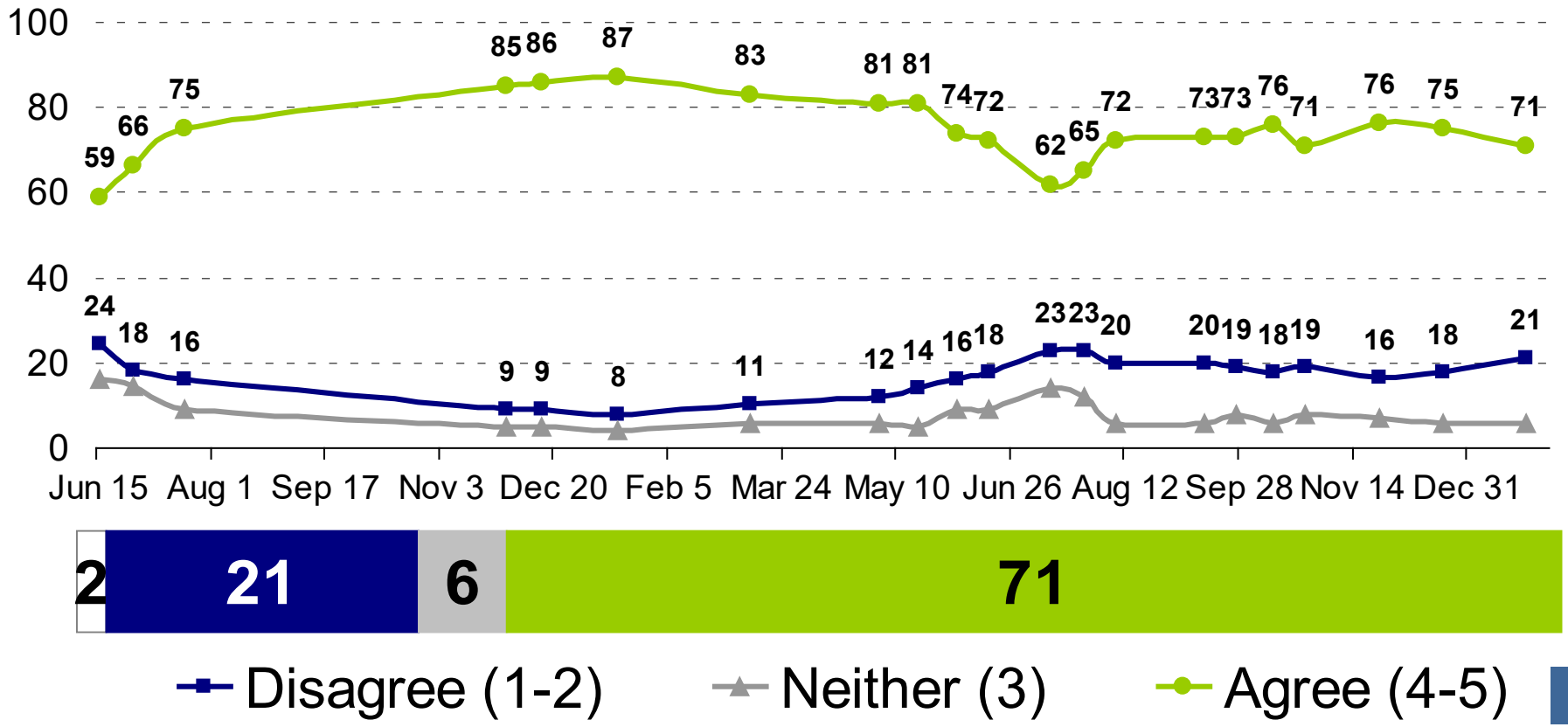
- Support for mask mandates remains strong
  - 71% of Canadians support the continued use of masks
- A 'health tax' on the unvaccinated yields mixed results and there is likely not enough public support to move ahead with this measure
- Curiously, just one in four Canadians (24%) support the use of remote learning in schools until the latest wave subsides

Copyright 2022
No reproduction without permission

Views on COVID-19 response
Compulsory use of masks

Q. *Please rate the extent to which you agree or disagree with the following statement:*

All Canadians should be required to wear masks in stores and while using public transit

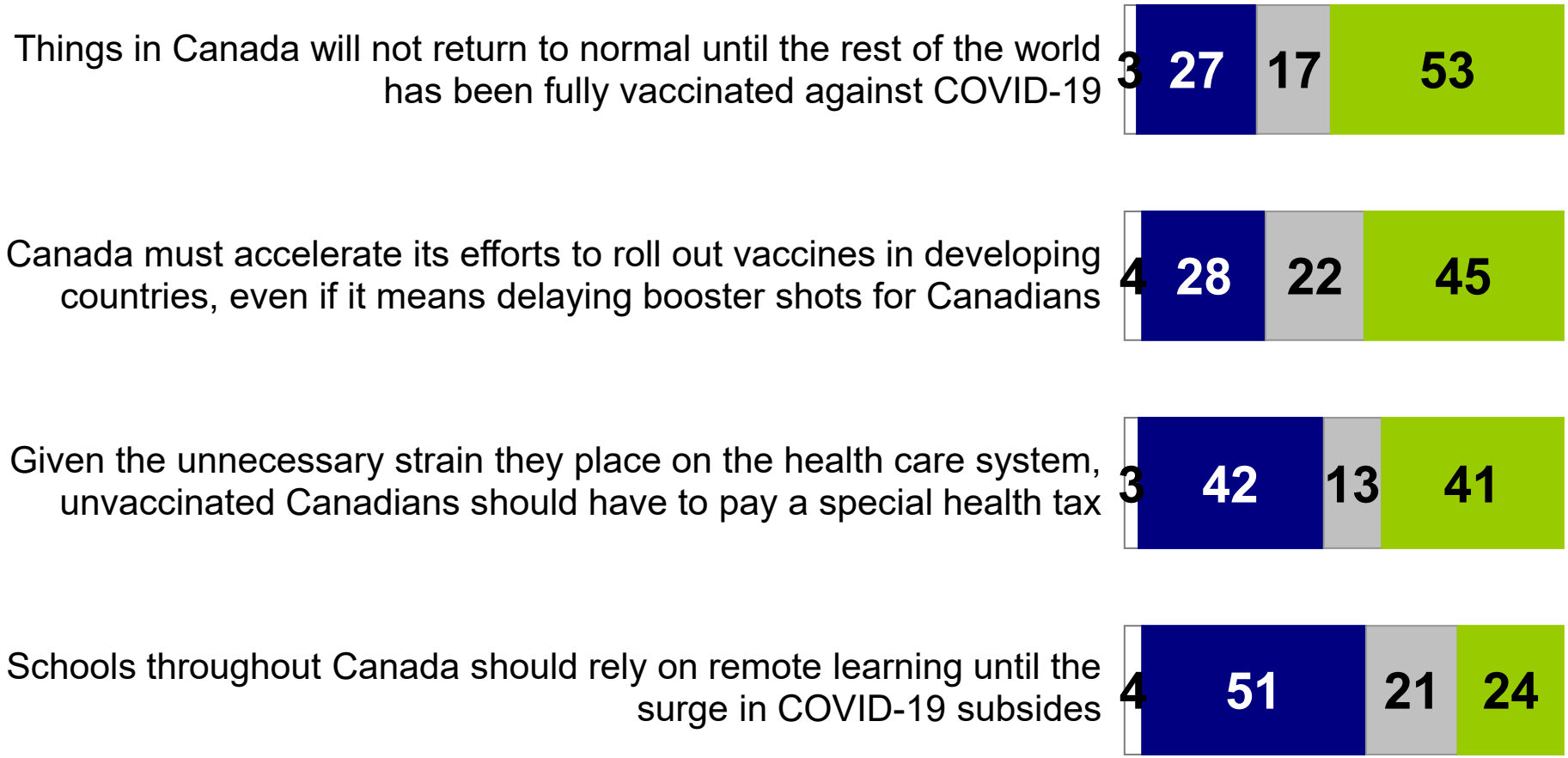


BASE: *Canadians; January 18-24, 2022, n=1,223, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Views on COVID-19 response

Q. *Please rate the extent to which you agree or disagree with the following statements:*

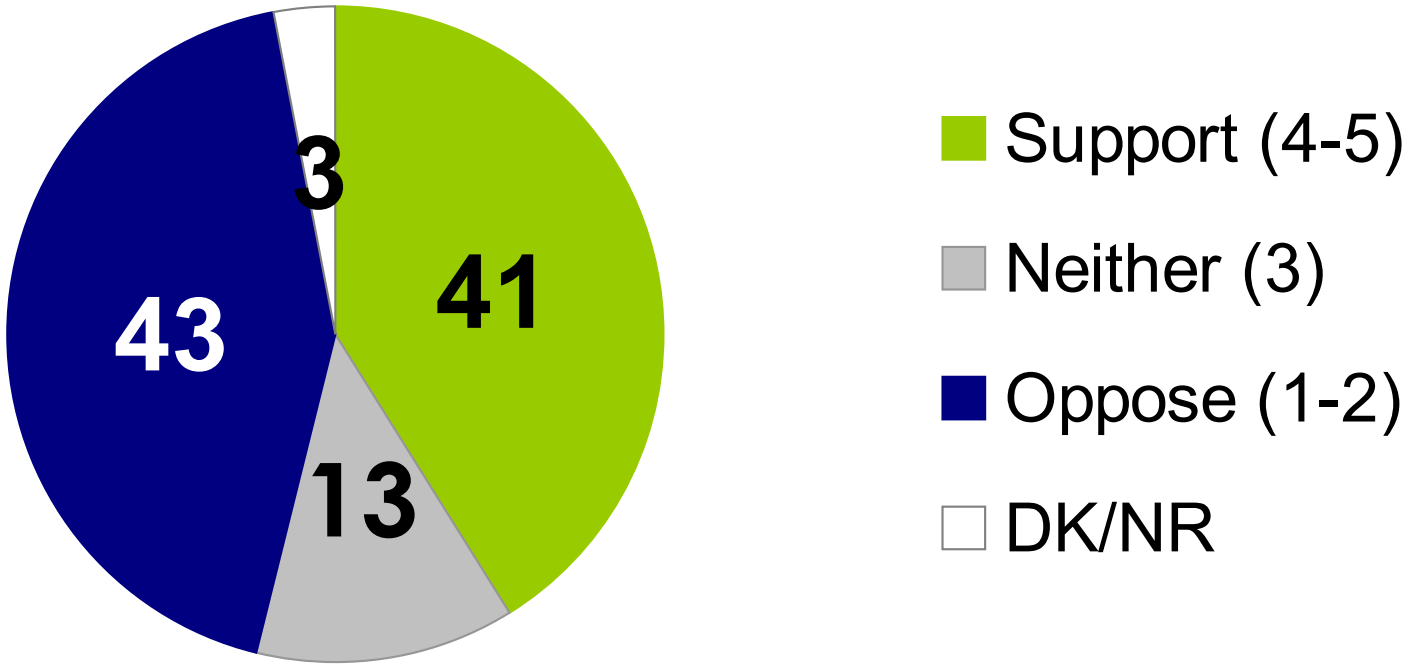


BASE: *Canadians; January 18-24, 2022, n=1,223, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Support for lower priority to unvaccinated patients

Q. *To what extent would you support or oppose given unvaccinated patients lower priority when it comes to medical resources?*



BASE: *Canadians; January 18-24, 2022, n=1,225, MOE +/- 2.8%, 19 times out of 20*

Copyright 2022
No reproduction without permission

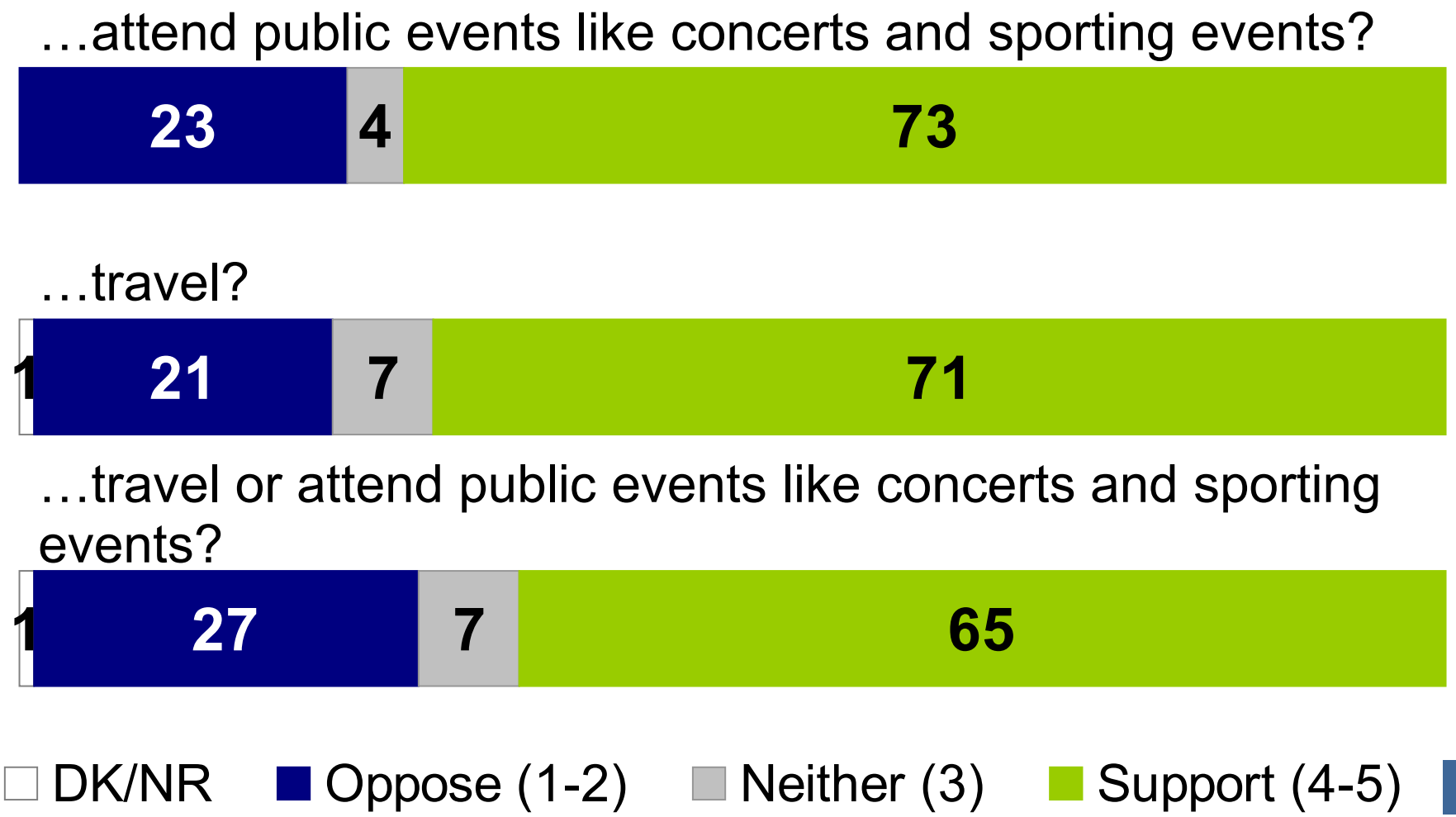
Attitudes to vaccine passports

- While not entirely clear, support for vaccine passports may be declining, though they still enjoy majority support
  - Two-thirds of Canadians (65%) support requiring proof of vaccination for travel and attending public events, a nine-point drop from December 2021
  - Nevertheless, vaccine mandates rank as the single most effective means of bringing an end to this critical period of the COVID-19 pandemic

Copyright 2022
No reproduction without permission

Support for vaccine passports

Q. *To what extent do you support or oppose requiring Canadians to carry proof of vaccination in order to…*

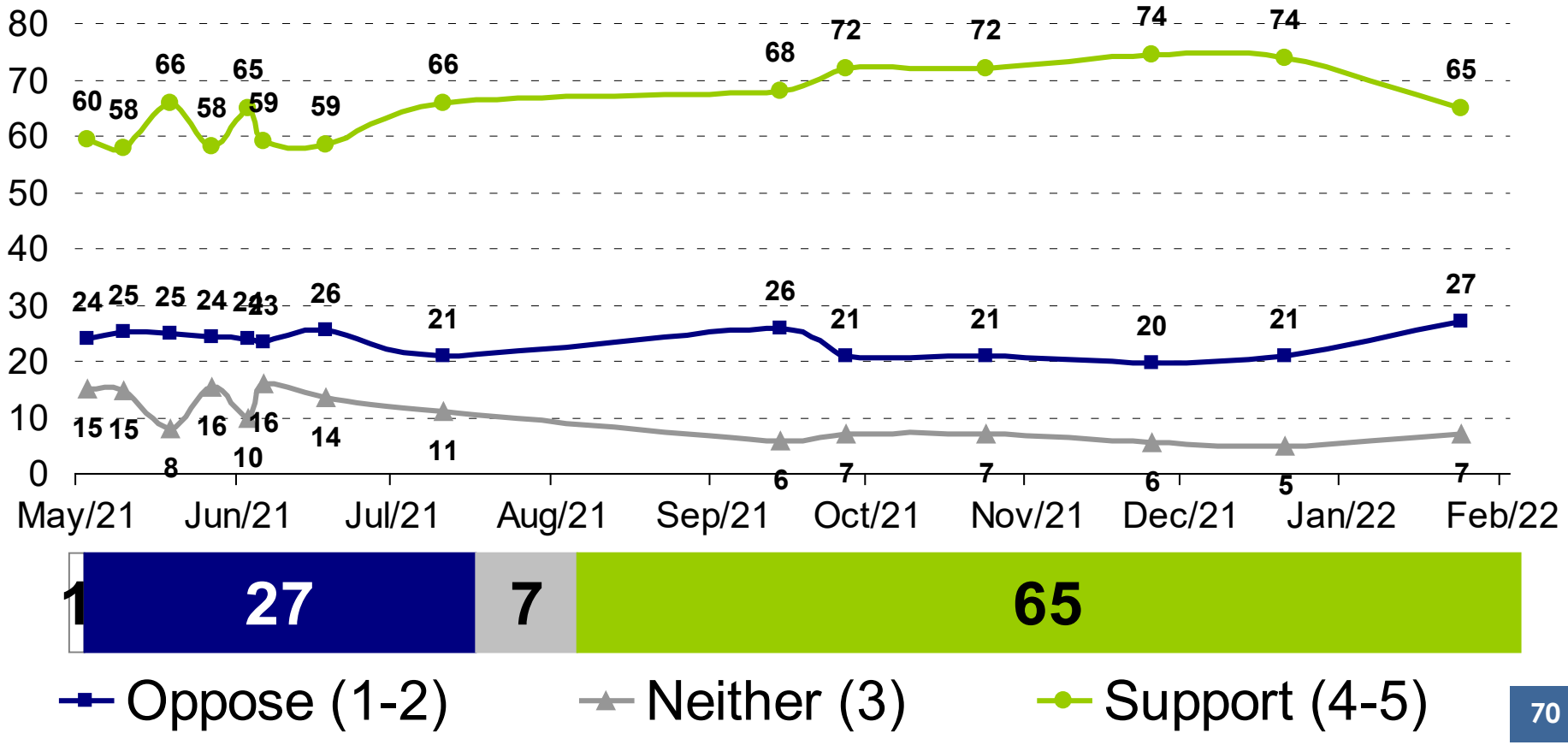


BASE: *Canadians (third-sample each); January 18-24, 2022, n=408, MOE +/- 4.9%,19 times out of 20*

Copyright 2022
No reproduction without permission

Tracking support for vaccine passports

Q. *To what extent do you support or oppose a proof-of-vaccination system where Canadians would be required to carry a vaccine passport in order to travel or attend public events?*

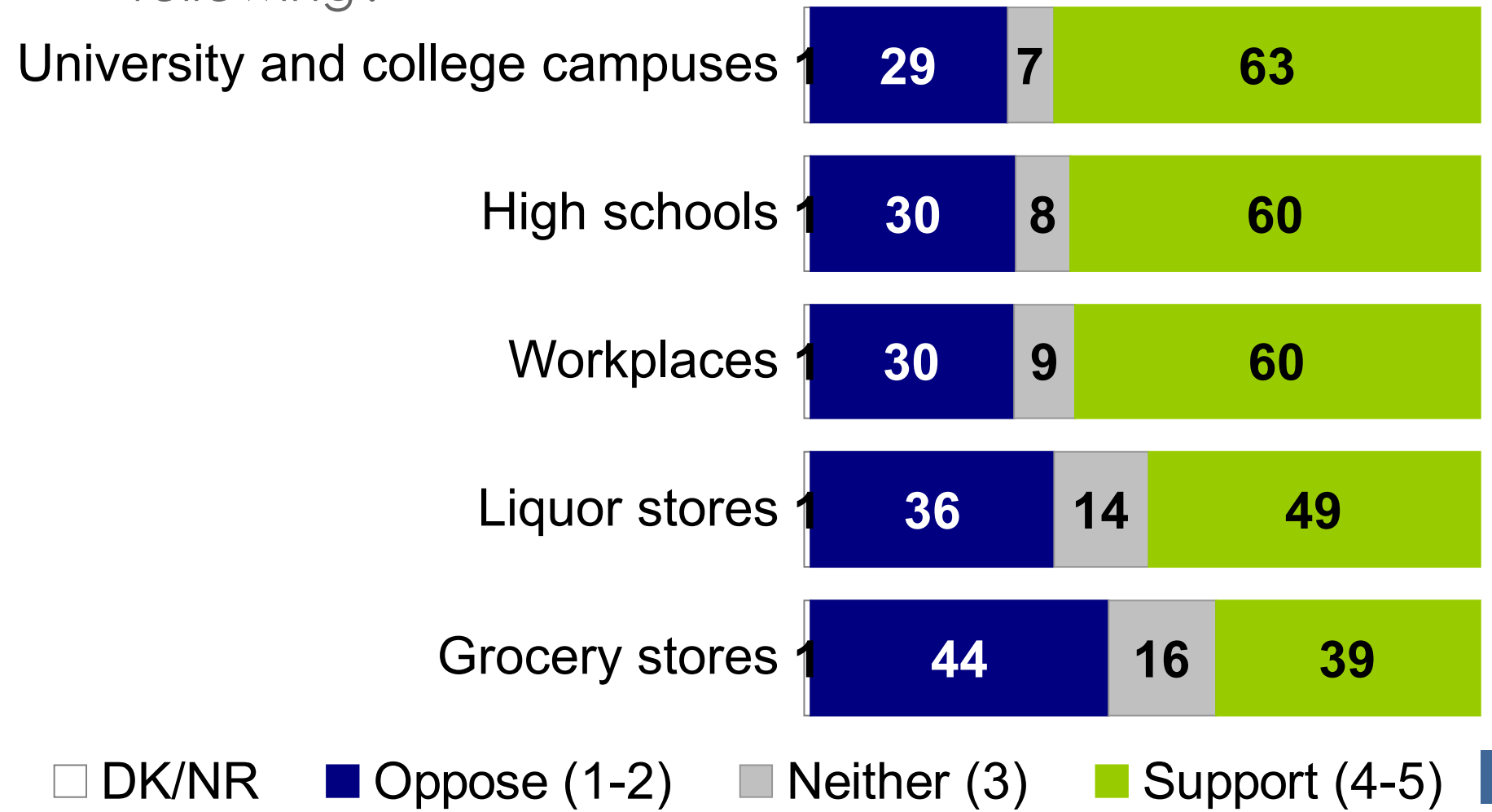


BASE: *Canadians (third-sample); January 18-24, 2022, n= 408, MOE +/- 4.9%,19 times out of 20*

Copyright 2022
No reproduction without permission

Support for vaccine passports by activity

Q. *To what extent would you support or oppose requiring Canadians proof of vaccination in order to visit the following?*

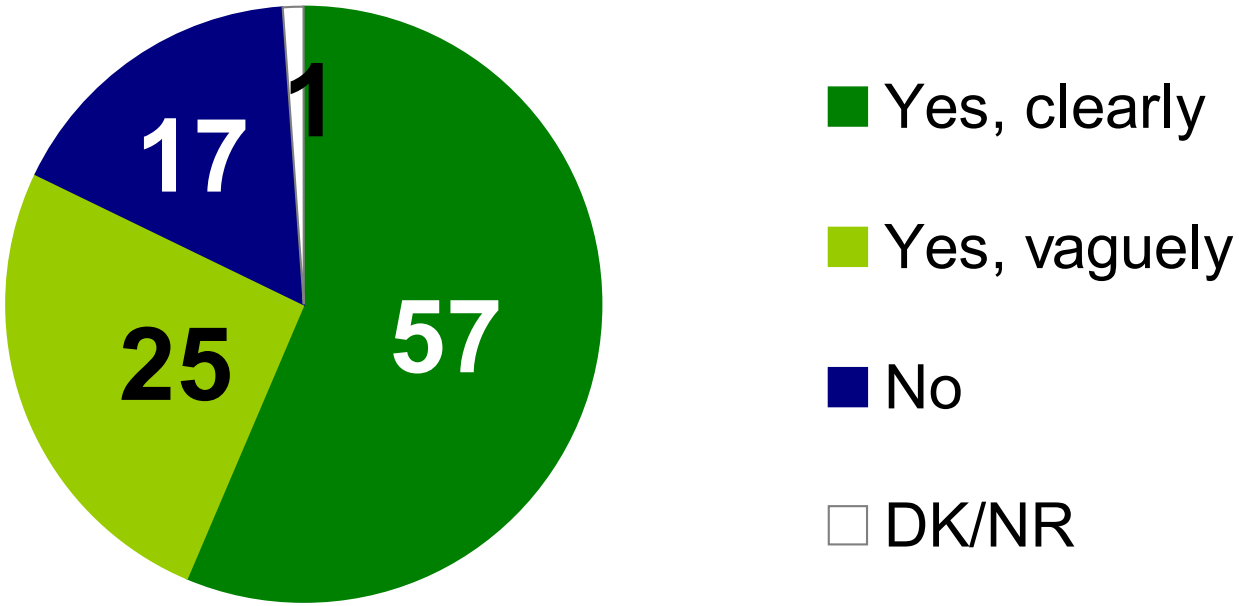


BASE: *Canadians; January 18-24, 2022, n=1,225, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Awareness of Pfizer oral treatment

Q. *As you may have heard, the Government of Canada recently announced that it placed an order for one million doses of Pfizer's new oral antiviral treatment, which has been shown to be 89% effective at reducing the risk of hospitalization and death from COVID-19 if administered within five days of infection. Do you recall hearing about this announcement?*

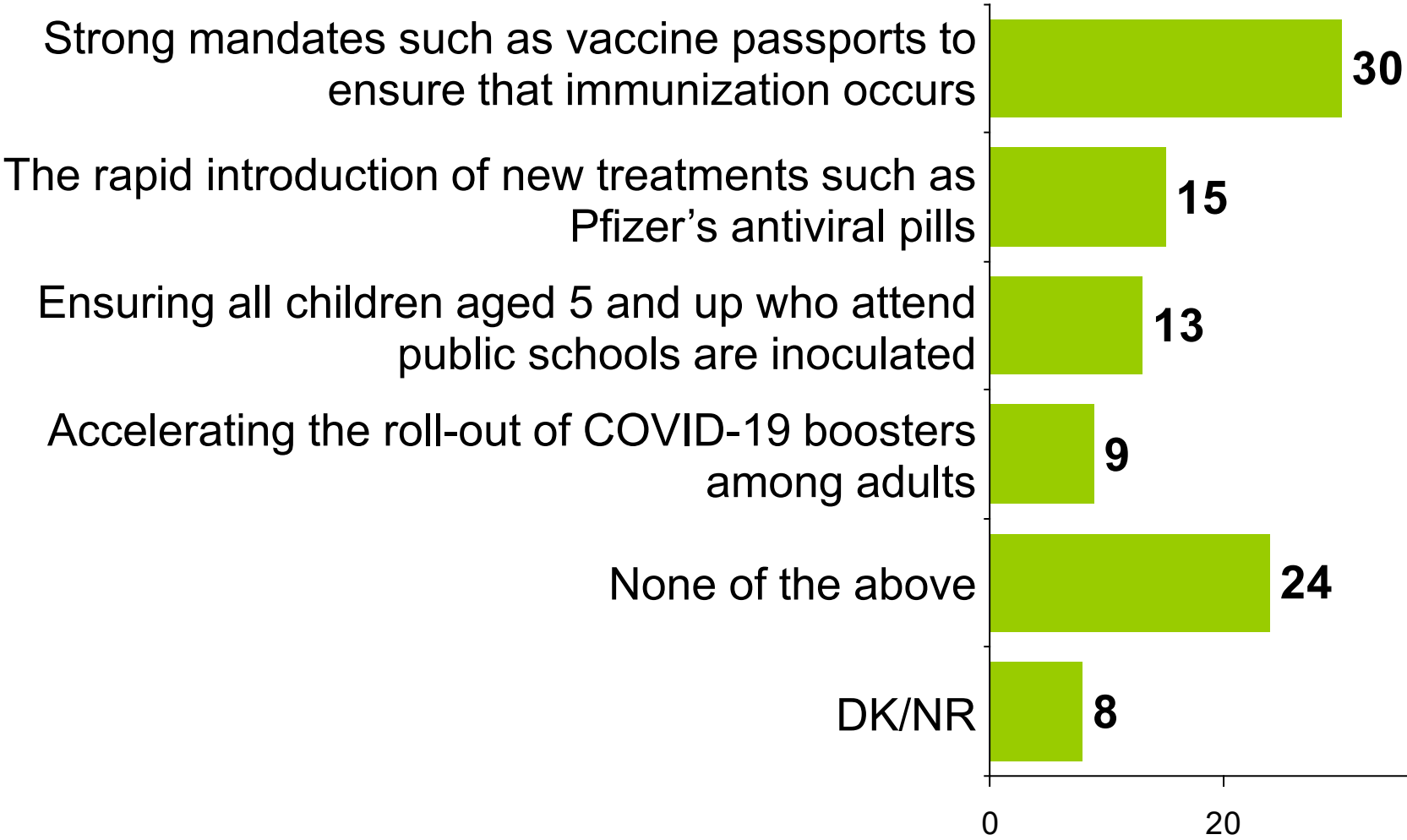


BASE: *Canadians; January 18-24, 2022, n=1,225, MOE +/- 2.8%, 19 times out of 20*

Copyright 2022
No reproduction without permission

Most effective actions to end the pandemic

Q. *Which of the following do you believe would be MOST effective in bringing an end to this critical period of COVID-19 pandemic?*



BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Support for mandatory vaccines

- Results reveal that half of Canadians (51%) would support compulsory vaccinations for all
  - Support is comparatively higher among those over 50, university graduates, and middle- and upper-class Canadians
  - Not surprisingly, mandatory vaccines are vehemently opposed by vaccine refusers (88% are opposed to the notion, compared to 29% among those who have been fully vaccinated)
- Importantly, however, support for vaccine passports is significantly higher (74% support the use of vaccine passports, compared to 51% who support mandatory vaccination)
  - This finding suggests that stricter mandates would be a more palatable approach to increasing vaccine uptake

Copyright 2022
No reproduction without permission

Mandatory vaccines vs. vaccine passports

Q. *To what extent would you support or oppose…?*

A proof-of-vaccination system where Canadians would be required to carry a vaccine passport in order to travel or attend public events



BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Mandatory COVID-19 vaccines for all eligible Canadians



BASE: *Canadians; January 7-17, 2022, n=2,612, MOE +/- 1.9%, 19 times out of 20*

DK/NR Disagree (1-2) Neither (3) Agree (4-5)

Copyright 2022
No reproduction without permission

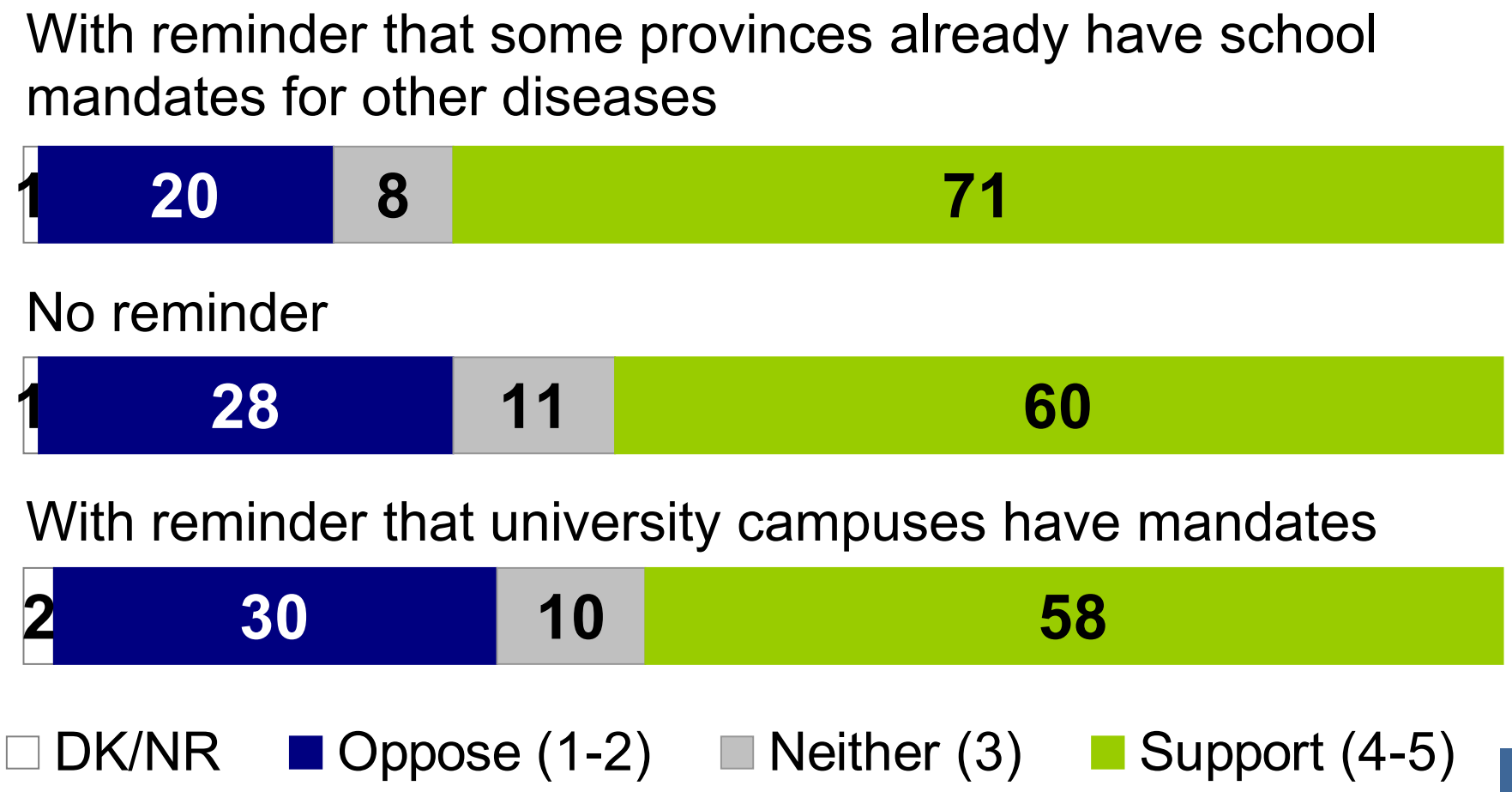
Attitudes to school mandates

- Results reveal strong support for vaccine mandates in schools, which rises significantly when respondents are reminded that some provinces already require vaccines for certain diseases, such as polio and measles

Copyright 2022
No reproduction without permission

Support for school vaccine mandates

Q. *To what extent would you support or oppose mandatory vaccinations for all students aged 5 and up who attend public schools?*

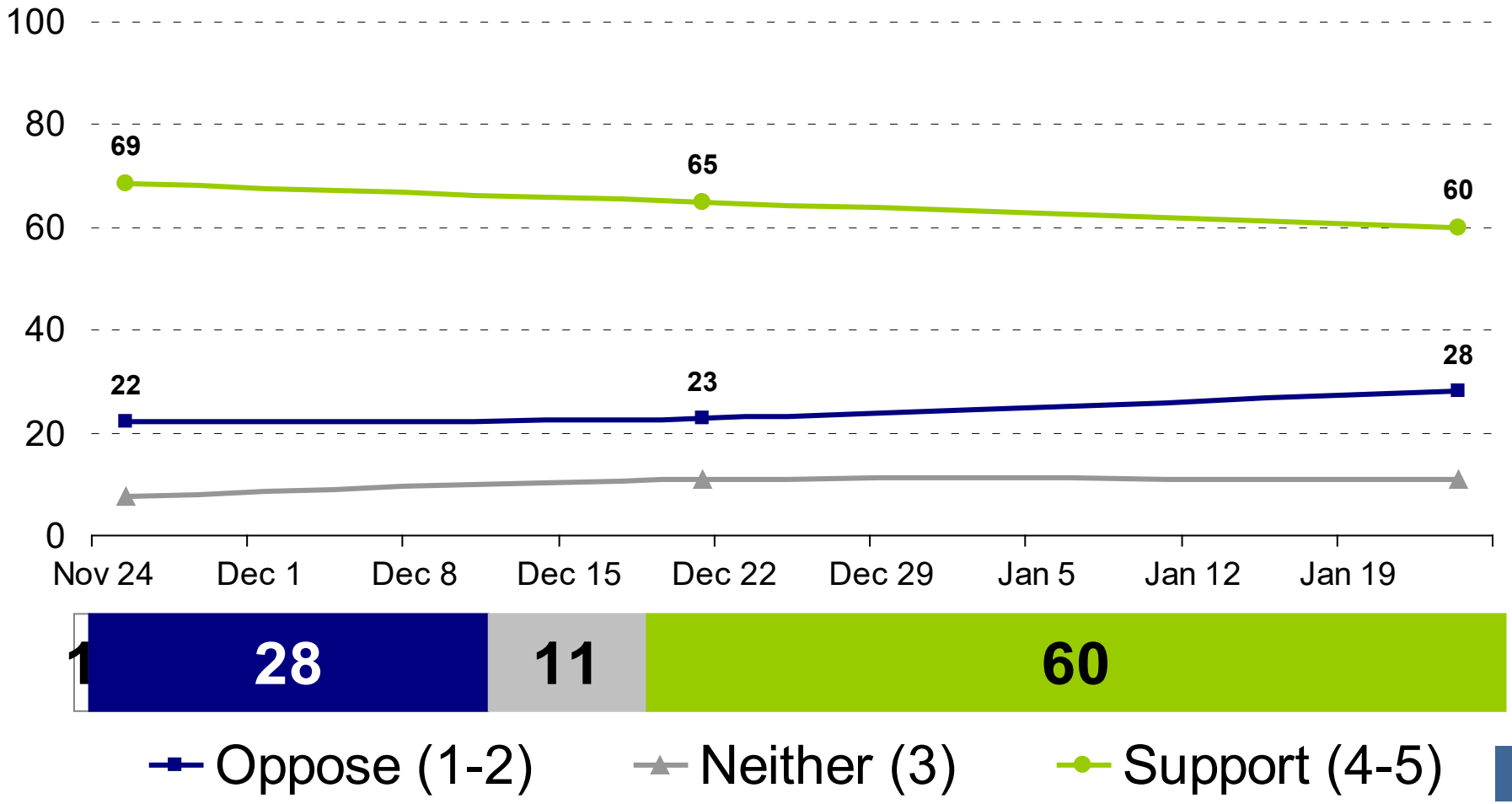


BASE: *Canadians (third-sample each); January 18-24, 2022, n=407-410, MOE +/- 4.8-4.9%,19 times out of 20*

Copyright 2022
No reproduction without permission

Tracking support for school mandates

Q. *To what extent would you support or oppose mandatory vaccinations for all students aged 5 and up who attend public schools?*



BASE: *Canadians (third-sample); January 18-24, 2022, n=408, MOE +/- 4.9%,19 times out of 20*

Copyright 2022
No reproduction without permission

1) General Outlook
2) Vaccine Acceptance
3) Approval of Government Response
4) Attitudes to Public Health Measures and Vaccine Mandates
5) **Disinformation**
6) Conclusions

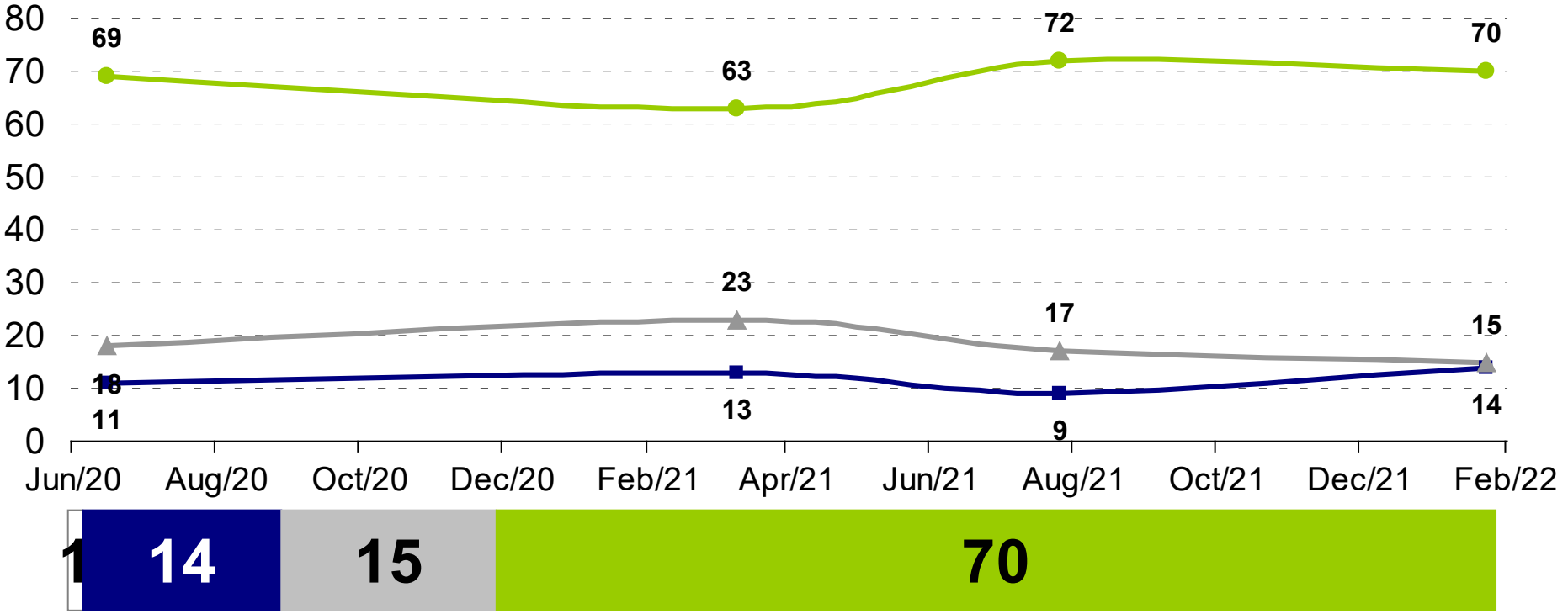
Disinformation

- The public are very concerned with the problem of disinformation, a problem that is denied in the world of vaccine refusers
- For this research, we have constructed an index of disinformation and it is clear that disinformation is not a minor problem
  - It is clear that disinformation is linked to mistrust, polarization, and vaccine refusal

Copyright 2022
No reproduction without permission

Perceived seriousness of disinformation

Q. *As you may know, the COVID-19 pandemic has led to a great deal of disinformation about the diagnosis and treatment of the disease, as well as various conspiracy theories about how the disease originated. Overall, how serious do you think this problem is?*

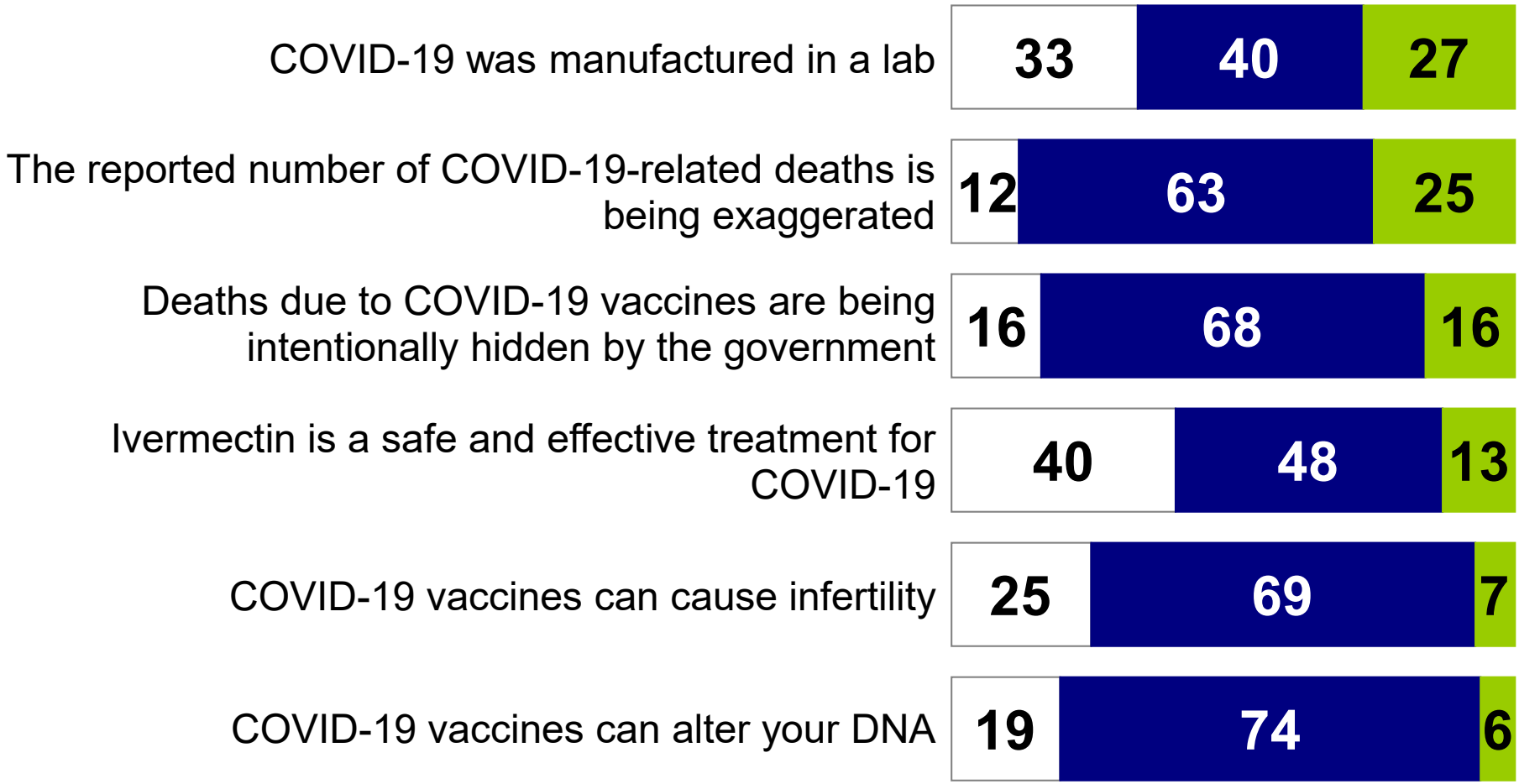


BASE: *Canadians; January 18-24, 2022, n=1,224, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Incidence of disinformation

Q. *To the best of your knowledge, are the following statements true or false?*



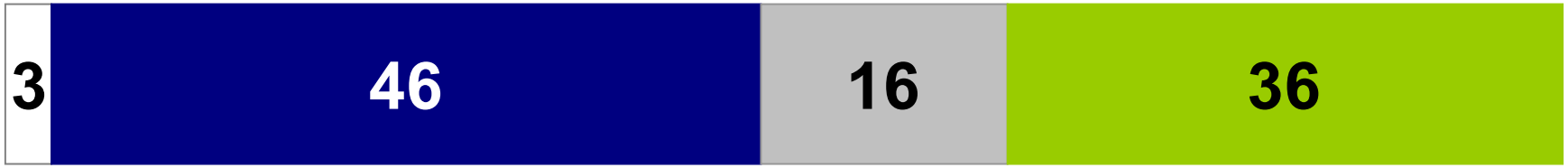
BASE: *Canadians; January 18-24, 2022, n=1,225, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Effectiveness of COVID-19 vaccines

Q. *Please rate the extent to which you agree or disagree with the following statements:*

The recent surge in COVID-19 cases means that COVID-19 vaccines are not as effective as initially thought



If vaccines are effective, it should make no difference to vaccinated individuals whether other people choose to get vaccinated



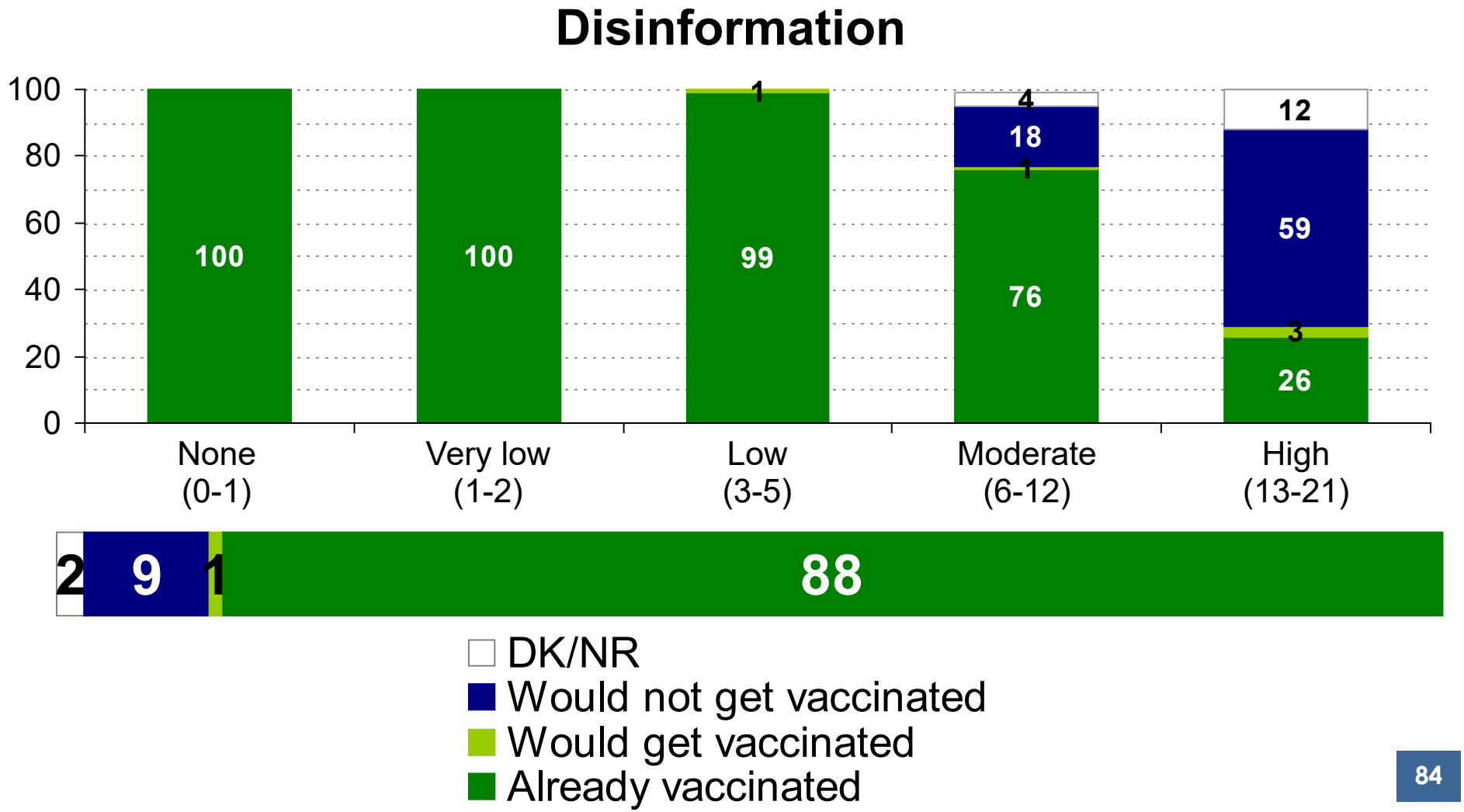
DK/NR Disagree (1-2) Neither (3) Agree (4-5)

BASE: *Canadians; January 18-24, 2022, n=1,223, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Vaccine acceptance by disinformation index

Q. *Have you received at least one dose of a COVID-19 vaccine? / Would you be willing to receive a COVID-19 vaccine?*



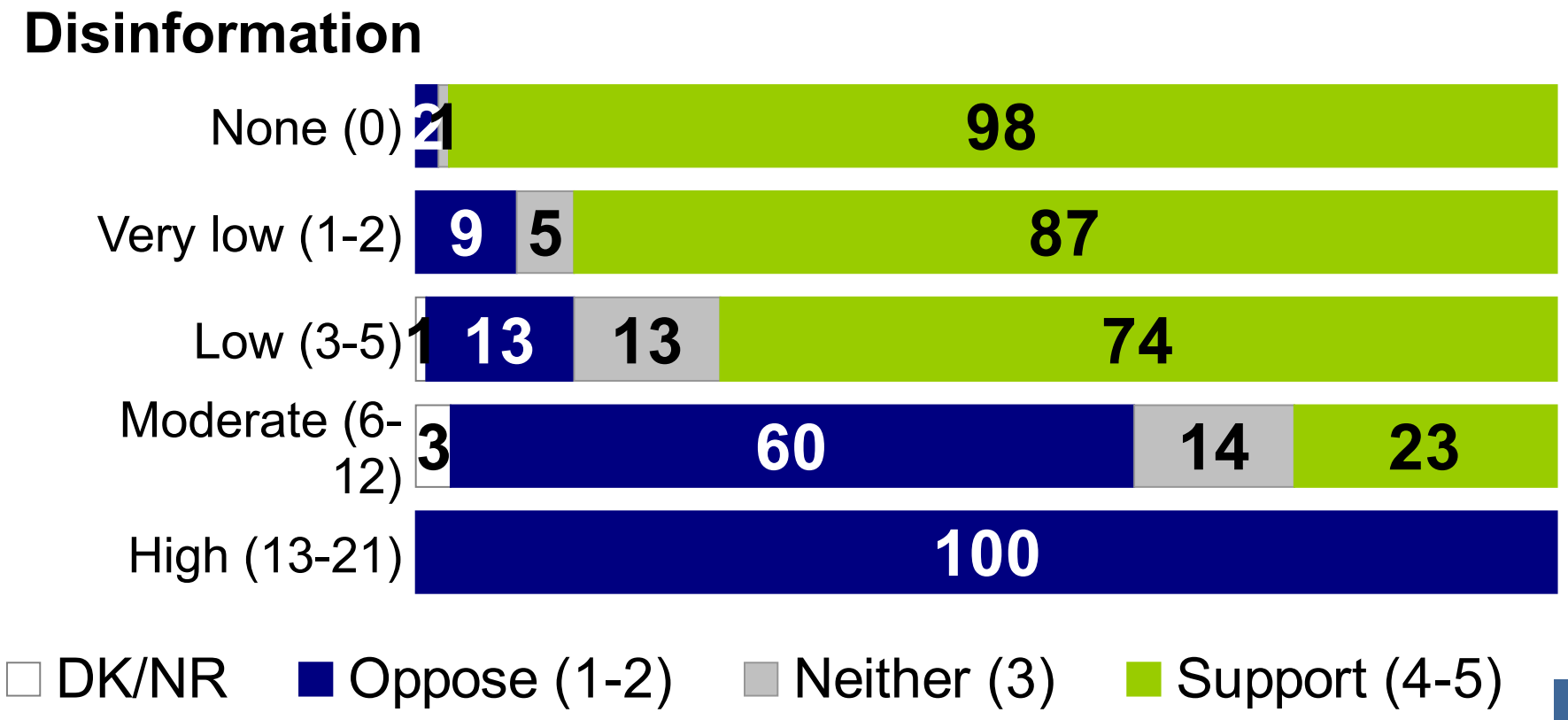
BASE: *Canadians; January 18-24, 2022, n=1,225, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Support for vaccine passports by disinformation index

Q. *To what extent do you support or oppose requiring Canadians to carry proof of vaccination in order to…*

…travel or attend public events like concerts and sporting events?

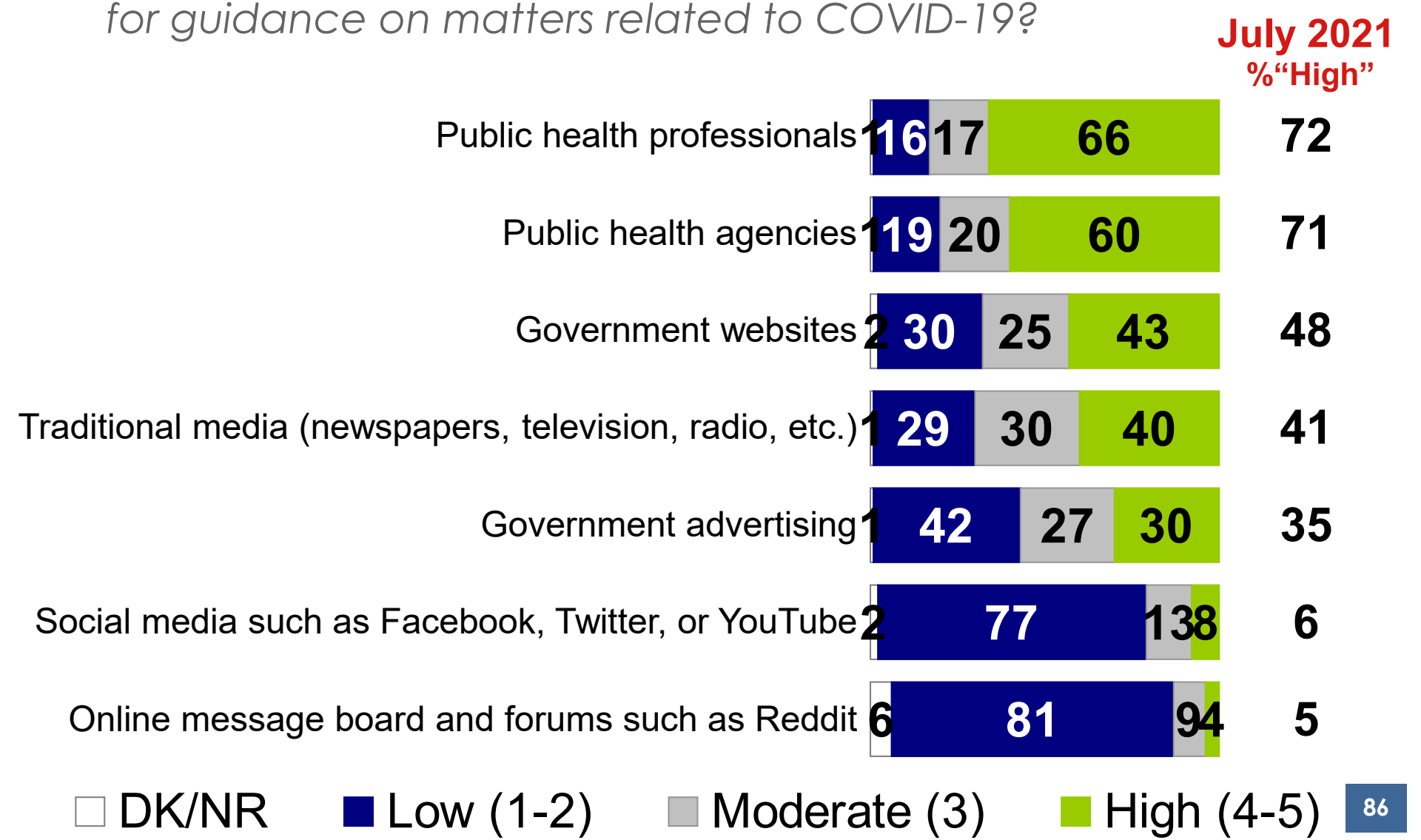


BASE: *Canadians (third-sample); January 18-24, 2022, n=408, MOE +/- 4.9%,19 times out of 20*

Copyright 2022
No reproduction without permission

Reliance on sources of information

Q. *To what extent do you rely on each of the following sources for guidance on matters related to COVID-19?*

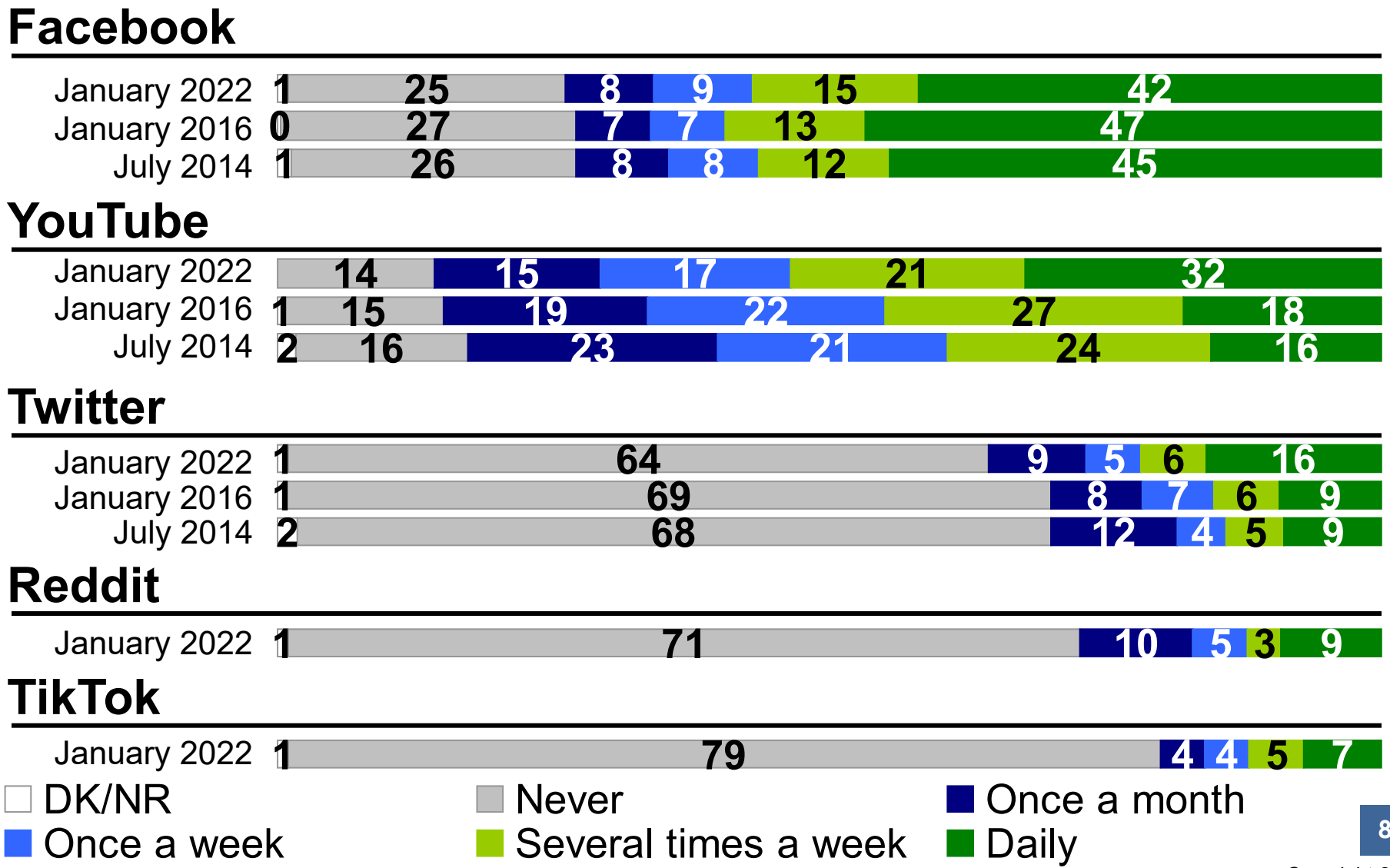


BASE: *Canadians; January 18-24, 2022, n=1,225, MOE +/- 2.8%,19 times out of 20*

Copyright 2022
No reproduction without permission

Tracking use of social media

Q. *How often do you use the following?*



BASE: *Canadians; January 18-24, 2022, n=1,225, MOE +/- 2.8%, 19 times out of 20*

Copyright 2022
No reproduction without permission

1) General Outlook
2) Vaccine Acceptance
3) Approval of Government Response
4) Attitudes to Public Health Measures and Vaccine Mandates
5) Disinformation
6) **Conclusions**

Conclusions (i)

- A period of relative normalcy is coming into view
  - The key hurdle is the asymmetric polarization which has caused a minority to adamantly reject the expert and majority consensus
  - Slowing rates of boosters, particularly amongst under 50 males and large, increasingly entrenched portion of parents objecting the vaccination of their children
  - The key drivers of these problems are disinformation and the mistrust and polarization it has produced
  - The public see mandates as the surest – but not only – path to normalcy

Copyright 2022
No reproduction without permission

Conclusions (ii)

- Although outlook on the economy and the pandemic have improved, there are some emerging areas of concern
- The brightening outlook has not dispelled the continuation of very high levels of stress and the improving outlook is very unevenly distributed through Canada
  - Racialized, disabled, poor, and working-class Canadians have a far bleaker outlook and some of this is becoming entrenched
  - There is a recurring problem with under-50 men, particularly, the non-university educated and those who live outside urban areas and the Prairies
  - The darker outlook is strongly linked to stress, a much lower commitment to vaccines in general (and boosters in particular), and deep dissatisfaction with national and federal direction

Copyright 2022
No reproduction without permission

Conclusions (iii)

- Another group that is displaying consistently weaker commitment to vaccinations and mandates is parents
  - It appears the larger the family, the more these problems express themselves
  - This finding is particularly concerning in the case of paediatric immunization and, more broadly, the immunization of those under 18
  - Paediatric vaccinations have only reached around half of eligible children and the vast majority of those who have not vaccinated their children say they won't
  - Results reveal similar resistance to vaccinating teenagers, though vaccine uptake is higher
- Current vaccination levels – particularly among children – are well short of necessary targets
  - It would appear that we are a trajectory for a longer pandemic than without this problem

Copyright 2022
No reproduction without permission

Conclusions (iv)

- The most central forces shaping these issues are a profound confluence of disinformation, deep economic pessimism, and a disturbing and growing trust deficit in these portions of Canada.
  - The relationship between disinformed views, distrust, and rejection of vaccines and continued careful behaviour is profoundly strong
  - Understanding the short-term prospects for addressing this problem is critical
- Examining the extent of disinformation and its sources suggests the tools of engagement, evidence, and reason will have little impact at this stage

Copyright 2022
No reproduction without permission

Conclusions (v)

- There is clear evidence that mandates (with avoidance of the harsher terms 'mandatory') are effective
  - Some of the newer, harsher approaches such as taxing the unvaccinated or restricting their access to grocery stores produce unnecessary polarization and weaker support than passports for travel, public events, and workplaces
  - Mandatory vaccines does have considerable resonance when it comes to schoolchildren, particularly when respondents are reminded of existing vaccine requirements in schools

Copyright 2022
No reproduction without permission

For more information:

FRANK GRAVES
EKOS Research Associates
fgraves@ekos.com
(613) 235-7215

Copyright 2021. No reproduction without permission.

ekos.com

Agence de la santé publique du Canada | Public Health Agency of Canada

Canada

InfoBulletin sur la confiance à l'égard des vaccins

Numéro 9 | janvier 2022 | Agence de la santé publique du Canada (ASPC)

Source de renseignements crédibles et opportuns sur les vaccins pour les fournisseurs de soins de santé et les décideurs de la santé publique afin de favoriser la confiance à l'égard des vaccins.

Merci d'être une source fiable d'information sur les vaccins dans l'ensemble des communautés canadiennes.

Dans ce numéro

Sujet tendance
- Infection et hospitalisation en pédiatrie

Article en vedette
- La vaccination vivement encouragée chez les personnes enceintes

Le coin de la confiance à l'égard des vaccins

Alerte au moniteur de la mésinformation / désinformation

Pleins feux sur la science

Mises à jour sur Omicron et la vaccination

Pleins feux sur la communauté

Webinaires de l'ASPC pour les fournisseurs de soins de santé

Restez à jour

Commentaires sur la confiance à l'égard des vaccins

Annexe
- Ressources en vedette
- Sources

Sujet tendance

Infections et hospitalisations pédiatriques

Certaines juridictions canadiennes ont signalé une augmentation des hospitalisations pédiatriques, en particulier dans les provinces les plus peuplées, c'est-à-dire l'Ontario, la Colombie-Britannique, l'Alberta et le Québec. Toutefois, cette hausse n'est pas nécessairement le reflet d'une augmentation de manifestations graves de la maladie chez les enfants. De nombreux cas de COVID-19 hospitalisés chez les enfants peuvent être fortuits, c'est-à-dire que les enfants ont été admis pour une autre raison (par exemple, une appendicite), mais que le dépistage de routine à l'admission a donné un résultat positif pour le COVID-19.



Étant donné la forte prévalence du variant Omicron dans la population, la probabilité d'avoir la COVID-19 est plus élevée à tout moment, y compris lorsqu'une personne est admise à l'hôpital.

Cependant, certains médecins et hôpitaux ont sonné l'alarme quant à une augmentation potentielle de la maladie grave chez les très jeunes enfants. Le 5 janvier, CHEO, l'hôpital SickKids, l'hôpital pour enfants McMaster et le centre des sciences de la santé de Kingston ont déclaré avoir admis un total de six bébés de moins de douze mois atteints de la COVID-19 depuis la mi-décembre. Tous les six sont nés de parents non vaccinés.

Pour en savoir plus, consultez l'article en vedette : La vaccination vivement encouragée chez les personnes enceintes.

Article en vedette

La vaccination vivement encouragée chez les personnes enceintes

Une augmentation du nombre d'hospitalisations de jeunes nourrissons nés de parents non vaccinés en Ontario au mois de décembre a incité plusieurs hôpitaux pour enfants à publier une déclaration commune dans laquelle ils exhortent les personnes enceintes à se faire vacciner contre la COVID-19 afin de se protéger et de protéger leur bébé.



La grossesse augmente le risque de conséquences graves de la COVID-19 pour la personne enceinte, y compris la nécessité d'une admission dans une unité de soins intensifs, d'une ventilation mécanique invasive ou d'une oxygénation par membrane extracorporelle (ECMO), et les personnes enceintes présentent un risque accru de décès dû à la COVID-19[1,2,3]. De plus, l'infection par le SRAS-CoV-2 pendant la grossesse a été associée à une augmentation des issues défavorables de la grossesse, telles qu'une augmentation des naissances prématurées, de la prééclampsie, de la mortinatalité et du faible poids à la naissance[4]. Il est difficile d'estimer la proportion de personnes enceintes vaccinées contre la COVID-19 au Canada et le nombre de doses de rappel reçus pendant la grossesse est inconnu.

Pour améliorer la protection contre le SRAS-CoV-2, y compris contre la souche Omicron, une dose de rappel est ecommandée chez les adultes de 18 ans et plus, y compris pendant la grossesse.

Aucun problème d'innocuité propre à la grossesse n'a été noté avec les vaccins contre la COVID-19. De nombreuses études démontrent qu'il n'y a pas eu d'augmentation du nombre de fausses couches, de fétus ou nouveaux-nés de petite taille pour l'âge gestationnel ou de mortinaissances associées à la vaccination à n'importe quel stade de la grossesse[5]. En outre, la vaccination pendant la grossesse peut conférer une protection supplémentaire aux nouveau-nés en leur transmettant des anticorps protecteurs à travers le placenta. Ces anticorps peuvent protéger le bébé après la naissance, tout comme les anticorps transmis par le lait humain à travers l'allaitement[6].

Pour en savoir plus, consulter les sites suivants :

- Déclaration de l'administratrice en chef de la santé publique du Canada – Importance de la vaccination contre la COVID-19 chez les personnes enceintes, les personnes qui ont récemment été enceintes et les personnes qui allaitent (26 novembre 2021)
- Déclaration de la Société des obstétriciens et gynécologues sur la vaccination contre la COVID-19 pendant la grossesse (révisée et réaffirmée le 4 novembre 2021)
- Note de service du médecin hygiéniste en chef de l'Ontario aux services de santé et aux hôpitaux demandant de donner la priorité aux femmes enceintes pour les doses de rappel (4 janvier 2022) (en anglais)



Discuter de la vaccination pendant la grossesse

- Commencez par écouter et poser des questions. Quelles sont les préoccupations spécifiques de la personne ? Comment comprend-elle son risque personnel de contracter ou être réinfectée par le COVID-19 et les impacts potentiels sur sa santé et celle de son bébé ?
- Utilisez votre relation avec la personne et votre connaissance d'elle comme point de départ. Adaptez vos conseils et votre discussion à ses préoccupations et à son contexte individuel (par exemple, le risque d'exposition sur le lieu de travail, dans la famille; les risques pour les membres vulnérables de la famille). Évitez le « déversement d'informations », qui peut être accablant.
- Laissez la conversation se dérouler sur plusieurs visites, si possible. Évitez de précipiter une décision ou de faire pression sur la personne. Invitez les membres hésitants de la famille à poser également des questions.
- Ne liez pas la vaccination pendant la grossesse au « bien commun » ou à la responsabilité collective. Concentrez-vous sur la santé et le bien-être de la famille.

Retourner à la page 1

Le coin de la confiance à l'égard des vaccins

Conseils, stratégies et renseignements fondés sur des données probantes pour promouvoir la confiance à l'égard des vaccins.

Le rôle des biais cognitifs dans les attitudes à l'égard des vaccins



Dans les prochains numéros de l'InfoBulletin sur la confiance à l'égard des vaccins, nous décrirons les principaux biais cognitifs et leur impact sur les attitudes et la prise de décisions en matière de vaccins, y compris la manière de les aborder avec les pairs et les patients.

Qu'est-ce qu'un biais cognitif?

Notre cerveau prend des raccourcis mentaux pour faire face à l'énorme volume d'informations que nous rencontrons chaque jour et le traiter efficacement.

Ces raccourcis (appelés heuristiques), qui peuvent être utiles dans la vie de tous les jours, peuvent également déformer nos perceptions et avoir un effet sur nos capacités de jugement et de prise de décisions. Les résultats sont souvent des « erreurs de jugement », appelées « biais cognitifs ».

Comment un biais cognitif influence-t-il les attitudes à l'égard des vaccins?

Les biais cognitifs peuvent influencer la manière dont nous traitons les informations relatives aux vaccins, les informations que nous utilisons pour guider notre prise de décisions, notre perception des risques et des avantages des vaccins, la manière dont nous comprenons les statistiques susceptibles d'éclairer nos calculs du risque, la manière dont nous sommes influencés par les messages sur les vaccins, etc.

Biais d'ancrage

Le biais d'ancrage, un type de biais cognitif, est la tendance à accorder une grande importance ou valeur au premier élément d'information que nous apprenons sur un sujet. Cette information originale sert ensuite de point de référence, ou « d'ancrage », à la façon dont nous interprétons et comprenons les nouveaux renseignements. Il s'agit d'un défi pour la confiance dans les vaccins en raison du grand nombre de mésinformations qui circulent. La simple exposition à des mésinformations ou à des désinformations sur le vaccin peut diminuer la confiance dans le vaccin et influencer le jugement et la perception des informations nouvelles ou plus exactes.

Comment aborder le biais d'ancrage

La « démystification au préalable » des mésinformations sur les vaccins peut être une stratégie efficace. Lorsque nous prévenons les gens à l'avance des mythes possibles sur les vaccins et des raisons pour lesquelles ils sont faux, nous renforçons leur résilience à la mésinformation et leur fournissons un point d'ancrage fondé sur des informations exactes. De plus amples informations sur le biais d'ancrage sont disponibles ici (en anglais).

Négligence de la taille de l'échantillon

La négligence de la taille de l'échantillon, un autre type de biais cognitif, est la tendance à ne pas considérer, ou à moins considérer, la fréquence d'une caractéristique dans un groupe lorsqu'on examine des informations précises relatives à des événements ou des individus. Par exemple, la plupart des infections par le SRAS-CoV-2 au Canada surviennent actuellement chez des personnes vaccinées. À première vue, cette information peut sembler indiquer que vous avez plus de chances de contracter la COVID-19 si vous êtes vacciné. Cependant, lorsque l'on prend en compte le nombre de cas chez les personnes vaccinées, il faut également tenir compte du nombre de personnes vaccinées (qui est très élevé). Lorsque vous divisez le nombre de cas chez les personnes vaccinées par le dénominateur approprié, qui est le nombre de personnes vaccinées, vous obtenez un taux chez les personnes vaccinées; cela vous donne une meilleure idée de l'impact sur les personnes vaccinées.

Vous pouvez ensuite comparer ce taux chez les personnes vaccinées au taux chez les personnes non vaccinées, qui correspond au nombre de cas chez les personnes non vaccinées divisé par le nombre de personnes non vaccinées.

Comment aborder la négligence de la taille de l'échantillon

Lorsque vous mentionnez un taux ou un risque dans une discussion avec d'autres personnes, assurez-vous que vous utilisez le bon dénominateur pour formuler votre raisonnement. Par exemple, le nombre de cas chez les vaccinés doit être déterminé sur la base d'un taux qui utilise le nombre de personnes vaccinées (qui est très élevé) comme dénominateur. Plus d'informations sur la négligence de la taille de l'échantillon et la COVID-19 sont disponibles ici.

Alerte au moniteur de la mésinformation/désinformation

Sources crédibles pour démystifier la désinformation et la mésinformation.

Les médias sociaux ont permis le partage généralisé de la mésinformation sur les vaccins, et les campagnes de désinformation et les inforobots étrangers ont accru sa prolifération[7]. Dans ce numéro, nous examinons les sources crédibles qui ont été utilisées pour démystifier une fausse rumeur qui a circulé sur les médias sociaux.

LE SAVIEZ-VOUS?

La **mésinformation** est une information fausse ou trompeuse, mais présentée comme un fait, quelle que soit l'intention.

La **désinformation** est une information créée et diffusée intentionnellement pour tromper ou induire en erreur.

La rumeur

Des messages sur les médias sociaux (en anglais seulement) circulant au début du mois de décembre affirmaient que 400 enfants (dont l'âge n'était pas précisé) avaient été traités en une semaine dans un hôpital de Calgary pour des effets indésirables liés aux vaccins contre la COVID-19. Ces messages prétendent que la source était un message d'un « ami dont la femme est infirmière ».

Comment cette rumeur a été démentie

Cette mésinformation a été corrigée par Alberta Health Services dans un message sur Twitter le 8 décembre 2021 (en anglais seulement). Alberta Health Services a confirmé qu'ils n'avaient pas eu d'hospitalisations pédiatriques liées à la vaccination contre la COVID-19 à cette époque.

Des données supplémentaires à l'appui du démenti de la rumeur se trouvent sur le site effets secondaires signalés après la vaccination contre la COVID-19 au Canada. Ce rapport de surveillance est mis à jour chaque semaine par l'Agence de la santé publique du Canada.

Il comprend tous les effets secondaires suivant l'immunisation (ESSI) possibles qui ont été signalés par les bureaux locaux de santé publique, y compris les effets qui ont nécessité une hospitalisation ou la prolongation d'une hospitalisation existante (qu'ils aient été liés aux vaccins ou non).

Pleins feux sur la science

Explications sur la science qui sous-tend les conseils sur les vaccins et la réponse de la santé publique.

La science des intervalles entre les vaccins



La récente vague du variant Omicron a amené certains à envisager de raccourcir les intervalles entre les rappels et les vaccins pédiatriques. Comprendre l'immunologie qui sous-tend les intervalles recommandés peut aider les fournisseurs de soins de santé à discuter des intervalles entre les vaccins avec leurs patients.

Comment les intervalles optimaux entre les vaccins au Canada ont été déterminés

Les intervalles entre les doses de vaccin sont souvent déterminés par des essais cliniques. Dans le contexte d'une crise de santé publique, les fabricants de vaccins ont choisi d'opter pour l'intervalle le plus court possible entre la première et la deuxième dose de la série primaire afin que les vaccins soient disponibles le plus rapidement possible; les intervalles recommandés par les fabricants sont de 21 jours pour le vaccin de Pfizer BioNTech (Comirnaty®) et de 28 jours pour le vaccin de Moderna (Spikevax™). Lorsqu'on a commencé à distribuer les vaccins au Canada, face à un approvisionnement initialement limité, le CCNI a recommandé un intervalle plus long entre les vaccins pour deux raisons :

- Pour permettre au plus grand nombre de personnes possible de recevoir la première dose, compte tenu de l'offre limitée.
- Les membres du CCNI ont conclu que des intervalles plus longs produiraient une meilleure réponse immunitaire sur la base de deux concepts immunologiques fondés sur des décennies de recherche : la maturation de l'affinité et la diminution de l'interférence immunitaire.

Maturation de l'affinité

Les vaccins fonctionnent en permettant à notre corps de se doter de défenses contre les agents pathogènes infectieux avant d'y être exposé. Ces défenses sont construites par étapes au fil du temps. Les défenses initiales qui apparaissent rapidement après la vaccination sont une sorte de « premier jet » et peuvent ne pas fournir une protection très efficace ou durable.

Toutefois, lorsque l'organisme est à nouveau exposé à l'antigène par une vaccination ou une infection, il réagit mieux en utilisant ses lymphocytes B mémoires qui ont été créés lors de la première exposition.

Un intervalle plus long entre les doses de vaccin permet une maturation optimale des lymphocytes B, appelée maturation de l'affinité, de sorte que lorsque le système immunitaire rencontre à nouveau le vaccin, il produit de meilleurs anticorps de liaison qui peuvent être plus protecteurs, plus durables et

avoir un spectre d'action plus large. Ces types d'anticorps peuvent offrir une meilleure protection en cas d'exposition au même variant ou à des variants différents du virus.

Diminution de l'interférence immunitaire

Les anticorps circulants atteignent leur maximum peu après la vaccination, puis commencent à diminuer. Si une deuxième dose de vaccin est introduite dans l'organisme alors que le taux d'anticorps circulants est encore élevé, ces anticorps peuvent masquer les sites de liaison sur l'antigène du vaccin, empêchant ainsi une bonne réponse au vaccin. En outre, les anticorps circulants peuvent également se lier à l'antigène, le marquant pour qu'il soit détruit, ce qui peut réduire la disponibilité de l'antigène et donc diminuer la réponse vaccinale. Le fait de laisser le temps aux anticorps circulants de diminuer entre les doses permettra d'éviter l'interférence immunitaire et d'optimiser les réponses vaccinales.

Le CCNI recommande les intervalles suivants entre les doses :

- Au moins 8 semaines entre la première et la deuxième dose de la série primaire pour les enfants âgés de 5 à 11 ans.
- 8 semaines entre la première et la deuxième dose de la série primaire pour les personnes âgées de 12 ans et plus.
- Un intervalle de 4 à 8 semaines entre chaque dose de la série primaire pour les personnes qui sont modérément ou gravement immunodéprimées.
- Au moins 6 mois entre la série primaire et le rappel chez les personnes âgées de 18 ans et plus.

Messages clés

La science des intervalles entre les vaccins

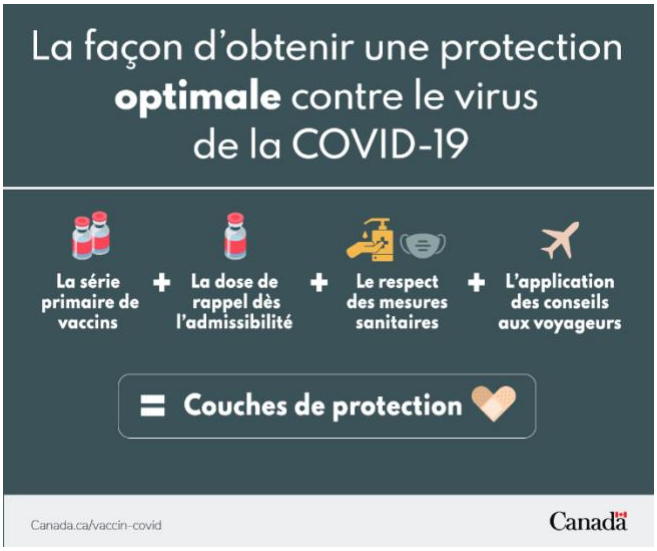
- Des intervalles plus longs entre les doses de vaccin peuvent permettre une meilleure réponse immunitaire, plus protectrice, contre une future infection. Cela peut être important pour améliorer la protection contre les variants préoccupants, actuels et futurs.
- Omicron est probablement un virus dominant dans la population pendant quelques mois et de nouveaux variants peuvent apparaître. Il sera important d'optimiser la protection à long terme et pas seulement pendant la vague actuelle.
- Les vaccins ne sont qu'un élément d'une intervention dynamique de santé publique. Pour réduire le risque, il demeure essentiel d'associer la vaccination à des mesures de santé publique ciblées au moment opportun à des pratiques de protection individuelle, en particulier le port d'un masque bien ajusté et bien construit lorsqu'on rencontrera probablement des personnes extérieures au ménage.

Mises à jour sur Omicron et la vaccination

Omicron et efficacité réelle des vaccins contre la COVID-19

Deux doses de vaccin contre la COVID-19 offrent une bonne protection contre les formes graves de la maladie et les hospitalisations causées par le variant Omicron, mais sont moins efficaces contre l'infection.

L'administration d'une dose de rappel à ARNm peut offrir une protection encore meilleure contre les formes graves de la maladie et les hospitalisations causées par le variant Omicron et améliorer la protection contre l'infection[8,9].



En raison de la grande transmissibilité du variant Omicron et de sa présence dans nos communautés, il est important que chacun continue à suivre les conseils de santé publique - **#MainsMasqueEspace.**

Vaccination contre la COVID-19 pour les enfants de 5 à 11 ans

Selon de nouvelles données probantes rassurantes sur l'innocuité en situation réelle, provenant des États-Unis et du Canada, le vaccin contre la COVID-19 pour les enfants de 5 à 11 ans présente un **bon profil d'innocuité** et est bien toléré.

Aux États-Unis, de très rares cas de myocardite ont été rapportés après l'administration du vaccin contre la COVID-19 de Pfizer-BioNTech (Comirnaty®) chez des enfants âgés de 5 à 11 ans, principalement après la deuxième dose chez les garçons. Ces rapports sont beaucoup moins fréquents que chez les adolescents de 12 à 17 ans et les jeunes adultes[10].

Quoi de neuf au CCNI?

Recommandation actualisée sur l'utilisation des vaccins contre la COVID-19 chez les enfants âgés de 5 à 11 ans

Le CCNI a renforcé sa recommandation sur l'utilisation du vaccin contre la COVID-19 pour les enfants de 5 à 11 ans, passant de discrétionnaire (peut être proposé) à forte (devrait être proposé). Selon sa recommandation actuelle, une **série complète du vaccin Comirnaty de Pfizer-BioNTech (10 mcg) devrait être administrée** aux enfants de 5 à 11 ans qui ne présentent pas de contre-indications au vaccin, en respectant un intervalle d'au moins 8 semaines entre la première et la deuxième dose.

Le CCNI maintient sa recommandation de respecter un **intervalle d'au moins 8 semaines** entre les doses pour ce groupe d'âge car il donne aux enfants la possibilité de développer une immunité meilleure et plus durable et réduit davantage le risque très rare de myocardite après la vaccination.

Une série primaire de 3 doses du vaccin contre la COVID-19 de Pfizer-BioNTech (Comirnaty®) (10 mcg) devrait être administrée aux enfants âgés de 5 à 11 ans qui sont modérément à sévèrement immunodéprimés en respectant un **intervalle de 4 à 8 semaines entre les doses.** Pour les personnes qui ont déjà reçu deux doses du vaccin contre la COVID-19 de Pfizer-BioNTech (Comirnaty®) (10 mcg), une troisième dose de ce vaccin (10 mcg) devrait être administrée 4 à 8 semaines après la deuxième dose.

- Un intervalle plus long entraînera probablement une meilleure réponse immunitaire et une plus longue durée de protection. Si un intervalle plus long est envisagé, il faut tenir compte des facteurs de risque d'exposition au virus, y compris l'épidémiologie locale, et du risque de complications graves.

Vaccination contre la COVID-19 pour les adolescents de 12 à 17 ans

D'après une étude américaine récente, la série de 2 doses de vaccin contre la COVID-19 de Pfizer-BioNTech (Comirnaty®) chez les adolescents a conféré une très bonne protection contre le syndrome inflammatoire multisystémique chez les enfants (SIM-C). D'après cette même étude, parmi les patients atteints du SIM-C gravement malades ayant besoin d'un maintien des fonctions vitales, aucun n'était vacciné[11].

Pour de plus amples renseignements sur le SIM-C, voir le récent article du Relevé des maladies transmissibles au Canada (RMTC) .

Le CCNI maintient sa recommandation d'administrer une série complète du vaccin à ARNm contre la COVID-19 aux adolescents âgés de 12 à 17 ans qui ne présentent pas de contre-indications au vaccin, avec un intervalle de 8 semaines entre la première et la deuxième dose.

Il est préférable d'utiliser le vaccin contre la COVID-19 de Pfizer-BioNTech (dose de 30 mcg) plutôt que le vaccin de Moderna (Spikevax™) (dose de 100 mcg) pour initier ou poursuivre la série primaire de vaccins à ARMm. En effet, le risque de myocardite/péricardite est plus faible avec le vaccin de Pfizer-BioNTech (Comirnaty®) qu'avec le vaccin de Moderna (Spikevax™).

Le CCNI continue de suivre de près l'évolution des données probantes sur les vaccins contre la COVID-19, y compris les données sur l'innocuité et l'efficacité réelle des doses de rappel chez les adolescents de moins de 18 ans, en particulier ceux qui présentent un risque plus élevé de maladie grave due à la COVID-19, et mettra à jour ses conseils si nécessaire.

Pleins feux sur la communauté

Mettre en lumière les projets innovants et les pratiques exemplaires des communautés partout au Canada.

Santé des enfants Canada : Vacciner les enfants en toute confiance

Avec le soutien du Fonds de partenariat d'immunisation (FPI) de l'ASPC, Santé des enfants Canada a élaboré le document « Vacciner les enfants en toute confiance : Capacité, communication et communauté ». Cette initiative offrira des interventions et des ressources adaptées pour améliorer l'accès, la sensibilisation et l'utilisation des connaissances et des ressources disponibles pour les fournisseurs de soins de santé de première ligne pour les enfants et les jeunes.

Elle vise à leur permettre de vacciner en toute sécurité et en toute confiance les enfants, y compris ceux qui sont exposés à un risque accru en raison de la COVID-19 et d'autres maladies infectieuses évitables par la vaccination.

Pour obtenir des outils utiles afin d'aider les communicateurs, les fournisseurs de vaccins et les familles en matière de vaccination pédiatrique, visitez le centre de ressources de Santé des enfants Canada.

Journée nationale de la vaccination pour les enfants

#KidsVaccinesDay

N.B. Le # est en anglais seulement.

Le 27 janvier 2022, Santé des enfants Canada, #LaSciencedAbord et The Sandbox Project (en anglais) ont uni leurs forces pour créer la Journée nationale de la vaccination pour les enfants. Ils encouragent chacun à participer aux événements de la journée par ses propres efforts et en faisant la promotion des programmes et des ressources en cours de planification à l'aide du mot-clic **#KidsVaccinesDay**.

Santé des enfants Canada organise une conférence gratuite d'une demi-journée – Vaccination Conversations Pop Up Event (en anglais) – afin de fournir aux fournisseurs de soins de santé les compétences, les outils et les informations nécessaires pour promouvoir et proposer en toute confiance les vaccinations aux enfants et à leurs familles.

#LaSciencedAbord organisera un événement gratuit, le webinaire LaSciencedAbord – Les enfants et la vaccination (en anglais) à 17 h HNP / 20 h HNE / 21 h HNA. Cet événement en direct répondra aux questions des enfants, des aidants naturels et des éducateurs sur les vaccins et la pandémie actuelle de COVID-19.

The Sandbox Project et la Young Canadians Roundtable on Health (YCRH) (en anglais) ont créé une base de données des ressources pour les enfants et les parents afin d'aider les enfants à comprendre l'importance et l'innocuité des vaccins, et de les rendre plus confiants lors de leurs rendez-vous.

À propos du Fonds de partenariat d'immunisation

Le Fonds de partenariat d'immunisation (FPI) de l'ASPC finance des projets qui améliorent l'accès aux vaccins et encouragent l'acceptation et l'utilisation des vaccins. Les projets financés renforcent les capacités des fournisseurs de soins de santé en tant que vaccinateurs et promoteurs de la vaccination, appuient la mise en place d'activités d'éducation, de promotion des vaccins et de sensibilisation liées à la COVID-19 dans la collectivité, et augmentent les capacités de communication sur les vaccins fondée sur des données probantes et culturellement adaptées.

Webinaires de l'ASPC pour les fournisseurs de soins de santé

L'ASPC, en collaboration avec le Centre canadien de ressources et d'échange sur les données probantes en vaccination (CANVax) et le Centre de collaboration nationale des maladies infectieuses (CCNMI), offre des webinaires animés par des experts qui visent à offrir aux fournisseurs de soins de santé des conseils cliniques sur des sujets clés liés aux vaccins.

Liste des webinaires

- Vaccin contre la COVID-19 autorisé pour usage pédiatrique au Canada
- Se préparer à la vaccination pédiatrique contre la COVID-19 et recommandations sur les doses de rappel pour adultes
- Revaccination avec des vaccins contre la COVID-19 après une anaphylaxie
- Contre-indications aux vaccins contre la COVID-19
- Vaccination contre la grippe saisonnière pour 2021-2022
- Répondre à la réticence à se faire vacciner contre la COVID-19 dans la pratique clinique

Abonnez-vous au bulletin d'information Une dose de CANVax et aux Alertes aux nouvelles du CCNMI (en anglais) pour rester au courant des prochains webinaires de l'ASPC.

Restez à jour

Abonnez-vous pour rester au courant des dernières directives et des derniers renseignements du **Guide canadien d'immunisation (GCI)** ou du **Comité consultatif national de l'immunisation (CCNI)**, y compris les recommandations, les déclarations et les analyses documentaires.

Le GCI est une ressource exhaustive sur l'immunisation. Son élaboration est fondée sur les recommandations et les déclarations de comités consultatifs spécialisés, dont le CCNI et le Comité consultatif de la médecine tropicale et de la médecine des voyages (CCMTMV).

Le CCNI formule des recommandations sur l'utilisation des vaccins dont l'administration chez l'homme est actuellement ou récemment approuvée au Canada, notamment en signalant les groupes à risque pour les maladies évitables par la vaccination qui devraient être la cible des campagnes de vaccination.

Commentaires sur la confiance à l'égard des vaccins

- Avez-vous des questions ou des commentaires?
- Avez-vous une réussite ou une meilleure pratique à communiquer à vos collègues à l'échelle du pays?
- Souhaitez-vous être ajouté à la liste de distribution pour recevoir directement l'InfoBulletin sur la confiance à l'égard des vaccins de l'ASPC?

Envoyez-nous un courriel à l'adresse : vaccination@phac-aspc.gc.ca

Veuillez noter que toute question médicale doit être adressée à votre fournisseur de soins de santé local et que toute question médicale urgente doit être adressée au 911 ou au service d'urgences local.

Annexe

Ressources en vedette

Chapitre sur la COVID-19 du Guide canadien d'immunisation

- Le 23 décembre 2021, **l'ASPC a publié un nouveau chapitre sur le vaccin contre la COVID-19 dans le Guide canadien d'immunisation**. Ce chapitre comprend toutes les recommandations du CCNI sur l'utilisation des vaccins contre la COVID-19 jusqu'au 29 octobre 2021 inclus.
- Ce chapitre marque un changement dans la manière dont les conseils du CCNI sur les vaccins contre la COVID-19 sont présentés aux fournisseurs de soins de santé, afin de rendre les informations plus accessibles et de les présenter dans un format similaire à celui utilisé pour les autres vaccins.
- Les futures directives du CCNI sur l'utilisation des vaccins contre la COVID-19 continueront d'être publiées sur la page Web du CCNI sous forme de courts énoncés ou de réponses rapides. Ces déclarations seront intégrées dans le chapitre consacré aux vaccins contre la COVID-19 du GCI dès que possible pour les prestataires de soins de santé. Les versions antérieures des recommandations du CCNI sur l'utilisation des vaccins contre la COVID-19 seront conservées sur la page Web du CCNI dans la section COVID-19.
- Le chapitre consacré aux vaccins contre la COVID-19 se trouve dans la Partie 4 : Agents d'immunisation active du Guide canadien d'immunisation**.**

Ressources pour l'enfance et la jeunesse

- Guide de référence rapide sur l'utilisation des vaccins contre la COVID-19 pour les enfants de 5 à 11 ans
- Guide de vaccination contre la COVID-19 pour les jeunes et les adultes (âgés de 12 ans et plus)
- COVID 19 : Prendre des décisions relatives à la vaccination des enfants de 5 à 11 ans – conseils pour les parents et tuteurs
- Le système CARD™ pour faire face à la peur et à l'anxiété liées aux aiguilles chez les enfants
- Trousse à outils de sensibilisation aux vaccins contre la COVID-19 pour les enfants (5-11 ans)

Ressources sur la fertilité et la grossesse

- Déclaration de la Société des obstétriciens et gynécologues du Canada sur la vaccination contre la COVID-19 pendant la grossesse
- Surveillance au Canada de la COVID-19 pendant la grossesse : épidémiologie, résultats pour la mère et le nourrisson (page disponible en français, données présentées en anglais)
- Vidéo « Des questions sur les vaccins contre la COVID-19» – Les vaccins COVID-19 peuvent-ils nuire à la fertilité?

Programme de soutien aux victimes d'une vaccination

- Il faut soutenir les Canadiens qui soutiennent la santé publique en se faisant vacciner s'ils subissent un préjudice grave et permanent à la suite d'une vaccination. Bien que rares, ces blessures peuvent se produire.

- Le Programme de soutien aux victimes d'une vaccination (PSVV), mis en place le 1er juin 2021, offre un soutien financier aux personnes qui ont subi une blessure grave et permanente après avoir reçu un vaccin autorisé par Santé Canada, administré au Canada, le 8 décembre 2020 ou après.

- Raymond Chabot Grant Thornton Consulting Inc, la tierce partie indépendante qui administre le Programme, a récemment publié les statistiques du programme sur son site Web, notamment des informations sur le nombre de demandes d'indemnisation reçues, le nombre de demandes d'indemnisation traitées et le montant des indemnités versées. Des informations sur le programme, y compris sur la manière de soumettre une demande d'indemnisation, ainsi que des statistiques complètes, sont disponibles à l'adresse suivante : soutienvinctimesvaccination.ca/fr/.

Sources

[1] . Allotey, E. Stallings, M. Bonet et coll., « Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis », *BMJ*, vol. 370, 2020, art. nº m3320.

[2] L.D. Zambrano, S. Ellington, P. Strid et coll., « Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–October 3, 2020 », *Morbidity and Mortality Weekly Report (MMWR)*, vol. 69, nº 44 (2020), p. 1641-1647.

[3] D. Money, *Surveillance canadienne de la COVID-19 pendant la grossesse: épidémiologie, effets sur la mère et l'enfant*, rapport nº 4, publié le 3 juin 2021, 2021.

[4] S.Q. Wei, M. Bilodeau-Bertrand, S. Liu et N. Auger, « The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis », *Canadian Medical Association Journal (CMAJ)*, vol. 193, nº 16 (2021), p. e540-e548. doi : https://doi.org/10.1503/cmaj.202604

[5] W. Fu, B. Sivajohan, E. McClymont, A. Albert, C. Elwood, G. Ogilvie et D. Money, « Systematic review of the safety, immunogenicity, and effectiveness of COVID-19 vaccines in pregnant and lactating individuals and their infants », *International Journal of Gynecology & Obstetrics*, 4 novembre 2021. doi : 10.1002/ijgo.14008. Publié en ligne avant impression. PMID : 34735722.

[6] W. Fu, B. Sivajohan, E. McClymont, A. Albert, C. Elwood, G. Ogilvie et D. Money, « Systematic review of the safety, immunogenicity, and effectiveness of COVID-19 vaccines in pregnant and lactating individuals and their infants », *International Journal of Gynecology & Obstetrics*, 4 novembre 2021. doi : 10.1002/ijgo.14008. Publié en ligne avant impression. PMID : 34735722.

[7] C. Betsch, N.T. Brewer, P. Brocard, P. Davies, W. Gaissmaier, N. Haase et M. Stryk, « Opportunities and challenges of Web 2.0 for vaccination decisions », *Vaccine*, vol. 30, nº 25 (2012), p. 3727-3733. doi : https://doi.org/10.1016/j.vaccine.2012.02.025

[8] UK Health Security Agency, *Effectiveness of 3 doses of COVID-19 vaccines against symptomatic COVID-19 and hospitalisation in adults aged 65 years and older*, gouvernement du Royaume-Uni, 15 novembre 2021. https://khub.net/documents/135939561/338928724/Effectiveness+of+3+doses+of+COVID-19+vaccines+against+symptomatic+COVID-19+and+hospitalisation+in+adults+aged+65+years+and+older.pdf/ab8f3558-1e16-465c-4b92-56334b6a832a

[9] UK Health Security Agency, *SARS-CoV-2 variants of concern and variants under investigation in England: Technical briefing 34*, gouvernement du Royaume-Uni, 14 janvier 2022. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1046623/Technical-Briefing-34-14January2022.pdf

[10] J.R. Su, *COVID-19 vaccine safety updates: Primary series in children and adolescents ages 5–11 and 12–15 years, and booster doses in adolescents ages 16–24 years*, Advisory Committee on Immunization Practices (ACIP), 5 janvier 2022. Données du Vaccine Adverse Event Reporting System (VEARS) présentées à l'ACIP. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-01-05/02-COVID-Su-508.pdf

[11] L.D. Zambrano, M.M. Newhams, S.M. Olson et coll., « Effectiveness of BNT162b2 (Pfizer-BioNTech) mRNA Vaccination Against Multisystem Inflammatory Syndrome in Children Among Persons Aged 12–18 Years — United States, July–December 2021 », *Morbidity and Mortality Weekly Report (MMWR)*, vol. 71, nº 2 (2022), p. 52-58. doi : http://dx.doi.org/10.15585/mmwr.mm7102e1

JAMA | Original Investigation

Association of COVID-19 Vaccination in Pregnancy With Adverse Peripartum Outcomes

Deshayne B. Fell, PhD; Tavleen Dhinsa, MSc; Gillian D. Alton, PhD; Eszter Török, PhD; Sheryll Dimanlig-Cruz, MSc; Annette K. Regan, PhD; Ann E. Sprague, PhD; Sarah A. Buchan, PhD; Jeffrey C. Kwong, MD; Sarah E. Wilson, MD; Siri E. Håberg, MD, PhD; Christopher A. Gravel, PhD; Kumanan Wilson, MD; Darine El-Chaâr, MD; Mark C. Walker, MD; Jon Barrett, MD; Shannon E. MacDonald, PhD; Nannette Okun, MD; Prakesh S. Shah, MD; Shelley D. Dougan, MSc; Sandra Dunn, PhD; Lise Bisnaire, PhD

IMPORTANCE There is limited comparative epidemiological evidence on outcomes associated with COVID-19 vaccination during pregnancy; monitoring pregnancy outcomes in large populations is required.

OBJECTIVE To evaluate peripartum outcomes following COVID-19 vaccination during pregnancy.

DESIGN, SETTING, AND PARTICIPANTS Population-based retrospective cohort study in Ontario, Canada, using a birth registry linked with the provincial COVID-19 immunization database. All births between December 14, 2020, and September 30, 2021, were included.

EXPOSURES COVID-19 vaccination during pregnancy, COVID-19 vaccination after pregnancy, and no vaccination.

MAIN OUTCOMES AND MEASURES Postpartum hemorrhage, chorioamnionitis, cesarean delivery (overall and emergency cesarean delivery), admission to neonatal intensive care unit (NICU), and low newborn 5-minute Apgar score (<7). Linear and robust Poisson regression was used to generate adjusted risk differences (aRDs) and risk ratios (aRRs), respectively, comparing cumulative incidence of outcomes in those who received COVID-19 vaccination during pregnancy with those vaccinated after pregnancy and those with no record of COVID-19 vaccination at any point. Inverse probability of treatment weights were used to adjust for confounding.

RESULTS Among 97 590 individuals (mean [SD] age, 31.9 [4.9] years), 22 660 (23%) received at least 1 dose of COVID-19 vaccine during pregnancy (63.6% received dose 1 in the third trimester; 99.8% received an mRNA vaccine). Comparing those vaccinated during vs after pregnancy (n = 44 815), there were no significantly increased risks of postpartum hemorrhage (incidence: 3.0% vs 3.0%; aRD, −0.28 per 100 individuals [95% CI, −0.59 to 0.03]; aRR, 0.91 [95% CI, 0.82-1.02]), chorioamnionitis (0.5% vs 0.5%; aRD, −0.04 per 100 individuals [95% CI, −0.17 to 0.09]; aRR, 0.92 [95% CI, 0.70-1.21]), cesarean delivery (30.8% vs 32.2%; aRD, −2.73 per 100 individuals [95% CI, −3.59 to −1.88]; aRR, 0.92 [95% CI, 0.89-0.95]), NICU admission (11.0% vs 13.3%; aRD, −1.89 per 100 newborns [95% CI, −2.49 to −1.30]; aRR, 0.85 [95% CI, 0.80-0.90]), or low Apgar score (1.8% vs 2.0%; aRD, −0.31 per 100 newborns [95% CI, −0.56 to −0.06]; aRR, 0.84 [95% CI, 0.73-0.97]). Findings were qualitatively similar when compared with individuals who did not receive COVID-19 vaccination at any point (n = 30 115).

CONCLUSIONS AND RELEVANCE In this population-based cohort study in Ontario, Canada, COVID-19 vaccination during pregnancy, compared with vaccination after pregnancy and with no vaccination, was not significantly associated with increased risk of adverse peripartum outcomes. Study interpretation should consider that the vaccinations received during pregnancy were primarily mRNA vaccines administered in the second and third trimester.

Editorial page 1451

Related articles pages 1469 and 1500

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Deshayne B. Fell, PhD, School of Epidemiology and Public Health, University of Ottawa, Scientist, Children's Hospital of Eastern Ontario (CHEO) Research Institute, ICES, Centre for Practice-Changing Research, 401 Smyth Rd, Room L1154, Ottawa, ON K1H 8L1, Canada (dfell@cheo.on.ca).

JAMA. 2022;327(15):1478-1487. doi:10.1001/jama.2022.4255
Published online March 24, 2022.

© 2022 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ on 06/22/2023

Pregnant individuals are at higher risk for COVID-19 complications, including hospitalization, intensive care unit (ICU) admission, and death, compared with nonpregnant individuals.[1,2] Significantly higher rates of adverse pregnancy outcomes, such as preterm birth and stillbirth, have also been observed after SARS-CoV-2 infection.[3,4] Vaccination during pregnancy is routinely recommended to prevent morbidity and mortality in both pregnant individuals and newborns from other infectious diseases, such as influenza and pertussis.[5] Since COVID-19 vaccines became available, many countries have also adopted recommendations for COVID-19 vaccination during pregnancy[6,7] to prevent severe COVID-19 and related complications in this population. Given the lack of prelicensure data specific to this population, ongoing safety monitoring is important to rule out potential risks of adverse maternal, fetal, and newborn outcomes. Emerging evidence from large epidemiological studies, to date, has not indicated any significantly increased risks of spontaneous abortion,[8,9] preterm birth,[10,11] or small-for-gestational-age birth[10,11] after COVID-19 vaccination during pregnancy; however, there is limited evidence from large populations on other outcomes after COVID-19 vaccination during pregnancy.

In Ontario—Canada's most populous province with universal, publicly-funded health care and approximately 140 000 births each year—pregnant individuals were designated a priority population for COVID-19 vaccination in late April 2021.[12] The purpose of this study was to evaluate the association between COVID-19 vaccination during pregnancy with maternal and neonatal peripartum outcomes occurring just before, during, or after delivery.

Key Points

Question Is COVID-19 vaccination during pregnancy associated with adverse peripartum outcomes?

Findings In this population-based retrospective cohort study of 97 590 individuals in Ontario, Canada, COVID-19 vaccination during pregnancy, compared with vaccination after pregnancy and with no vaccination, was not significantly associated with increased risk of postpartum hemorrhage, chorioamnionitis, cesarean delivery, admission to neonatal intensive care unit, or low newborn 5-minute Apgar score.

Meaning COVID-19 vaccination during pregnancy was not significantly associated with an increased risk of adverse peripartum outcomes.

Methods

This study used routinely collected data by province-wide registries, and no additional data were collected from patients. The research ethics board of the Children's Hospital of Eastern Ontario granted ethics approval and waived informed consent. We followed standardized guidance for reporting observational studies.[13]

Study Design and Population

This population-based retrospective cohort study used the Better Outcomes Registry & Network Ontario birth registry[14] linked with the provincial COVID-19 immunization database (COVaxON). We identified all pregnancy records in the birth registry with a birth date or expected due date on or after December 14, 2020 (when the COVID-19 vaccination program began in Ontario[15]), and excluded ongoing pregnancies as of September 30, 2021, individuals who became pregnant less than 42 weeks before the end of the study period (ie, those with a last menstrual period after December 9, 2020) to avoid cohort truncation bias,[16] records with documented gestational age less than 20 weeks at birth, and pregnancy terminations (**Figure 1**).

Data Sources

The Better Outcomes Registry & Network Ontario Information System collects extensive information on all live births and stillbirths from more than 250 hospitals, birth centers, midwifery practice groups, and prenatal screening laboratories across Ontario.[14] Available data include maternal demographics, health behaviors, preexisting health problems, pregnancy history, obstetric complications, interventions, and birth outcomes. These data are collected from medical records, clinical forms, and patient interview.[14,17] Using the maternal postal code, we linked the study population to Statistics Canada's 2016 Census, to obtain information on rural/urban residence and neighborhood income, and to the Ontario Marginalization Index, which provides 4 area-based measures reflecting social and economic marginalization.[18] Using unique health card numbers, we deterministically linked the study population with COVID-19 vaccination records in COVaxON up to September 30, 2021. Information on vaccine product, number of doses, and date(s) of vaccination are reported directly into COVaxON at the time of immunization. In a sensitivity analysis, we also deterministically linked with the Public Health Case and Contact Management Solution[19] to ascertain laboratory-confirmed COVID-19 during pregnancy.

Measures

Exposure

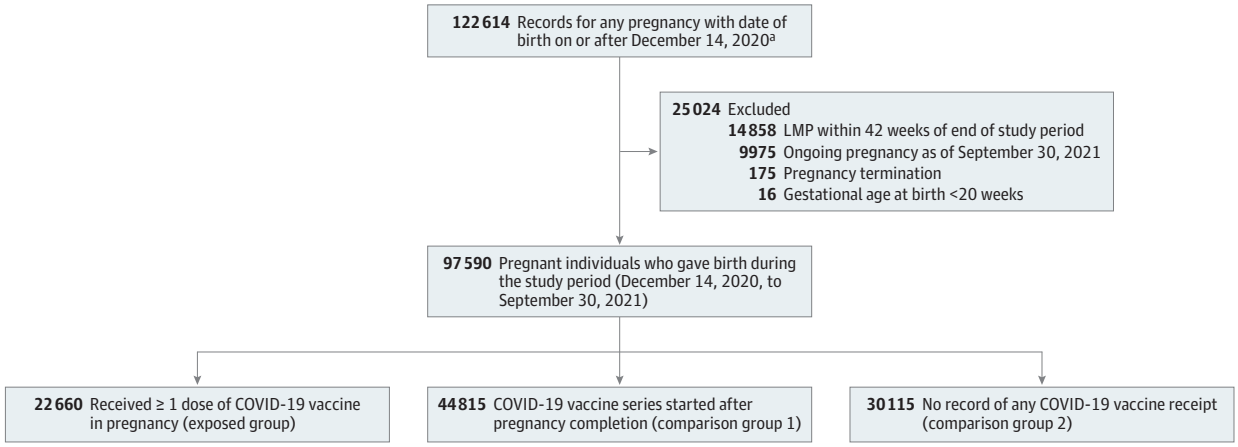
Ontario's COVID-19 vaccination program began on December 14, 2020 (Pfizer-BioNTech [BNT162b2] became available on December 14, 2020; Moderna [mRNA-1273], December 28, 2020; and AstraZeneca [AZD1222], February 26, 2021).[20,21] Pregnant people in early priority groups, such as front-line clinicians, were immediately eligible for vaccination[22]; however, it was not offered to the general population of pregnant individuals until April 23, 2021, when pregnancy became prioritized in Ontario's vaccination program.[12] Due to a limited vaccine supply in Canada during the first half of 2021, extended dose intervals and heterologous vaccine products to complete a series were recommended, where necessary.[23,24]

We determined the gestational timing of doses received during pregnancy using vaccination dates from COVaxON and the estimated date of birth recorded in the birth registry. COVID-19 vaccination was considered to have occurred during pregnancy if 1 or more doses were administered between

© 2022 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ on 06/22/2023

Figure 1. Flow of Individuals in a Study of the Association of COVID-19 Vaccination in Pregnancy With Adverse Peripartum Outcomes



[a] These records represent all pregnant individuals (ie, 1 record per pregnant individual) and were used to evaluate obstetric outcomes (postpartum hemorrhage, chorioamnionitis, cesarean delivery, and emergency cesarean delivery).

the estimated date of conception up to 1 day before birth (conception date was estimated by adding 14 days to the last menstrual period date). Based on previous studies, we anticipated that baseline characteristics of individuals who were vaccinated during pregnancy would systematically differ from those who were unvaccinated during pregnancy.[25,26] Because vaccine eligibility and supply was limited in earlier study months, we hypothesized that individuals vaccinated after pregnancy would be more similar to those vaccinated during pregnancy than to those never vaccinated at any time. Therefore, we stratified the unvaccinated during pregnancy group into 2 comparison groups: (1) those vaccinated after pregnancy (comparison group 1) and (2) those with no record of any COVID-19 vaccination by September 30, 2021 (comparison group 2).

Outcomes

Assessing potential risks of vaccination during pregnancy requires careful consideration of the timing of vaccination relative to gestational exposure windows.[27] Because pregnant people were only prioritized for COVID-19 vaccination in late April 2021[12] and the study period included births up to September 30, 2021, vaccinated pregnancies occurred later in calendar time (eFigure 1 in the Supplement) and the majority of individuals in this group were vaccinated during the third trimester (**Figure 2**). This precluded assessment of outcomes with earlier gestational onset, such as those related to abnormal placentation; thus, we evaluated peripartum outcomes occurring just before, during, or after delivery that could plausibly be associated with later pregnancy vaccination (ie, vaccination during the second or third trimester). Obstetric outcomes included postpartum hemorrhage, chorioamnionitis, cesarean delivery, and emergency cesarean delivery (indications in eTable 1 in the Supplement); newborn outcomes included neonatal ICU (NICU) admission and low newborn 5-minute Apgar score (<7).

Covariates

We included covariates potentially associated with pregnancy outcomes and vaccination behavior in propensity scores to account for confounding. Covariates obtained from the birth registry included maternal age at delivery (in years); prepregnancy body mass index; self-reported maternal smoking status and substance use during pregnancy; public health unit region; preexisting maternal health conditions (asthma, chronic hypertension, diabetes, heart disease, thyroid disease); parity; and multiple birth. Covariates obtained from the Canadian Census included rural/urban residence and neighborhood-level income quintile. Covariates obtained from the Ontario Marginalization Index included neighborhood-level quintiles for residential instability (family or housing instability), material deprivation (inability to access and attain basic material needs), dependency (receipt of income support), and ethnic concentration (geographic areas with high concentrations of recent immigrants and/or "visible minorities," defined by Statistics Canada as persons, other than Aboriginal peoples, who self-identify as "non-Caucasian" or "non-White," including individuals identifying as South Asian, Chinese, Black, Filipino, Arab, Latin American, Southeast Asian, West Asian, Korean, Japanese, or other).[18] See eAppendix 1 in the Supplement for details.

Statistical Analyses

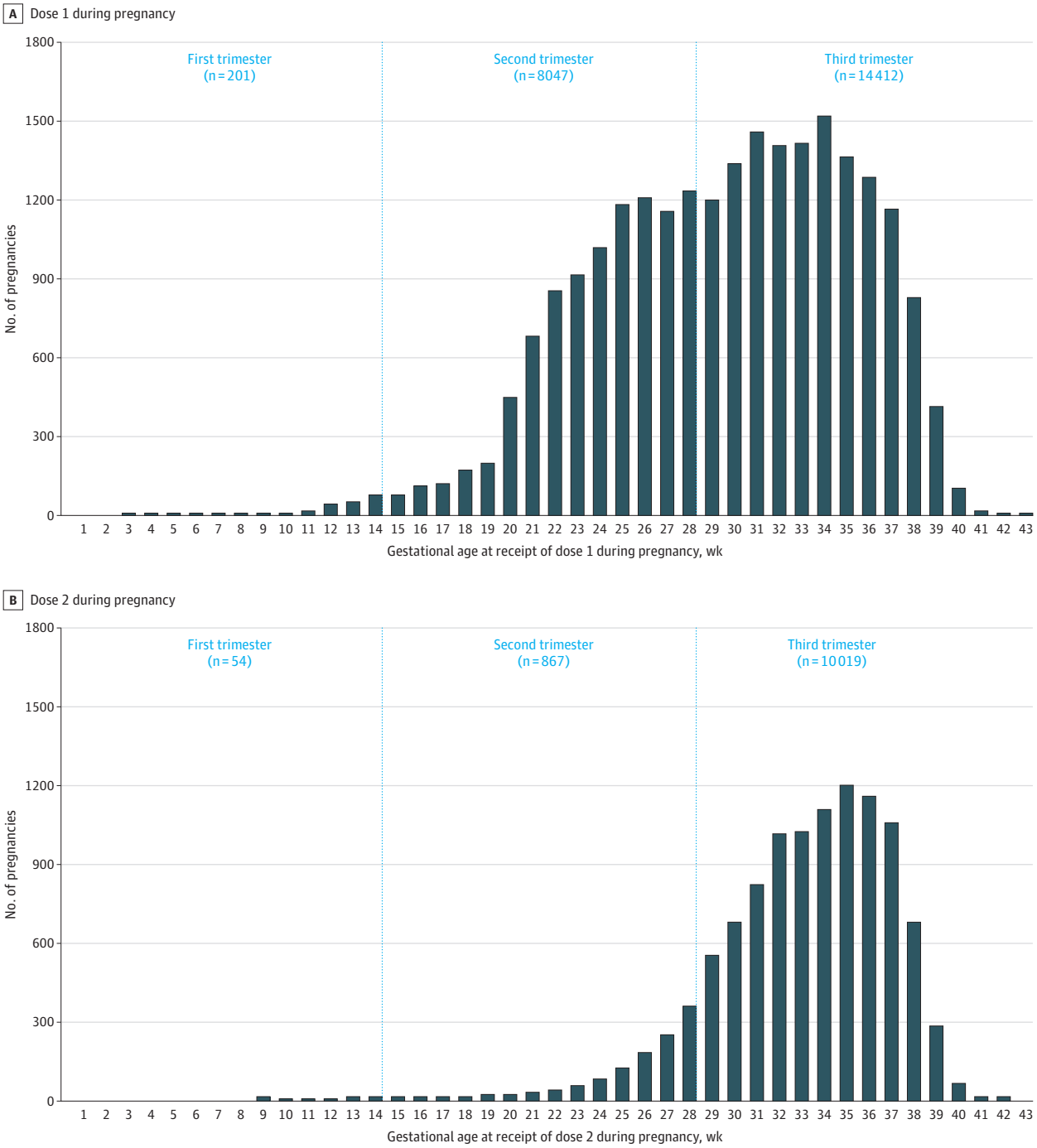
The number of pregnancies was the unit of analysis for obstetric outcomes, while it was all live births (1 record per infant, including multiples) for newborn outcomes. We compared the distribution of all baseline characteristics in pregnant individuals across exposure groups using standardized differences; an absolute standardized difference less than 0.1 was considered indicative of balance across groups.[28]

Unadjusted cumulative incidence rates for all outcomes by exposure group were computed; we used linear and log

© 2022 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ on 06/22/2023

Figure 2. Gestational Age at COVID-19 Vaccination in a Study of the Association of COVID-19 Vaccination in Pregnancy With Adverse Peripartum Outcomes



A, Median (IQR) gestational age at dose 1 was 213 (180-242) days. Counts for gestational weeks 2 and 3 have been combined to permit reporting (cell counts <6 cannot be reported). B, Median (IQR) gestational age at dose 2 was 238 (218-255) days. Counts for gestational weeks 2 to 9 have been combined to permit reporting (cell counts <6 cannot be reported).

Poisson regression (with robust variance estimation) to compute unadjusted risk differences (RDs) and risk ratios (RRs), respectively. Propensity score methods were used to account for potential confounding bias; 2 sets of propensity scores were computed, representing the predicted probability of COVID-19 vaccination during pregnancy relative to each comparison group. In addition to the variables listed previously, we included 2 temporal variables: calendar month of estimated conception and a flag denoting pregnancy completion prior to April 23, 2021. Multiple imputation was used to address missing

© 2022 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ on 06/22/2023

covariate values (details about multiple imputation and propensity score methods provided in eAppendix 2 in the Supplement). Both sets of propensity scores were developed from each of the 5 imputed data sets and used to compute inverse probability of treatment weights, which were stabilized and trimmed to the first and 99th percentiles.[28]

Regression models incorporating stabilized weights from each of the imputed data sets were used to generate adjusted coefficients and standard errors, which were combined to produce adjusted estimates and 95% CIs. In subgroup analyses, we stratified by number of doses received during pregnancy, vaccine product received for dose 1, and trimester during which dose 1 was received. In sensitivity analyses, we applied alternate trimming values to the stabilized weights and ran conventional multivariable adjusted models instead of using weights. We also repeated the main analyses with additional adjustment for maternal age and calendar time (due to residual imbalances in these variables after weighting), time since vaccination (to account for gestational timing of vaccination), confirmed COVID-19 during pregnancy, and gestational age at birth. In addition, we carried out a post hoc assessment of the robustness of the propensity scores to the potential influence of calendar time due to changes in vaccine eligibility. Because of the potential for type I error due to multiple comparisons, findings should be interpreted as exploratory. Precision around point estimates was provided using 2-sided 95% CIs; estimates were considered statistically significant when the 95% CI excluded the null value. Analyses were conducted using SAS, version 9.4 (SAS Institute).

Results

There were 122 614 pregnant individuals in Ontario with a birth date or expected due date on or after December 14, 2020. There were 97 590 individuals remaining after exclusion of those who did not meet inclusion criteria (Figure 1), of whom 22 660 (23%) received at least 1 dose of COVID-19 vaccine during pregnancy and 74 930 (77%) had not been vaccinated by pregnancy completion (44 815 [46%] were vaccinated after pregnancy [comparison group 1] and 30 115 [31%] were not vaccinated at any point [comparison group 2]). The study flow diagram for newborn outcomes is provided in eFigure 2 in the Supplement.

Compared with individuals vaccinated after pregnancy (comparison group 1), those vaccinated during pregnancy were less likely to be younger than 30 years (23.7% vs 32.2%) and more likely to reside in neighborhoods with higher incomes (quintile 5: 21.3% vs 17.4%) and lower material deprivation (quintile 1: 28.6% vs 23.7%). Compared with individuals who were never vaccinated (comparison group 2), those vaccinated during pregnancy were more likely to reside in neighborhoods with higher incomes (quintile 5: 21.3% vs 13.1%) and lower material deprivation (quintile 1: 28.6% vs 16.9%) and were more likely to be nulliparous (46.1% vs 37.8%). They were also less likely to be younger than 30 years (23.7% vs 42.6%), smoke during pregnancy (3.3% vs 11.4%), and live in a rural setting (13.2% vs 18.3%) (**Table 1**). Following propensity score weighting, baseline characteristics were well-balanced across groups; all standardized differences, other than maternal age and calendar time, were less than 0.1 (eTable 3 and eFigure 3 in the Supplement) and there was adequate overlap in propensity score distributions by exposure group after weighting (eFigure 4 in the Supplement).

Of the 22 660 individuals vaccinated during pregnancy, 766 (3.4%) received only dose 1, 10 954 (48.3%) received dose 1 during pregnancy and dose 2 after pregnancy, and 10 940 (48.3%) received both doses during pregnancy. Overall, 63.6% of individuals vaccinated during pregnancy received dose 1 in the third trimester, at a median gestation of 213 days (30 weeks); 79.9% received BNT162b2 for dose 1, 19.9% received mRNA-1273, and less than 1% received another product (eTable 4 in the Supplement).

Compared with 44 815 individuals who initiated their COVID-19 vaccine series after pregnancy (comparison group 1), there was no significant association between COVID-19 vaccination during pregnancy and postpartum hemorrhage; the cumulative incidence of postpartum hemorrhage in both groups was 3.0%, the adjusted RR was 0.91 (95% CI, 0.82-1.02), and the adjusted RD was −0.28 per 100 individuals (95% CI, −0.59 to 0.03) (**Table 2**). COVID-19 vaccination during pregnancy was not significantly associated with a higher risk of chorioamnionitis (0.5% vs 0.5%; aRR, 0.92 [95% CI, 0.70-1.21]; aRD, −0.04 per 100 individuals [95% CI, −0.17 to 0.09]), cesarean delivery (30.8% vs 32.2%; aRR, 0.92 [95% CI, 0.89-0.95]; aRD, −2.73 per 100 individuals [95% CI, −3.59 to −1.88]), or emergency cesarean delivery (15.3% vs 16.4%; aRR, 0.89 [95% CI, 0.84-0.94]; aRD, −1.81 per 100 individuals [95% CI, −2.54 to −1.08]). Rates of adverse newborn outcomes were lower among those born to individuals vaccinated during pregnancy (Table 2); after adjustment for confounding, the significantly lower risk persisted for both NICU admission (11.0% vs 13.3%; aRR, 0.85 [95% CI, 0.80-0.90]; aRD, −1.89 per 100 newborns [95% CI, −2.49 to −1.30]) and low 5-minute Apgar score (<7) (1.8% vs 2.0%; aRR, 0.84 [95% CI, 0.73-0.97]; aRD, −0.31 per 100 newborns [95% CI, −0.56 to −0.06]). Compared with the 30 115 individuals who were never vaccinated (comparison group 2), there were no significantly increased risks of any of the outcomes in those vaccinated during pregnancy; most CIs included the null value, except for risk of emergency cesarean delivery (15.3% vs 14.2%; aRR, 0.91 [95% CI, 0.87-0.96]; aRD, −1.35 per 100 individuals [95% CI, −2.06 to −0.63]) and NICU admission (11.0% vs 12.8%; aRR, 0.92 [95% CI, 0.87-0.97]; aRD, −0.93 per 100 newborns [95% CI, −1.52 to −0.35]), which were both significantly lower among individuals who were vaccinated during pregnancy (**Table 3**).

Subgroup and Sensitivity Analyses

In subgroup analyses comparing individuals vaccinated during pregnancy with those vaccinated after pregnancy (comparison group 1), there were no statistically significant increases in study outcomes when those vaccinated during pregnancy were stratified by number of doses received, vaccine product, or trimester of vaccination for dose 1 (eTable 5 in the Supplement). Results from sensitivity analyses did not

© 2022 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ on 06/22/2023

Table 1. Unweighted Distribution of Baseline Characteristics of the Study Population[a,b]

Characteristic	Received ≥1 dose of COVID-19 vaccine during pregnancy, No. (%) (n = 22 660)	Not vaccinated during pregnancy			
		Initiated COVID-19 vaccine series after pregnancy, No. (%) (n = 44 815)	Standardized difference[c]	Not vaccinated with COVID-19 vaccine at any time, No. (%) (n = 30 115)	Standardized difference[d]
Maternal age, y					
<25	914 (4.0)	3284 (7.3)	0.14	4224 (14.0)	0.35
25-29	4468 (19.7)	11 138 (24.9)	0.12	8606 (28.6)	0.21
30-34	10 344 (45.6)	18 528 (41.3)	0.09	10 230 (34.0)	0.24
35-39	5864 (25.9)	9831 (21.9)	0.09	5565 (18.5)	0.18
≥40	1070 (4.7)	2034 (4.5)	0.01	1490 (4.9)	0.01
Mean (SD)	32.8 (4.3)	32.0 (4.8)	0.15	31.0 (5.5)	0.31
Estimated date of conception					
Before June 2020	27 (0.1)	14 591 (32.6)	0.98	6644 (22.1)	0.75
June-July 2020	467 (2.1)	15 981 (35.7)	0.95	6530 (21.7)	0.64
August-September 2020	7367 (32.5)	8886 (19.8)	0.29	6660 (22.1)	0.23
October-November 2020	10 925 (48.2)	4511 (10.1)	0.92	7374 (24.5)	0.51
December 2020 or later	3874 (17.1)	846 (1.9)	0.54	2907 (9.7)	0.22
Gave birth before April 23[e]	542 (2.4)	32 051 (71.5)	2.05	13 789 (45.8)	1.18
Nulliparous	10 382/22 531 (46.1)	20 614/44 635 (46.2)	0.00	11 351/29 999 (37.8)	0.17
Multiple birth	328 (1.4)	656 (1.5)	0.00	408 (1.4)	0.01
Preexisting maternal medical condition[f,g]	2763 (12.2)	5121 (11.4)	0.02	2931 (9.7)	0.08
Thyroid disease	1531 (6.8)	2711 (6.0)	0.03	1266 (4.2)	0.11
Asthma	935 (4.1)	1675 (3.7)	0.02	1211 (4.0)	0.01
Diabetes	234 (1.0)	526 (1.2)	0.01	310 (1.0)	0.00
Chronic hypertension	202 (0.9)	452 (1.0)	0.01	277 (0.9)	0.00
Heart disease	43 (0.2)	30 (0.1)	0.03	36 (0.1)	0.02
Smoked during pregnancy	723/22 058 (3.3)	2277/44 044 (5.2)	0.10	3380/29 593 (11.4)	0.31
Substance use during pregnancy[h]	648/21 805 (3.0)	1629/42 344 (3.8)	0.04	2392/28 920 (8.3)	0.23
Maternal BMI ≥30.0	4096/20 478 (20.0)	8350/40 129 (20.8)	0.01	5693/26 507 (21.5)	0.02
Neighborhood median family income quintiles					
1 (lowest)	3497/22 542 (15.5)	8449/44 572 (19.0)	0.09	7740/29 354 (26.4)	0.26
2	4165/22 542 (18.5)	8903/44 572 (20.0)	0.04	6417/29 354 (21.9)	0.07
3	4837/22 542 (21.5)	9717/44 572 (21.8)	0.01	5987/29 354 (20.4)	0.04
4	5247/22 542 (23.3)	9729/44 572 (21.8)	0.03	5354/29 354 (18.2)	0.13
5 (highest)	4796/22 542 (21.3)	7774/44 572 (17.4)	0.10	3856/29 354 (13.1)	0.22
Rural residence	2991 (13.2)	5954/44 808 (13.3)	0.00	5425/29 629 (18.3)	0.13
Material deprivation quintile[i]					
1 (least deprived)	6388/22 333 (28.6)	10 496/44 200 (23.7)	0.11	4705/27 921 (16.9)	0.31
2	5092/22 333 (22.8)	9323/44 200 (21.1)	0.04	4958/27 921 (17.8)	0.15
3	4071/22 333 (18.2)	8350/44 200 (18.9)	0.02	5103/27 921 (18.3)	0.03
4	3642/22 333 (16.3)	7997/44 200 (18.1)	0.05	5572/27 921 (20.0)	0.06
5 (most deprived)	3140/22 333 (14.1)	8034/44 200 (18.2)	0.11	7583/27 921 (27.2)	0.29
History of COVID-19 infection during pregnancy	689 (3.0)	1582 (3.5)	0.03	1061 (3.5)	0.03
Gestational age at birth, mean (SD), wk	38.8 (1.6)	38.6 (1.8)	0.09	38.8 (1.8)	0.01
Birth weight, mean (SD), g	3368 (526.7)	3325 (563.3)	0.06	3351 (557.2)	0.03

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

[a] For variables with missing values, data are presented as the numerator over the denominator of nonmissing values.

[b] Additional baseline characteristics are presented in the Supplement (eTable 2 in Supplement).

[c] Absolute standardized difference between those who received ≥1 dose of COVID-19 vaccine during pregnancy and those who initiated COVID-19 vaccine series after pregnancy. Standardized difference >0.10 indicates an imbalance in the distribution between these 2 groups.

[d] Absolute standardized difference between those who received ≥1 dose of COVID-19 vaccine during pregnancy and those who had not received any COVID-19 vaccine at any time. Standardized difference >0.10 indicates an imbalance in the distribution between these 2 groups.

[e] Captures timing of pregnancy relative to April 23, 2021; pregnant individuals were designated a high-priority population for COVID-19 vaccination on April 23, 2021.

[f] Composite of asthma, chronic hypertension, diabetes, heart disease, or thyroid disease. Sum of individual conditions does not equal the total number of individuals with any condition, because categories were not mutually exclusive.

[g] Includes individuals with any preexisting maternal medical condition.

[h] Self-reported cannabis, opioid, or alcohol use during pregnancy.

[i] Based on Canadian Census data. It refers to individuals and communities being unable to access and attain basic material needs and is closely connected to poverty.

© 2022 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ on 06/22/2023

Table 2. Risk of Adverse Peripartum Outcomes Among Individuals Who Received at Least 1 Dose During Pregnancy Compared With Those Who Initiated COVID-19 Vaccine Series After Pregnancy

Outcome	No. (%)		Risk ratio (95% CI)		
	Received ≥1 dose of COVID-19 vaccine during pregnancy	Initiated COVID-19 vaccine series after pregnancy (comparison group 1)	Crude	Adjusted[a]	Adjusted risk difference per 100 (95% CI)[a]
Pregnant individuals with a live birth or stillbirth, No.	22 660	44 815			
Postpartum hemorrhage	677 (3.0)	1351 (3.0)	0.99 (0.90 to 1.09)	0.91 (0.82 to 1.02)	−0.28 (−0.59 to 0.03)
Chorioamnionitis	101 (0.5)	214 (0.5)	0.93 (0.74 to 1.18)	0.92 (0.70 to 1.21)	−0.04 (−0.17 to 0.09)
Cesarean delivery	6988 (30.8)	14 427 (32.2)	0.96 (0.93 to 0.99)	0.92 (0.89 to 0.95)	−2.73 (−3.59 to −1.88)
Emergency cesarean delivery	2829 (15.3)	5943 (16.4)	0.93 (0.89 to 0.98)	0.89 (0.84 to 0.94)	−1.81 (−2.54 to −1.08)
Liveborn infants, No.	22 746	44 943			
NICU admission	2508 (11.0)	5969 (13.3)	0.83 (0.79 to 0.87)	0.85 (0.80 to 0.90)	−1.89 (−2.49 to −1.30)
Low 5-min Apgar score (<7)[b]	403/22 334 (1.8)	894/44 344 (2.0)	0.89 (0.79 to 1.00)	0.84 (0.73 to 0.97)	−0.31 (−0.56 to −0.06)

Abbreviation: NICU, neonatal intensive care unit.

[a] Adjusted using stabilized inverse probability of treatment weights.

[b] The Apgar scoring system is a standardized method to assess the status of newborns immediately after birth. It comprises 5 components (skin color, heart rate, reflexes, muscle tone, and respiration), each of which is given a score of 0, 1, or 2 (with 10 being the highest possible score).

Table 3. Risk of Adverse Peripartum Outcomes Among Individuals Who Received at Least 1 Dose During Pregnancy Compared With Those Not Vaccinated With COVID-19 Vaccine at Any Time

Outcome	No. (%)		Risk ratio (95% CI)		
	Received ≥1 dose of COVID-19 vaccine during pregnancy	Not vaccinated with COVID-19 vaccine at any time (comparison group 2)	Crude	Adjusted[a]	Adjusted risk difference per 100 (95% CI)[a]
Pregnant individuals with a live birth or stillbirth, No.	22 660	30 115			
Postpartum hemorrhage	677 (3.0)	1008 (3.4)	0.89 (0.81 to 0.98)	0.90 (0.81 to 1.00)	−0.32 (−0.64 to −0.01)
Chorioamnionitis	101 (0.5)	90 (0.3)	1.49 (1.12 to 1.98)	1.20 (0.90 to 1.59)	0.07 (−0.04 to 0.19)
Cesarean delivery	6988 (30.8)	8583 (28.5)	1.08 (1.05 to 1.12)	0.97 (0.94 to 1.00)	−0.97 (−1.81 to −0.14)
Emergency cesarean delivery	2829 (15.3)	3548 (14.2)	1.08 (1.03 to 1.14)	0.91 (0.87 to 0.96)	−1.35 (−2.06 to −0.63)
Liveborn infants, No.	22 746	30 109			
NICU admission	2508 (11.0)	3852 (12.8)	0.86 (0.82 to 0.91)	0.92 (0.87 to 0.97)	−0.93 (−1.52 to −0.35)
Low 5-min Apgar score (<7)[b]	403/22 334 (1.8)	588/29 588 (2.0)	0.91 (0.80 to 1.03)	0.88 (0.77 to 1.01)	−0.23 (−0.47 to 0.02)

Abbreviation: NICU, neonatal intensive care unit.

[a] Adjusted using stabilized inverse probability of treatment weights.

[b] The Apgar scoring system is a standardized method to assess the status of newborns immediately after birth. It comprises 5 components (skin color, heart rate, reflexes, muscle tone, and respiration), each of which is given a score of 0, 1, or 2 (with 10 being the highest possible score).

qualitatively differ from the original results (eTable 6 in the Supplement). Results from subgroup analyses comparing individuals vaccinated during pregnancy with those never vaccinated (comparison group 2) were consistent with results from the main analyses (eTable 7 in the Supplement). The magnitude and direction of point estimates from sensitivity analyses were similar to the main analyses, with the exception of an increase in NICU admission among infants born to vaccinated individuals when adjusted for time since dose 1 (aRR, 1.16 [95% CI, 1.07-1.26]; eTable 8 in the Supplement). The post hoc assessment of alternate propensity score specifications yielded weighted distributions and standardized differences that were similar to those from original analyses, supporting the robustness of the propensity scores to the effect of calendar time (eFigure 5 in the Supplement).

Discussion

In this large population-based study that included more than 22 000 individuals who received at least 1 dose of COVID-19 vaccine during pregnancy, vaccination was not significantly associated with any increased risk of postpartum hemorrhage, chorioamnionitis, cesarean delivery, NICU admission, or low 5-minute Apgar score. The results were largely unchanged when stratified according to the number of doses

© 2022 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ on 06/22/2023

received during pregnancy, vaccine product, or the trimester when dose 1 was received. Moreover, the interpretations did not change when the comparison group was individuals who were vaccinated after pregnancy (who were more similar to those vaccinated during pregnancy with respect to baseline characteristics, but had different calendar timing of pregnancy) or individuals who had not received a COVID-19 vaccine at any point by the end of September 2021 (who were more similar to those vaccinated during pregnancy with respect to calendar timing of pregnancy, but had different baseline characteristics). The results were robust to sensitivity analyses designed to account for potential residual confounding by factors such as maternal age, calendar time, time since vaccination, gestational length, and COVID-19 during pregnancy.

COVID-19 vaccine effectiveness has been shown to be high in pregnant people, similar to the general population.[29,30] Because COVID-19 vaccine–derived maternal antibodies cross the placenta,[31] vaccination during pregnancy could potentially protect newborns in the early months of life, similar to well-established benefits of influenza and pertussis vaccination during pregnancy.[32,33] Large epidemiological studies of COVID-19 vaccination during pregnancy available to date have not identified significantly increased risks of preterm birth or small-for-gestational-age birth overall[10,11] or when stratified by the number of doses received during pregnancy or trimester of vaccination (second or third trimester).[10] Miscarriage risk after COVID-19 vaccination during early pregnancy has been assessed by 2 large population-based case-control studies, neither of which found evidence of increased odds of spontaneous abortion associated with having received a COVID-19 vaccine; these conclusions remained unchanged regardless of number of doses received or mRNA vaccine product.[8,9] These findings are consistent with the large body of research on influenza and pertussis immunization during pregnancy, in which no significant associations with adverse maternal, fetal, or neonatal outcomes have been identified.[34-39]

Strengths of this study include the large number of individuals vaccinated during pregnancy. The data sources, which were population-based, limited potential selection bias and provided detailed information on clinical and sociodemographic variables. COVID-19 vaccination was ascertained through linkage with the database that captures all immunization events in Ontario, regardless of where they were received; thus, exposure misclassification is unlikely.

Limitations

This study has several limitations. First, the study relied on clinician-assigned outcome diagnoses recorded in the birth registry; therefore, misclassification of some outcomes is possible—particularly chorioamnionitis, which is difficult to diagnose, and postpartum hemorrhage, which may be incompletely documented. Assuming any outcome misclassification is nondifferential, estimates could be biased toward the null, potentially obscuring an increase in risk; however, given that these outcomes are uncommon and likely measured with high specificity, misclassification would have a small effect.[40] Second, given the observational nature of this study, causality cannot be inferred and findings should be interpreted cautiously. Despite achieving good balance of baseline covariates in weighted analyses, propensity score derivation was limited to variables available in the study databases. Third, although important potential confounders such as smoking, body mass index, and socioeconomic indicators were included, there was no information on other health-related behaviors such as influenza vaccination during recent seasons; thus, residual confounding remains possible. Fourth, there was an increase in risk of NICU admission in one sensitivity analysis; however, given the robustness of the results to all other sensitivity analyses, this may represent type I error due to the many statistical comparisons. Fifth, individuals in this study were predominantly vaccinated during the second and third trimesters; because pregnant people were only prioritized for COVID-19 vaccination in late April 2021, pregnancies with earlier gestational vaccination are still ongoing. As more individuals vaccinated earlier in pregnancy give birth (expected in late 2021/early 2022), other important obstetric and perinatal outcomes with earlier gestational origin and earlier gestational timing of vaccination during pregnancy will be evaluated.

Conclusions

In this population-based cohort study in Ontario, Canada, COVID-19 vaccination during pregnancy, compared with vaccination after pregnancy and with no vaccination, was not significantly associated with increased risk of adverse peripartum outcomes. Study interpretation should consider that the vaccinations received during pregnancy were primarily mRNA vaccines administered in the second and third trimester.

ARTICLE INFORMATION

Accepted for Publication: March 4, 2022.

Published Online: March 24, 2022. doi:10.1001/jama.2022.4255

Author Affiliations: School of Epidemiology and Public Health, University of Ottawa, Ottawa, Ontario, Canada (Fell, Dimanlig-Cruz, Gravel, El-Chaâr, Walker); Children's Hospital of Eastern Ontario (CHEO) Research Institute, Ottawa, Ontario, Canada (Fell, Dhinsa, Alton, Török, Dimanlig-Cruz, Sprague, Walker, Dougan, Dunn, Bisnaire); Better Outcomes Registry & Network (BORN) Ontario, Ottawa, Ontario, Canada (Dhinsa, Alton, Török, Dimanlig-Cruz, Sprague, Walker, Dougan, Dunn, Bisnaire); School of Nursing and Health Professions, University of San Francisco, San Francisco, California (Regan); Department of Epidemiology, UCLA Fielding School of Public Health, Los Angeles, California (Regan); Public Health Ontario, Toronto, Ontario, Canada (Buchan, Kwong, S. E. Wilson); Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada (Buchan, Kwong, S. E. Wilson); ICES, Toronto, Ontario, Canada (Kwong); Department of Family and Community Medicine, University of Toronto, Toronto, Ontario, Canada (Kwong); Centre for Fertility and Health, Norwegian Institute of Public Health, Oslo, Norway (Håberg); Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Quebec, Canada (Gravel); Department of Medicine, University of Ottawa, Ottawa, Ontario, Canada (K. Wilson); Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada (K. Wilson, El-Chaâr, Walker); Bruyère Research Institute, Ottawa, Ontario, Canada (K. Wilson); Department of Obstetrics and Gynecology, University of Ottawa, Ottawa, Ontario, Canada (El-Chaâr, Walker); Department of Obstetrics and Gynecology, McMaster University, Hamilton, Ontario, Canada (Barrett); Faculty of

© 2022 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ on 06/22/2023

Nursing, University of Alberta, Edmonton, Alberta, Canada (MacDonald); School of Public Health, University of Alberta, Edmonton, Alberta, Canada (MacDonald); Department of Pediatrics, University of Calgary, Calgary, Alberta, Canada (MacDonald); Department of Obstetrics and Gynaecology, University of Toronto, Toronto, Ontario, Canada (Okun); Department of Pediatrics, Mount Sinai Hospital, Toronto, Ontario, Canada (Shah); Department of Pediatrics, University of Toronto, Toronto, Ontario, Canada (Shah); Maternal-infant Care Research Centre, Department of Pediatrics, Mount Sinai Hospital, Toronto, Ontario, Canada (Shah); Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada (Shah); School of Nursing, University of Ottawa, Ottawa, Ontario, Canada (Dunn).

Author Contributions: Dr Fell had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Fell, Alton, Regan, Sprague, Kwong, Gravel, K. Wilson, El-Chaar, Barrett, MacDonald, Okun, Dougan, Bisnaire.
Acquisition, analysis, or interpretation of data: Fell, Dhinsa, Alton, Török, Dimanlig-Cruz, Regan, Sprague, Buchan, Kwong, S. Wilson, Håberg, Gravel, Walker, Barrett, MacDonald, Okun, Shah, Dougan, Dunn.
Drafting of the manuscript: Fell, Dhinsa, Török, Dimanlig-Cruz, Sprague.
Critical revision of the manuscript for important intellectual content: Fell, Dhinsa, Alton, Regan, Sprague, Buchan, Kwong, S. Wilson, Håberg, Gravel, K. Wilson, El-Chaar, Walker, Barrett, MacDonald, Okun, Shah, Dougan, Dunn, Bisnaire.
Statistical analysis: Fell, Dhinsa, Alton, Dimanlig-Cruz, Gravel.
Obtained funding: Fell, Sprague.
Administrative, technical, or material support: Fell, Török, Walker, Dougan, Dunn, Bisnaire.
Supervision: Fell, Håberg.
Other - Clinical input: El-Chaar.

Conflict of Interest Disclosures: Dr Regan reported receiving grants from the National Institutes of Health/National Institute of Allergy and Infectious Diseases and grants from EuroQol outside the submitted work. Dr Sprague reported receiving grants from the COVID-19 Immunity Task Force and funding from the Ministry of Health of Ontario Better Outcomes Registry & Network (BORN) Ontario during the conduct of the study. Dr Håberg reported receiving grants from NordForsk (project number 105545) during the conduct of the study. Dr K. Wilson reported being CEO of CANImmunize Inc and being on the advisory board for Medicago. Dr Dougan reported receiving grants from the COVID-19 Immunity Task Force during the conduct of the study. No other disclosures were reported.

Funding/Support: This study was supported by funding from the Public Health Agency of Canada, through the Vaccine Surveillance Reference Group and the COVID-19 Immunity Task Force. Dr Håberg was partly funded by the Norwegian Research Council (project numbers 324312 and 262700).

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: Parts of this article are based on data and information compiled and provided by BORN Ontario and the Ontario Ministry of Health; however, the analyses, conclusions, opinions, and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred.

Additional Contributions: The authors thank the Ontario Ministry of Health for granting access to the COVaxON database and the Public Health Case and Contact Management Solution. The authors also thank maternal-newborn hospitals and midwifery practice groups in Ontario for providing maternal-newborn data to BORN Ontario. In addition, the authors thank BORN Ontario staff for their assistance with data extraction, linkage, code review, and results review.

REFERENCES

1. Centers for Disease Control and Prevention. Precautions for people with certain medical conditions. Accessed February 22, 2022. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

2. Allotey J, Stallings E, Bonet M, et al; for PregCOV-19 Living Systematic Review Consortium. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. 2020;370:m3320. doi:10.1136/bmj.m3320

3. Karasek D, Baer RJ, McLemore MR, et al. The association of COVID-19 infection in pregnancy with preterm birth: a retrospective cohort study in California. *Lancet Reg Health Am*. 2021;2:100027.

4. Villar J, Ariff S, Gunier RB, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: the INTERCOVID multinational cohort study. *JAMA Pediatr*. 2021;175(8):817-826. doi:10.1001/jamapediatrics.2021.1050

5. Omer SB. Maternal immunization. *N Engl J Med*. 2017;376(25):2497.

6. World Health Organization Department of Reproductive Health and Research. On the use of COVID-19 mRNA vaccines in pregnancy. Accessed February 22, 2022. https://www.who.int/news-room/news-updates

7. Berman Institute of Bioethics Center for Immunization Research. COVID-19 maternal immunization tracker. Accessed February 22, 2022. http://www.comitglobal.org.

8. Magnus MC, Gjessing HK, Eide HN, Wilcox AJ, Fell DB, Håberg SE. Covid-19 vaccination during pregnancy and first-trimester miscarriage. *N Engl J Med*. 2021;385(21):2008-2010. doi:10.1056/NEJMc2114466

9. Kharbanda EO, Haapala J, DeSilva M, et al. Spontaneous abortion following COVID-19 vaccination during pregnancy. *JAMA*. 2021;326(16):1629-1631. doi:10.1001/jama.2021.15494

10. Lipkind HS, Vazquez-Benitez G, DeSilva M, et al. Receipt of COVID-19 vaccine during pregnancy and preterm or small-for-gestational-age at birth: eight integrated health care organizations, United States, December 15, 2020-July 22, 2021. *MMWR Morb Mortal Wkly Rep*. 2022;71(1):26-30. doi:10.15585/mmwr.mm7101e1

11. Goldshtein I, Steinberg DM, Kuint J, et al. Association of BNT162b2 COVID-19 Vaccination During Pregnancy With Neonatal and Early Infant Outcomes. *JAMA Pediatr*. Published online February 10, 2022. doi:10.1001/jamapediatrics.2022.0001

12. Ontario Ministry of Health. COVID-19: guidance for prioritization of phase 2 populations for COVID-19 vaccination. Accessed February 22, 2022. https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/vaccine/COVID-19_Phase_2_vaccination_prioritization.pdf

13. Benchimol EI, Smeeth L, Guttmann A, et al; RECORD Working Committee. The reporting of studies conducted using observational routinely-collected health data (RECORD) statement. *PLoS Med*. 2015;12(10):e1001885. doi:10.1371/journal.pmed.1001885

14. Murphy MSQ, Fell DB, Sprague AE, et al. Data resource profile: Better Outcomes Registry & Network (BORN) Ontario. *Int J Epidemiol*. 2021;50(5):1416-1417h. doi:10.1093/ije/dyab033

15. Office of the Premier of Ontario. Ontario delivers first COVID-19 vaccine in the country. Accessed February 22, 2022. https://news.ontario.ca/en/statement/59635/ontario-delivers-first-covid-19-vaccines-to-frontline-health-workers

16. Neophytou AM, Kioumourtzoglou M-A, Goin DE, Darwin KC, Casey JA. Educational note: addressing special cases of bias that frequently occur in perinatal epidemiology. *Int J Epidemiol*. 2021;50(1):337-345. doi:10.1093/ije/dyaa252

17. Dunn S, Lanes A, Sprague AE, et al. Data accuracy in the Ontario Birth Registry: a chart re-abstraction study. *BMC Health Serv Res*. 2019;19(1):1001. doi:10.1186/s12913-019-4825-3

18. Public Health Ontario. Ontario marginalization index. Accessed February 22, 2022. https://www.publichealthontario.ca/en/data-and-analysis/health-equity/ontario-marginalization-index

19. Ontario Ministry of Health. Protecting Ontarians through enhanced case and contact management. Accessed February 22, 2022. https://www.ontario.ca/page/case-and-contact-management-strategy

20. Ontario Ministry of Health. Ontario's COVID-19 vaccination plan. Accessed February 22, 2022. https://covid-19.ontario.ca/ontarios-covid-19-vaccination-plan#our-three-phased-vaccination-plan)

21. Health Canada. Approved COVID-19 vaccines. Accessed February 22, 2022. https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines.html

22. National Advisory Committee on Immunization. Recommendations on the use of COVID-19 vaccines. Accessed February 22, 2022. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines.html#a7

23. National Advisory Committee on Immunization. NACI rapid response: extended dose intervals for COVID-19 vaccines to optimize early vaccine rollout and population protection in Canada. Accessed February 22, 2022. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/rapid-response-extended-dose-

© 2022 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ on 06/22/2023

intervals-covid-19-vaccines-early-rollout-population-protection.html

24. National Advisory Committee on Immunization. NACI rapid response: interchangeability of authorized COVID-19 vaccines. Accessed February 22, 2022. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines/rapid-response-interchangeability.html

25. Walsh LK, Donelle J, Dodds L, et al. Health outcomes of young children born to mothers who received 2009 pandemic H1N1 influenza vaccination during pregnancy: retrospective cohort study. *BMJ*. 2019;366:l4151. doi:10.1136/bmj.l4151

26. Savitz DA, Fell DB, Ortiz JR, Bhat N. Does influenza vaccination improve pregnancy outcome? methodological issues and research needs. *Vaccine*. 2015;33(47):6430-6435. doi:10.1016/j.vaccine.2015.08.041

27. Kharbanda EO, Vazquez-Benitez G, Lipkind H, Naleway A, Lee G, Nordin JD; Vaccine Safety Datalink Team. Inactivated influenza vaccine during pregnancy and risks for adverse obstetric events. *Obstet Gynecol*. 2013;122(3):659-667. doi:10.1097/AOG.0b013e3182a1118a

28. Austin PC, Stuart EA. Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. *Stat Med*. 2015;34(28):3661-3679. doi:10.1002/sim.6607

29. Dagan N, Barda N, Biron-Shental T, et al. Effectiveness of the BNT162b2 mRNA COVID-19 vaccine in pregnancy. *Nat Med*. 2021;27(10):1693-1695. doi:10.1038/s41591-021-01490-8

30. Goldshtein I, Nevo D, Steinberg DM, et al. Association between BNT162b2 vaccination and incidence of SARS-CoV-2 infection in pregnant women. *JAMA*. 2021;326(8):728-735. doi:10.1001/jama.2021.11035

31. Gray KJ, Bordt EA, Atyeo C, et al. Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study. *Am J Obstet Gynecol*. 2021;225(3):303.e1-303.e17. doi:10.1016/j.ajog.2021.03.023

32. Regan AK, Munoz FM. Efficacy and safety of influenza vaccination during pregnancy: realizing the potential of maternal influenza immunization. *Expert Rev Vaccines*. 2021;20(6):649-660. doi:10.1080/14760584.2021.1915138

33. Baxter R, Bartlett J, Fireman B, Lewis E, Klein NP. Effectiveness of vaccination during pregnancy to prevent infant pertussis. *Pediatrics*. 2017;139(5):e20164091. doi:10.1542/peds.2016-4091

34. Giles ML, Krishnaswamy S, Macartney K, Cheng A. The safety of inactivated influenza vaccines in pregnancy for birth outcomes: a systematic review. *Hum Vaccin Immunother*. 2019;15(3):687-699. doi:10.1080/21645515.2018.1540807

35. McMillan M, Porritt K, Kralik D, Costi L, Marshall H. Influenza vaccination during pregnancy: a systematic review of fetal death, spontaneous abortion, and congenital malformation safety outcomes. *Vaccine*. 2015;33(18):2108-2117. doi:10.1016/j.vaccine.2015.02.068

36. Griffin JB, Yu L, Watson D, et al. Pertussis immunisation in pregnancy safety (PIPS) study: a retrospective cohort study of safety outcomes in pregnant women vaccinated with Tdap vaccine. *Vaccine*. 2018;36(34):5173-5179. doi:10.1016/j.vaccine.2018.07.011

37. Sukumaran L, McCarthy NL, Kharbanda EO, et al. Safety of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis and influenza vaccinations in pregnancy. *Obstet Gynecol*. 2015;126(5):1069-1074. doi:10.1097/AOG.0000000000001066

38. Vygen-Bonnet S, Hellenbrand W, Garbe E, et al. Safety and effectiveness of acellular pertussis vaccination during pregnancy: a systematic review. *BMC Infect Dis*. 2020;20(1):136. doi:10.1186/s12879-020-4824-3

39. Fakhraei R, Crowcroft N, Bolotin S, et al. Obstetric and perinatal health outcomes after pertussis vaccination during pregnancy in Ontario, Canada: a retrospective cohort study. *CMAJ Open*. 2021;9(2):E349. doi:10.9778/cmajo.20200239

40. Validity in epidemiologic studies: nondifferential misclassification. In: Rothman K, Greenland S, Lash T, eds. *Modern Epidemiology*. 3rd ed. Lippincott Williams & Wilkins; 2008:139-143.

© 2022 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ on 06/22/2023

Risque d'accouchement avant terme chez les femmes atteintes de la COVID-19

Révision des recommandations
Juin 2022

Réalisation: Codjo Djignéfa Djade, Maria Tran, Isabelle Rouleau

Institut national de santé publique Québec

Objectifs de la demande

- La demande visait à fournir des données probantes permettant de déterminer si les recommandations doivent être modulées en fonction du statut vaccinal
- Pour répondre à cette demande, nous avons estimé :
  - le risque d'accouchement avant terme (AAT) chez les femmes enceintes infectées par la COVID-19 durant la grossesse
  - l'effet du statut vaccinal sur le risque d'AAT

Institut national de santé publique Québec

Population à l'étude

- Nouvelle grossesse débutée à partir du 1er septembre 2020 et dont l'accouchement a eu lieu dans un centre hospitalier du Québec avant le 31 décembre 2021
    - Exposées au SRAS-CoV-2 après le déconfinement
    - Peu ou pas exposées à la souche Omicron
- Données de Med-Echo, appariées au registre de vaccination, à la TSP et aux données de laboratoire
- Les femmes ayant une infection présumée au SRAS-CoV-2 (dans TSP ou dans leurs données d'accouchement) ont été exclues

Institut national de santé publique Québec

Population à l'étude

- Nouvelle grossesse débutée à partir du 1er septembre 2020 et dont l'accouchement a eu lieu dans un centre hospitalier du Québec avant le 31 décembre 2021
  - **Date d'accouchement:** Date de l'accouchement vaginal ou de la césarienne inscrite dans Med-Echo ou la date d'admission si la date d'intervention est manquante
  - **Début de grossesse:** Date d'accouchement moins l'âge gestationnel (Nb semaines * 7 jours)

Institut national de santé publique Québec

Définitions des variables d'intérêt

- **Risque d'AAT:** correspond à la proportion d'accouchements avec un age gestationnel < 37 semaines
- **Infection (confirmée) :** Résultat de laboratoire positif au SRAS-CoV-2 (selon la date du premier prélèvement +)
- **Statut vaccinal:** Statut relativement moment de l'infection
  - **Vaccinée (1 dose):** si > 14 jours avant
  - **Vaccinée (2 doses):** si > 7 jours avant
  - **Vaccinée (3 doses):** si > 7 jours avant
- **Deuxième trimestre :** Semaines 14-26 (PMSD)

Institut national de santé publique Québec

Séquence des événements

- Pour chaque grossesse, on a ordonné les événements en fonction de leur date de début, d'accouchement, de vaccination (par dose), d'infection (prélèvement +)
- On a fait l'inventaire des différentes séquences obtenues en distinguant le nombre d'expositions survenues avant, pendant et après la grossesse
- Les séquences similaires ont été regroupées et réévaluées en fonction de la validité des doses lors de l'infection

Institut national de santé publique Québec

Description de la population

- 47 658 accouchements répertoriés (par 47 653 femmes)
  - 3 963 (8,3%) d'accouchements avant terme
  - 5 730 (12,0%) cas de COVID-19
  - 1 649 (3,5%) de cas de COVID-19 durant la grossesse
    - 656 (39%) au premier trimestre
    - 456 (28%) au deuxième trimestre
    - 537 (33%) au troisième trimestre

Institut national de santé publique Québec

Risque d'AAT post-infection (anténatale)

Catégorie	Exp prénatale	Exp anténatale	Nb AAT	Nb Naissances	
Non infectées non vaccinées			**1793**	**19281**	**9,3%**
Exp0_A	Aucune	Aucune	576	6598	8,7%
Exp0_B	Aucune	Aucune (Exp en postnatal)	1217	12683	9,6%
Expositions prénatales et anténatales					
Catégorie	**Exp prénatale**	**Exp anténatale**	**Nb AAT**	**Nb Naissances**	
Infection anténatale (Non vaccinées)			**122**	**1564**	**7,8%**
Exp3_A1	NV	Infection	87	985	8,8%
Exp3_B1	NV	Infection < dose 1	20	321	6,2%
Exp3_C	NV	Infection < doses 1+2	15	258	5,8%
Infection anténatale (Vaccinées 1 dose)			**6**	**70**	**8,6%**
Exp2_A2	Dose 1	Infection	1	6	16,7%
Exp2_B2	Dose 1	Infection < dose 2	0	3	0,0%
Exp3_B1	NV	Dose 1 < Infection	3	34	8,8%
Exp3_C	NV	Dose 1 < Infection < dose 2	2	27	7,4%
Infection anténatale (Vaccinées 2 doses)			**9**	**131**	**6,9%**
Exp2_B2	Dose 1	Dose 2 < Infection	1	13	7,7%
Exp3_C	NV	2 doses < Infection	7	116	6,0%
Exp3_D	NV	2 doses < Infection < dose 3	1	2	50,0%

→ **Risque de base (Pandémique)**
(Non infectées, non vaccinées)
9,3 %

→ **Non vaccinées (0 dose)**
7,8 %

→ **Vaccinées (1 dose)**
8,6 %

→ **Vaccinées (2 doses)**
6,9 %

Risque de base d'AAT sans COVID

Risque de base d'AAT avec COVID

Risque d'AAT post-infection (prénatale)

Catégorie	Prénatale	Anténatale	Nb AAT	Nb Naissances	
Infection prénatales (Non vaccinées)			**114**	**1371**	**8,3%**
Exp1_A1	Infection	-	48	620	7,7%
Exp_2A1	Infection	Dose 1	28	353	7,9%
Exp_2B1	Infection	Deux doses	21	289	7,3%
Exp_2C1	Infection	Trois doses	0	2	0,0%
Exp1_B1	Infection < Dose 1	-	11	50	22,0%
Exp1_C1	Infection < Deux doses	-	0	1	0,0%
Exp_2B4	Infection < Dose 1	Dose 2	6	55	10,9%
Exp_2C2	Infection < Dose 1	Doses 2 et 3	0	1	0,0%

Risque d'AAT
(Infection prénatale)
8,3 %

Non vaccinées
7,7%

Vaccinées
15,9 %

Constats

- Le risque d'AAT ne semble pas être augmenté chez les femmes qui contractent la COVID-19 pendant la grossesse

  Infection anténatale: RR 0,83 (0,70 – 1,00)

- Parmi les femmes qui contractent la COVID-19 pendant la grossesse, le risque d'AAT pourrait être plus faible chez celles ayant reçu deux doses de vaccin avant de faire l'infection

  Vaccinée (1 dose): RR 1,09 (0,50 – 2,41)

  Vaccinée (2 doses): RR 0,88 (0,46 – 1,69)

Institut national de santé publique Québec

Limites

- Le risque de base d'AAT est plus élevé que celui des grossesses pré-pandémie (7,2%) ou pré/post-pandémie (7,0%).
  - Comparativement à 2019-2020, on voit une augmentation non significative du risque d'AAT post-infection : RR 1,09 (0,91 – 1,29)
- Le risque d'AAT post-infection chez femmes partiellement vaccinées doit être interprété avec prudence
- Les femmes avec ATCD de vaccination avant la grossesse ont des taux d'AAT systématiquement plus élevés que les autres:
  - Groupes prioritaires: TdeS à haut risque vaccinées avant avril 2021
  - Grossesses en cours censurées au 31 décembre

Institut national de santé publique Québec

Merci!

Isabelle Rouleau



Éric Bédard

De: MSSS - Protection <protection@msss.gouv.qc.ca>
Envoyé: 12 août 2022 10:33
Objet: Répondants ESPRI - Article CANVAS MCI COVID-19 chez les femmes enceintes
Pièces jointes: 22TLID0347_Sadarangani.pdf; 22TLID0347_appendix.pdf

Catégories: Demande d'accès Information

ATTENTION: L'origine de cette communication est de source externe. Veuillez vous assurer que l'expéditeur et le contenu, incluant les pièces jointes, sont légitimes avant même de les ouvrir ou de les télécharger.

Santé et Services sociaux Québec

Objet : Répondants ESPRI – Article CANVAS MCI COVID-19 chez les femmes enceintes
Destinataires : Répondants ESPRI
CC : Groupe central ESPRI

Bonjour,

Nous partageons avec vous un article nouvellement publié dans *The Lancet Infectious Diseases* par notre collègue Dr Gaston De Serres et ses collaborateurs. L'article " Safety of COVID-19 vaccines in pregnancy : a Canadian National Vaccine Safety (CANVAS) network cohort study " présente les résultats de la surveillance active CANVAS des MCI chez les femmes enceintes dans 7 provinces (dont le Québec) dans le cadre de la campagne de vaccination contre la COVID-19.

Bonne lecture,

Frédérique Armellin-Ducharme pour

Eveline Toth, M.Sc

Directrice par intérim de la vigie sanitaire
Direction de la vigie sanitaire
Direction générale adjointe de la protection de la santé publique
Ministère de la santé et des services sociaux du Québec
201, boul. Crémazie Est, bureau 2.03
Montréal (Québec) H2M 1L2
Téléphone: 514 864-4544
Télécopieur: 514 864-2778
Cellulaire : 514-838-6375
Courriel: eveline.toth@msss.gouv.qc.ca

Safety of COVID-19 vaccines in pregnancy: a Canadian National Vaccine Safety (CANVAS) network cohort study

Manish Sadarangani, Phyumar Soe, Hennady P Shulha, Louis Valiquette, Otto G Vanderkooi, James D Kellner, Matthew P Muller, Karina A Top, Jennifer E Isenor, Allison McGeer, Mike Irvine, Gaston De Serres, Kimberly Marty, Julie A Bettinger, for the Canadian Immunization Research Network

Summary

Background Pregnant individuals have been receiving COVID-19 vaccines following pre-authorisation clinical trials in non-pregnant people. This study aimed to determine the frequency and nature of significant health events among pregnant females after COVID-19 vaccination, compared with unvaccinated pregnant controls and vaccinated non-pregnant individuals.

Methods We did an observational cohort study, set in seven Canadian provinces and territories including Ontario, Quebec, British Columbia, Alberta, Nova Scotia, Yukon, and Prince Edward Island. Eligibility criteria for vaccinated individuals were a first dose of a COVID-19 vaccine within the previous 7 days; an active email address and telephone number; ability to communicate in English or French; and residence in the aforementioned provinces or territories. Study participants were pregnant and non-pregnant females aged 15–49 years. Individuals were able to participate as controls if they were unvaccinated and fulfilled the other criteria. Data were collected primarily by self-reported survey after both vaccine doses, with telephone follow-up for those reporting any medically attended event. Participants reported significant health events (new or worsening of a health event sufficient to cause work or school absenteeism, medical consultation, or prevent daily activities) occurring within 7 days of vaccination or within the past 7 days for unvaccinated individuals. We employed multivariable logistic regression to examine significant health events associated with mRNA vaccines, adjusting for age group, previous SARS-CoV-2 infection, and trimester, as appropriate.

Findings As of Nov 4, 2021, 191 360 women aged 15–49 years with known pregnancy status had completed the first vaccine dose survey and 94 937 had completed the second dose survey. 180 388 received one dose and 94 262 received a second dose of an mRNA vaccine, with 5597 pregnant participants receiving dose one and 3108 receiving dose two, and 174 765 non-pregnant participants receiving dose one and 91 131 receiving dose two. Of 6179 included unvaccinated control participants, 339 were pregnant and 5840 were not pregnant. Overall, 226 (4·0%) of 5597 vaccinated pregnant females reported a significant health event after dose one of an mRNA vaccine, and 227 (7·3%) of 3108 after dose two, compared with 11 (3·2%) of 339 pregnant unvaccinated females. Pregnant vaccinated females had an increased odds of a significant health event within 7 days of the vaccine after dose two of mRNA-1273 (adjusted odds ratio [aOR] 4·4 [95% CI 2·4–8·3]) compared with pregnant unvaccinated controls within the past 7 days, but not after dose one of mRNA-1273 or any dose of BNT162b2. Pregnant vaccinated females had decreased odds of a significant health event compared with non-pregnant vaccinated females after both dose one (aOR 0·63 [95% CI 0·55–0·72]) and dose two (aOR 0·62 [0·54–0·71]) of any mRNA vaccination. There were no significant differences in any analyses when restricted to events which led to medical attention.

Interpretation COVID-19 mRNA vaccines have a good safety profile in pregnancy. These data can be used to appropriately inform pregnant people regarding reactogenicity of COVID-19 vaccines during pregnancy, and should be considered alongside effectiveness and immunogenicity data to make appropriate recommendations about best use of COVID-19 vaccines in pregnancy.

Funding Canadian Institutes of Health Research, Public Health Agency of Canada.

Copyright © 2022 Elsevier Ltd. All rights reserved.

Lancet Infect Dis 2022

Published **Online** August 11, 2022 https://doi.org/10.1016/S1473-3099(22)00426-1

See **Online/Comment** https://doi.org/10.1016/S1473-3099(22)00443-1

Vaccine Evaluation Center, BC Children's Hospital Research Institute, Vancouver, BC, Canada (M Sadarangani DPhil, P Soe MSc, H P Shulha PhD, K Marty BSc, Prof J A Bettinger PhD); **Department of Pediatrics, University of British Columbia, Vancouver, BC, Canada** (M Sadarangani, P Soe, K Marty, Prof J A Bettinger); **Department of Microbiology and Infectious Diseases, Universitaire de Sherbrooke, Sherbrooke, QC, Canada** (Prof L Valiquette MD); **Alberta Children's Hospital Research Institute, Calgary, AB, Canada** (O G Vanderkooi MD, Prof J D Kellner MD); **Department of Pediatrics, University of Calgary, Calgary, AB, Canada** (O G Vanderkooi, Prof J D Kellner); **Department of Medicine, Unity Health Toronto, Toronto, ON, Canada** (M P Muller MD); **Department of Medicine** (M P Muller), **and Department of Microbiology** (Prof A McGeer MD), **University of Toronto, Toronto, ON, Canada); Canadian Center for Vaccinology, IWK Health, Halifax, NS, Canada** (K A Top MD, J E Isenor PharmD); **Department of Pediatrics** (K A Top) **and College of Pharmacy** (J E Isenor), **Dalhousie University, Halifax, NS, Canada; Sinai Health System, Toronto, ON, Canada** (Prof A McGeer); **BC Centre for Disease Control, Vancouver, BC, Canada** (M Irvine PhD); **CHU de Québec-Université Laval, Quebec, QC, Canada** (Prof G De Serres MD); **Institut national de santé publique du Québec, QC, Canada** (Prof G De Serres)

Introduction

The COVID-19 pandemic has disproportionately affected pregnant people, who are at higher risk of severe disease compared with similarly aged non-pregnant individuals. Pregnancy leads to an increased risk of hospital admission with COVID-19, intensive care unit admission, mechanical ventilation, and death, due to changes in cardiopulmonary and immunological physiology.[1] Additionally, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection increases risk of adverse pregnancy outcomes such as hypertension, pre-eclampsia, impaired fetal growth, and preterm birth.[2]

COVID-19 vaccines have been available in Canada since December, 2020.[3] Multiple expert groups published

Correspondence to:
Dr Manish Sadarangani, Vaccine Evaluation Center, BC Children's Hospital Research Institute, Vancouver, BC V5Z 4H4, Canada
msadarangani@bcchr.ubc.ca

Research in context

Evidence before this study

We searched the peer-reviewed (PubMed) and pre-print (MedRxiv) literature for studies published in English related to safety, reactogenicity, and tolerability of COVID-19 vaccines in pregnant people between Nov 1, 2021, and May 9, 2022, with no date restrictions, and using search terms "COVID-19", "vaccine" and "pregnancy", combined with "safety", "reactogenicity", "adverse events" or "tolerability". In addition to identified primary research articles, we also further reviewed citations from review articles that had not been identified in our search. Of studies involving direct collection of data from participants, we found several observational studies that described rates of adverse events after first and second doses or booster doses of mRNA vaccines in pregnancy. Most studies included a pregnant cohort only (except two that reported on vaccine-specific adverse events instead of adverse pregnancy outcomes, with smaller cohorts than our study), with some studies also including a non-pregnant vaccinated group. There were some additional studies using data from administrative databases without individual participant verification. Most studies described all adverse events reported, with limited differentiation of significant/severe/serious adverse events. Most comparisons of adverse pregnancy outcomes in vaccinated compared with unvaccinated pregnant people utilised historical control data, with no studies including a contemporaneous pregnant, unvaccinated control group.

Added value of this study

Our study included a sample of 5625 pregnant, vaccinated females aged 15–49 years, compared with 185 735 non-pregnant vaccinated females and 339 pregnant unvaccinated controls of a similar age. All data were collected during the study period, using standardised surveys, enabling direct comparison between groups. We also actively follow-up individuals with severe adverse events to enable detailed descriptions. Our study focused on significant health events—new or worsening health events following vaccination sufficient to cause work or school absenteeism, medical consultation, or prevent daily activities—and included sensitivity analyses restricted to events leading to medical consultation. Our data provide reassuring evidence that COVID-19 mRNA vaccines are safe in pregnancy, with lower rates of significant adverse events following immunisation in pregnant people than non-pregnant vaccine recipients for both mRNA vaccines used in Canada, after dose one and dose two. Although rates of significant adverse events following immunisation were highest after dose two for mRNA-1273 recipients, both mRNA vaccines are highly immunogenic and effective in pregnancy. Given the increased rate of significant complications related to COVID-19 in pregnancy, high vaccine coverage in this group is important for protection of the pregnant person and young infant.

Implications of all the available evidence

These data can be used in combination with previously published data to provide accurate information to pregnant females receiving COVID-19 vaccines regarding the rates of significant health events occurring after vaccination, putting the information in the context of an unvaccinated control group, with similar rates of health events other than after a second dose of mRNA-1273. The data also provides reassurance that the rate of significant health events is lower in pregnant people than non-pregnant individuals after vaccination, with similar rates of medical consultation for all comparisons.

positive recommendations for use of COVID-19 vaccines in pregnancy early on in vaccine deployment, based largely on previously established safety of inactivated vaccines in pregnancy, several decades of use of vaccines in pregnancy (such as tetanus toxoid, influenza, and tetanus-diphtheria-pertussis), and reassuring data from the small number of incidental pregnancies occurring during pre-authorisation trials.[4,5] Data from large cohorts requires post-implementation studies, and data has been accruing on the safety of mRNA vaccines during pregnancy.[6–8] These are primarily descriptive studies, relying on comparisons with historic rates of adverse events and mostly without a contemporaneous control group to enable comparison with background rates of adverse events following immunisation.

The Canadian National Vaccine Safety (CANVAS) Network was established during the 2009 influenza pandemic to provide rapid, real-time safety data during rollout of immunisation programmes, and has monitored the safety of seasonal influenza vaccines in Canada and other emergency campaigns, such as for a capsular group B meningococcal vaccine.[9] CANVAS obtains information via surveys administered to vaccinated and unvaccinated individuals. The CANVAS Network has been monitoring COVID-19 vaccine safety in Canada since the start of the vaccine rollout.[10] The focus of this study and other CANVAS studies has been significant adverse events occurring in the week following immunisation that affect work or schooling, or that require medical attention. Distinguishing components of the CANVAS approach are active follow-up of individuals with important health events and active enrolment of a control group to enable comparisons with unvaccinated individuals in a similar time frame. The aim of this analysis was to compare rates of health events in (1) vaccinated pregnant females and vaccinated non-pregnant females of the same age and (2) vaccinated and unvaccinated (control) pregnant females.

Methods

Study design and participants

In this ongoing observational cohort study, we actively recruited participants from seven Canadian provinces

and territories accounting for more than 75% of the national population including Ontario, Quebec, British Columbia, Alberta, Nova Scotia, Yukon, and Prince Edward Island.[10] At the time of this analysis, the study was open to anyone eligible for a COVID-19 vaccine, which included individuals aged 12 years and older. Vaccinated individuals were eligible if they received the first dose of a COVID-19 vaccine within the previous 7 days; had an active email address and telephone number; were able to communicate in English or French; and reside in the aforementioned provinces or territories. Individuals were able to participate as controls if they were unvaccinated and fulfilled the other three criteria. Individuals were able to contribute to both vaccinated and control groups if they initially enrolled prior to vaccination and subsequently enrolled after vaccination. Individuals who enrolled as control participants and expected to be vaccinated within the next 6 months completed a retrospective control survey. All other control participants were followed prospectively. All participants provided informed consent electronically. Each study site obtained approval from Research Ethics Boards (British Columbia and Yukon: UBC Children's & Women's, Ref: H20-03704; Quebec: Centre Intégré univrsitaire de santé et de services sociaux de l'Estrie, Ref: MP-31-2021-4044; Nova Scotia and Prince Edward Island: Health PEI and IWK Health Research, Ref: 1026400; Alberta: Conjoint Health REB, University of Calgary, Ref: REB20-2177; Ontario: Unity Health Toronto, Ref: 20-334). The study protocol has previously been published.

Procedures

Recruitment methods for COVID-19 vaccinated participants included: (1) passive recruitment via information provided at immunisation clinics; (2) electronic invitation when an appointment was made for vaccination; and (3) electronic invitation after vaccination using names obtained from the relevant immunisation registry. Control participants were: (1) previous CANVAS study participants who indicated their agreement to be contacted for research; (2) users of the CANImmunize app; (3) enrolled via the study website and (4) recruited from volunteer databases. A detailed description of recruitment procedures has been previously published.[10] Study enrolment commenced on Dec 22, 2020. Of relevance to this analysis, vaccinated participants were surveyed via email for the occurrence of adverse events following immunisation during the 7 days following each dose of COVID-19 vaccine. All participants were asked about injection site reactions, but only those that indicated they had a significant health event were requested to provide further details. Control participants were requested to note the occurrence of health problems in the previous 7 days, also via email. We did a telephone follow-up for those who reported any medically attended event. We sent up to two automatic reminders every 72 h for all non-responders to address loss to follow-up. Survey data were collected in a secure REDCap (Research Electronic Data Capture) database.[11,12] Data collected relevant to this analysis included age group, sex, gender, ethnicity, self-reported previous laboratory-confirmed SARS-CoV-2 infection, pregnancy and lactation status, general health status, COVID-19 vaccine brand administered, occurrence or worsening of health events, and requirement for medical attention and hospital admission related to the health event.

Outcomes

The primary endpoint was a significant health event, defined as a new or worsening health event sufficient to cause work or school absenteeism, medical consultation, or prevent daily activities in the previous 7 days (for controls) or the 7 days following vaccination for those that received a COVID-19 vaccine. The secondary endpoint was defined as any serious health event (an event resulting in emergency department visit or hospital admission) in the previous 7 days. Two types of exposures were analysed: (1) vaccination status among pregnant people, and (2) pregnancy status among vaccinated people.

For the purposes of this analysis, we included all females reporting a pregnancy on any survey, and non-pregnant females in the same age groups (15–49 years). When comparing health event rates among pregnant people, the same pregnant control group was used to compare with vaccinated pregnant people who received a first or second dose of a COVID-19 vaccine. For statistical modelling, the analysis was restricted to those who received any mRNA vaccines (BNT162b2 [Pfizer] and mRNA-1273 [Moderna]) because very few pregnant people reported receiving the ChAdox1-S [AstraZeneca] vaccine. For pregnant participants who reported experiencing a miscarriage following both dose one and dose two, only the first report was included to avoid duplicate counting from individuals reporting the same miscarriage twice, given the relatively short interval between vaccine doses.

For **previously published protocol** see https://bmjopen.bmj.com/content/12/1/e051254.long

For the **CANVAS study website** see www.canvas-covid.ca

Statistical analysis

We estimated rates of significant and serious health events including all symptoms following the first and second doses of COVID-19 vaccines. To examine associations between the outcomes and the exposures, two sets of univariable and multivariable logistic regression models were built for each type of exposure (vaccination status among pregnant people and pregnancy status among vaccinated people). When fitting multivariable models, we adjusted known or expected covariates such as age group, previous SARS-CoV-2 infection, and trimester of pregnancy, as appropriate. Three different vaccine groups were evaluated: (1) BNT162b2, (2) mRNA-1273, and (3) any mRNA vaccine. The estimated odds ratio (OR) and

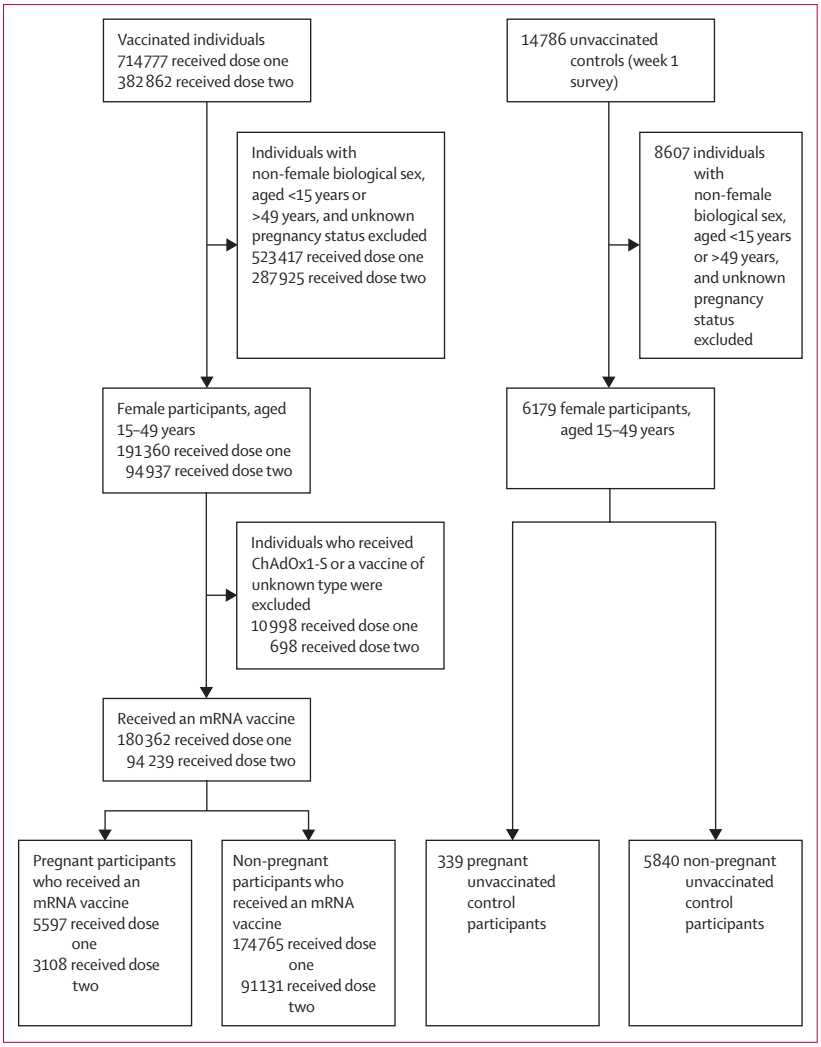


Figure 1: **Study profile**
Flow chart depicting the analytical samples (dose one and dose two) for examining adverse events following immunisation associated with COVID-19 vaccine. Non-pregnant controls were not included in the regression analysis.

See Online for appendix

95% CIs were reported. We did complete case analysis because no variable had more than 2% of missing data. We verified the absence of multicollinearity with variance inflation factor using a cut-off point of less than 5. To evaluate the robustness of findings, we did two sensitivity analyses. In the first, our primary end point (significant health event) was restricted to new or worsening health events also resulting in medical consultation in the previous 7 days. We repeated the same analysis after the first and second doses of COVID-19 vaccines. In the second analysis, we restricted the dataset of pregnant people to those who reported being in excellent health and compared this with the results from the primary analysis. Data cleaning was done in SAS version 9.4 (SAS Institute) and analysis was completed in R software version 4.1.1 (R foundation for Statistical Computing, Vienna, Austria).

Role of funding source
The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

As of Nov 4, 2021, a total of 191360 women aged 15–49 years with known pregnancy status had completed the first vaccine does survey and 94937 had completed the second dose survey (figure 1). A total of 5625 (2·9%) of 191360 and 3114 (3·3%) of 94937 women reported being pregnant at the time of receiving the first and second doses of COVID-19 vaccines (appendix p 1). Of these, most pregnant participants had received BNT162b2 (3414 received dose one and 1892 received dose two) or mRNA-1273 (2183 received dose one and 1216 received dose two) COVID-19 vaccines and few individuals reported receiving ChAdOx1-S (25 received dose one and six received dose two). Among the enrolled unvaccinated control participants, a total of 6179 females aged 15–49 years had completed 7-day surveys. Of these, 339 (5·5%) reported being pregnant during the survey period (appendix p 1). Among both vaccinated and control groups, pregnant individuals in all three trimesters were well represented (table 1).

Most respondents in both control and vaccinated groups were aged 30–49 (ranging from 65900 [61·5%] of 107121 in not-pregnant individuals receiving dose one of BNT162b2 to 288 [85·0%] of 339 in the pregnant control group) and reported being in excellent/very good/good health (ranging from 44362 [83·6%] of 53077 in not-pregnant individuals receiving dose two of BNT162b2 to 333 [98·2%] of 339 in the pregnant control group; table 1). The ethnic origin of more than half of participants in both vaccinated and control groups was unknown because the question regarding ethnicity was introduced only in the dose two survey questionnaires and was optional. Among those who reported their ethnicity, the majority were White, followed by East Asian, and South Asian. Prevalence of previous SARS-CoV-2 infection varied between 2·3% and 4·6% (table 1).

Overall, 226 (4·0%) of 5597 mRNA-vaccinated pregnant females reported a significant health event within 7 days after dose one of an mRNA vaccine, and 227 (7·3%) of 3108 after dose two (table 1). The rates were similar after dose one for both mRNA vaccines (137 [4·0%] of 3414 for BNT162b2 and 89 [4·1%] of 2183 for mRNA-1273), but higher for mRNA-1273 (147 [12·1%] of 1216) than BNT162b2 (80 [4·2%] of 1892) after dose two. The most common significant health events after dose two of mRNA-1273 in pregnant females were feeling unwell or malaise or myalgia (139 [11·4%] of 1216), headache or migraine (103 [8·5%] of 1216), and respiratory tract infection (68 [5·6%] of 1216; table 2). Among pregnant and vaccinated participants who reported significant health events, most of them recognised their symptoms

	Pregnant control group (n=339)	Dose 1						Dose 2					
		Any mRNA		BNT162b2		mRNA-1273		Any mRNA		BNT162b2		mRNA-1273	
		Not pregnant (n=174 765)	Pregnant (n=5597)	Not pregnant (n=107 121)	Pregnant (n=3414)	Not pregnant (67 644)	Pregnant (n=2183)	Not pregnant (91 131)	Pregnant (n=3108)	Not pregnant (n=53 077)	Pregnant (n=1892)	Not pregnant (38 054)	Pregnant (n=1216)
Health events													
Significant health event	11 (3·2%)	10 950 (6·3%)	226 (4·0%)	6501 (6·1%)	137 (4·0%)	4449 (6·6%)	89 (4·1%)	10 254 (11·3%)	227 (7·3%)	4121 (7·8%)	80 (4·2%)	6133 (16·1%)	147 (12·1%)
Severe health event	4 (1·2%)	2439 (1·4%)	78 (1·4%)	1392 (1·3%)	45 (1·3%)	1047 (1·5%)	33 (1·5%)	1257 (1·4%)	47 (1·5%)	663 (1·2%)	22 (1·2%)	594 (1·6%)	25 (2·1%)
Serious health event	2 (0·6%)	733 (0·4%)	31 (0·6%)	421 (0·4%)	18 (0·5%)	312 (0·5%)	13 (0·6%)	343 (0·4%)	19 (0·6%)	192 (0·4%)	8 (0·4%)	151 (0·4%)	11 (0·9%)
Trimester*													
1st trimester	6 (1·8%)	..	81 (1·4%)	..	47 (1·4%)	..	34 (1·6%)	..	67 (2·2%)	..	23 (1·2%)	..	44 (3·6%)
2nd trimester	3 (0·9%)	..	96 (1·7%)	..	56 (1·6%)	..	40 (1·8%)	..	86 (2·8%)	..	29 (1·5%)	..	57 (4·7%)
3rd trimester	2 (0·6%)	..	48 (0·9%)	..	34 (1·0%)	..	14 (0·6%)	..	74 (2·4%)	..	28 (1·5%)	..	46 (3·8%)
Unknown	..	..	1 (<0·1%)	..	..	..	1 (<0·1%)	..	..	..	..	..	..
Age groups, years													
15–29	51 (15·0%)	59 263 (33·9%)	1417 (25·3%)	41 221 (38·5%)	796 (23·3%)	18 042 (26·7%)	621 (28·4%)	26 324 (28·9%)	716 (23·0%)	17 008 (32·0%)	422 (22·3%)	9316 (24·5%)	294 (24·2%)
30–49	288 (85·0%)	115 502 (66·1%)	4180 (74·7%)	65 900 (61·5%)	2618 (76·7%)	49 602 (73·3%)	1562 (71·6%)	64 807 (71·1%)	2392 (77·0%)	36 069 (68·0%)	1470 (77·7%)	28 738 (75·5%)	922 (75·8%)
Gender													
Woman	338 (99·7%)	170 674 (97·7%)	5579 (99·7%)	104 279 (97·3%)	3403 (99·7%)	66 395 (98·2%)	2176 (99·7%)	89 176 (97·9%)	3091 (99·5%)	51 914 (97·8%)	1881 (99·4%)	37 262 (97·9%)	1210 (99·5%)
Man	0	819 (0·5%)	3 (0·1%)	561 (0·5%)	1 (<0·1%)	258 (0·4%)	2 (0·1%)	341 (0·4%)	1 (<0·1%)	215 (0·4%)	1 (0·1%)	126 (0·3%)	0
Non-binary	1 (0·3%)	2380 (1·4%)	12 (0·2%)	1698 (1·6%)	9 (0·3%)	682 (1·0%)	3 (0·1%)	1254 (1·4%)	13 (0·4%)	737 (1·4%)	8 (0·4%)	517 (1·4%)	5 (0·4%)
Two-spirit	0	148 (0·1%)	0	96 (0·1%)	0	52 (0·1%)	0	49 (0·1%)	0	33 (0·1%)	0	16 (<0·1%)	0
Other	0	139 (0·1%)	1 (<0·1%)	101 (0·1%)	0	38 (0·1%)	1 (<0·1%)	69 (0·1%)	0	40 (0·1%)	0	29 (0·1%)	0
Unknown	0	605 (0·3%)	2 (<0·1%)	386 (0·4%)	1 (<0·1%)	219 (0·3%)	1 (<0·1%)	242 (0·3%)	3 (0·1%)	138 (0·3%)	2 (0·1%)	104 (0·3%)	1 (0·1%)

(Table 1 continues on next page)

	Pregnant control group (n=339)	Dose 1						Dose 2					
		Any mRNA		BNT162b2		mRNA-1273		Any mRNA		BNT162b2		mRNA-1273	
		Not pregnant (n=174765)	Pregnant (n=5597)	Not pregnant (n=107121)	Pregnant (n=3414)	Not pregnant (67644)	Pregnant (n=2183)	Not pregnant (91131)	Pregnant (n=3108)	Not pregnant (n=53077)	Pregnant (n=1892)	Not pregnant (38054)	Pregnant (n=1216)
(Continued from previous page)													
Ethnicity													
White	22 (6·5%)	47539 (27·2%)	1818 (32·5%)	29421 (27·5%)	1166 (34·2%)	18118 (26·8%)	652 (29·9%)	50779 (55·7%)	1778 (57·2%)	25645 (48·3%)	957 (50·6%)	25134 (66·0%)	821 (67·5%)
Black	2 (0·6%)	1155 (0·7%)	18 (0·3%)	802 (0·7%)	12 (0·4%)	353 (0·5%)	6 (0·3%)	1169 (1·3%)	22 (0·7%)	692 (1·3%)	14 (0·7%)	477 (1·3%)	8 (0·7%)
East Asian	0	3367 (1·9%)	117 (2·1%)	2427 (2·3%)	87 (2·5%)	940 (1·4%)	30 (1·4%)	3471 (3·8%)	106 (3·4%)	2213 (4·2%)	72 (3·8%)	1258 (3·3%)	34 (2·8%)
South Asian	0	1977 (1·1%)	95 (1·7%)	1502 (1·4%)	81 (2·4%)	475 (0·7%)	14 (0·6%)	2041 (2·2%)	104 (3·3%)	1325 (2·5%)	83 (4·4%)	716 (1·9%)	21 (1·7%)
South-East Asian	1 (0·3%)	1552 (0·9%)	47 (0·8%)	1121 (1·0%)	36 (1·1%)	431 (0·6%)	11 (0·5%)	1587 (1·7%)	45 (1·4%)	995 (1·9%)	27 (1·4%)	592 (1·6%)	18 (1·5%)
Indigenous	0	699 (0·4%)	22 (0·4%)	476 (0·4%)	18 (0·5%)	223 (0·3%)	4 (0·2%)	703 (0·8%)	21 (0·7%)	436 (0·8%)	13 (0·7%)	267 (0·7%)	8 (0·7%)
Middle Eastern	0	1352 (0·8%)	44 (0·8%)	821 (0·8%)	30 (0·9%)	531 (0·8%)	14 (0·6%)	1361 (1·5%)	44 (1·4%)	751 (1·4%)	25 (1·3%)	610 (1·6%)	19 (1·6%)
Latino	0	1392 (0·8%)	48 (0·9%)	807 (0·8%)	23 (0·7%)	585 (0·9%)	25 (1·1%)	1460 (1·6%)	50 (1·6%)	736 (1·4%)	19 (1·0%)	724 (1·9%)	31 (2·5%)
Mixed	0	2714 (1·6%)	92 (1·6%)	1888 (1·8%)	68 (2·0%)	826 (1·2%)	24 (1·1%)	2800 (3·1%)	88 (2·8%)	1619 (3·1%)	53 (2·8%)	1181 (3·1%)	35 (2·9%)
Unknown or other	314 (92·6%)	113018 (64·7%)	3296 (58·9%)	67856 (63·3%)	1893 (55·4%)	45162 (66·8%)	1403 (64·3%)	25758 (28·3%)	850 (27·3%)	18665 (35·2%)	629 (33·2%)	7095 (18·6%)	221 (18·2%)
Health status													
Excellent, very good, or good	333 (98·2%)	151446 (86·7%)	5029 (89·9%)	91266 (85·2%)	2961 (86·7%)	60180 (89·0%)	2068 (94·7%)	77911 (85·5%)	2747 (88·4%)	44362 (83·6%)	1617 (85·5%)	33549 (88·2%)	1130 (92·9%)
Fair, poor, or unknown	6 (1·8%)	23319 (13·3%)	568 (10·1%)	15855 (14·8%)	453 (13·3%)	7464 (11·0%)	115 (5·3%)	13220 (14·5%)	361 (11·6%)	8715 (16·4%)	275 (14·5%)	4505 (11·8%)	86 (7·1%)
Province													
Alberta	37 (10·9%)	28987 (16·6%)	778 (13·9%)	22129 (20·7%)	650 (19·0%)	6858 (10·1%)	128 (5·9%)	17260 (18·9%)	544 (17·5%)	12052 (22·7%)	422 (22·3%)	5208 (13·7%)	122 (10·0%)
Ontario	178 (52·5%)	44184 (25·3%)	2080 (37·2%)	36571 (34·1%)	1636 (47·9%)	7613 (11·3%)	444 (20·3%)	32324 (35·5%)	1318 (42·4%)	20445 (38·5%)	888 (46·9%)	11879 (31·2%)	430 (35·4%)
Quebec	4 (1·2%)	65501 (37·5%)	1464 (26·2%)	21446 (20·0%)	174 (5·1%)	44055 (65·1%)	1290 (59·1%)	27621 (30·3%)	664 (21·4%)	11609 (21·9%)	188 (9·9%)	16012 (42·1%)	476 (39·1%)
British Columbia and Yukon	85 (25·1%)	31287 (17·9%)	1132 (20·2%)	23197 (21·7%)	834 (24·4%)	8090 (12·0%)	298 (13·7%)	10393 (11·4%)	484 (15·6%)	7437 (14·0%)	341 (18·0%)	2956 (7·8%)	143 (11·8%)
Prince Edward Island and Nova Scotia	35 (10·3%)	4806 (2·7%)	143 (2·6%)	3778 (3·5%)	120 (3·5%)	1028 (1·5%)	23 (1·1%)	3533 (3·9%)	98 (3·2%)	1534 (2·9%)	53 (2·8%)	1999 (5·3%)	45 (3·7%)

(Table 1 continues on next page)

	Pregnant control group (n=339)	Dose 1						Dose 2					
		Any mRNA		BNT162b2		mRNA-1273		Any mRNA		BNT162b2		mRNA-1273	
		Not pregnant (n=174765)	Pregnant (n=5597)	Not pregnant (n=107121)	Pregnant (n=3414)	Not pregnant (67644)	Pregnant (n=2183)	Not pregnant (91131)	Pregnant (n=3108)	Not pregnant (n=53077)	Pregnant (n=1892)	Not pregnant (38054)	Pregnant (n=1216)
(Continued from previous page)													
History of SARS-COV-2 infection													
No	331 (97·6%)	167100/174516 (95·8%)	5434/5592 (97·2%)	102013/106965 (95·4%)	3310/3409 (97·1%)	65087/67551 (96·4%)	2124 (97·3%)	87891/91072 (96·5%)	3009/3106 (96·9%)	50993/53048 (96·1%)	1821/1890 (96·3%)	36898/38024 (97·0%)	1188 (97·7%)
Yes	8 (2·4%)	7416/174516 (4·2%)	158/5592 (2·8%)	4952/106965 (4·6%)	99/3409 (2·9%)	2464/67551 (3·6%)	59 (2·7%)	3181/91072 (3·5%)	97/3106 (3·1%)	2055/53048 (3·9%)	69/1890 (3·7%)	1126/38024 (3·0%)	28 (2·3%)

Data are n (%) or n/N (%). Significant health event indicates a new or worsening health event sufficient to cause work or school absenteeism, medical consultation, or prevent daily activities within 7 days after vaccination for vaccinated participants and in the previous 7 days for control groups. Severe health event is a subgroup of significant health events and indicates a new or worsening a health event resulting in medical consultation within 7 days after vaccination for vaccinated participants and in the previous 7 days for control groups. Serious health event indicates any event resulting in emergency department visit or admission to hospital within 7 days after vaccination for vaccinated participants and in the previous 7 days for control groups. *Breakdown of trimester data applies only to significant health events.

Table 1: **Baseline demographics and health events in study populations**

within 24 h following vaccination (overall 130 [57·5%] of 226 after dose one and 187 [82·4%] of 227 after dose two of an mRNA vaccine) and the majority (124 [54·9%] of 226 after dose one and 168 [74·0%] of 227) resolved within 3 days (appendix p 2). In comparison, 11 (3·2%) of 339 pregnant unvaccinated participants (controls) reported similar events in the 7 days before survey completion (table 1). Of these, two (18·2%) reported their symptoms as resolved at least 24 h before the control survey and nine (81·8%) reported their events as on-going for at least 6 days (appendix 2). The reported serious health events were rare (between eight [0·4%] of 1892 and 11 [0·9%] of 1216 across various pregnant groups; table 1) and occurred at similar rates in vaccinated pregnant individuals and unvaccinated controls, and after dose one and dose two for all vaccine types (table 1; appendix p 3).

Miscarriage or stillbirth was the most frequently reported adverse pregnancy outcome and it was reported at similar rates between control (seven [2·1%] of 339) and vaccinated groups within seven days after dose one of any mRNA vaccine (83 [1·5%] of 5597; table 3). Almost all pregnancy losses (73 [88%] of 83; occurred during the first trimester. There were an additional 175 (5·6%) of 3114 individuals who reported experiencing miscarriage or stillbirth between the first COVID-19 vaccine dose and completion of the second (dose two) survey (up to 10 days after dose two), although precise timing of these events relative to vaccination was not collected. Other adverse pregnancy outcomes such as vaginal bleeding, abnormal fetal heart rate, and reduced fetal movement were rarely reported within 7 days following any mRNA vaccination (table 3).

In the multivariable analysis adjusting for age group, previous SARS-CoV-2 infection, and trimester, we observed an increased risk of significant health events within 7 days after the second dose of any mRNA vaccine (adjusted OR [aOR] 2·4 [95% CI 1·3–4·5]) or the second dose of mRNA-1273 COVID-19 vaccination (aOR 4·4 [2·4–8·3]) among pregnant vaccinated individuals, compared with pregnant unvaccinated controls (figure 2A). The first dose of any mRNA vaccine (mRNA-1273 or BNT162b2) and either dose of BNT162b2 were not associated with increased risk of significant health events. Similarly, we found no significant association between vaccination status and serious health events in pregnant people (figure 2A).

In the sensitivity analysis, both univariable and multivariable models among pregnant individuals with excellent health status revealed similar findings to those in the main analysis. The increase in significant health events after dose two of any mRNA vaccine and mRNA-1273 was no longer observed when we restricted our outcome variable to events requiring medical consultation (any mRNA vaccine: aOR 1·26 [95% CI 0·45–3·52] and mRNA-1273 vaccine: aOR 1·81 [0·62–5·28]; appendix p 4).

	Pregnant control group (n=339)	Dose 1			Dose 2		
		Any mRNA (n=5597)	BNT162b2 (n=3414)	mRNA-1273 (n=2183)	Any mRNA (n=3108)	BNT162b2 (n=1892)	mRNA-1273 (n=1216)
Health events							
Injection site reactions	NA	4515 (80·7%)	2631 (77·1%)	1884 (86·3%)	2440 (78·5%)	1430 (75·6%)	1010 (83·1%)
Significant health events*	11 (3·2%)	226 (4·0%)	137 (4·0%)	89 (4·1%)	227 (7·3%)	80 (4·2%)	147 (12·1%)
General							
Feeling unwell, malaise, or myalgia	3 (0·9%)	168 (3·0%)	104 (3·0%)	64 (2·9%)	205 (6·6%)	66 (3·5%)	139 (11·4%)
Fever	1 (0·3%)	34 (0·6%)	21 (0·6%)	13 (0·6%)	73 (2·3%)	18 (1·0%)	55 (4·5%)
Arthritis or joint pain	2 (0·6%)	31 (0·6%)	16 (0·5%)	15 (0·7%)	57 (1·8%)	19 (1·0%)	38 (3·1%)
Jaundice	0	1 (<0·1%)	0	1 (<0·1%)	0	0	0
Neurological							
Headache or migraine	2 (0·6%)	128 (2·3%)	82 (2·4%)	46 (2·1%)	144 (4·6)	41(2·2%)	103 (8·5%)
Dizziness or vertigo	1 (0·3%)	49 (0·9%)	30 (0·9%)	19 (0·9%)	41 (1·3%)	16 (0·8%)	25 (2·1%)
Paresthesia	0	24 (0·4%)	16 (0·5%)	8 (0·4%)	27 (0·9%)	12 (0·6%)	15 (1·2%)
Fainting	0	8 (0·1%)	4 (0·1%)	4 (0·2%)	2 (0·1%)	0	2 (0·2%)
Inability to walk	0	7 (0·1%)	2 (0·1%)	5 (0·2%)	8 (0·3%)	2 (0·1%)	6 (0·5%)
Loss of taste or smell	0	10 (0·2%)	9 (0·3%)	1 (<0·1%)	4 (0·1%)	1 (0·1%)	3 (0·2%)
Loss of vision	0	4 (0·1%)	2 (0·1%)	2 (0·1%)	1 (<0·1%)	0	1 (0·1%)
Sudden unilateral facial weakness or paralysis	0	1 (<0·1%)	0	1 (<0·1%)	3 (0·1%)	2 (0·1%)	1 (0·1%)
Seizure or convulsions	0	1 (<0·1%)	0	1 (<0·5%)	0	0	0
Other neurological symptoms†	0	9 (0·2%)	5 (0·1%)	4 (0·2%)	3(0·1%)	1 (0·1%)	2 (0·2%)
Infection							
Respiratory tract infection	3 (0·9%)	91 (1·6%)	61 (1·8%)	30 (1·4%)	98 (3·2%)	30 (1·6%)	68 (5·6%)
Shingles	0	1 (<0·1%)	0	1 (<0·1%)	1 (<0·1%)	0	1 (0·1%)
Urinary tract infection symptoms	0	6 (0·1%)	2 (0·1%)	4 (0·2%)	2 (0·1%)	0	2 (0·2%)
Cardio-respiratory							
Chest pain or palpitations	1 (0·3%)	38 (0·7%)	24 (0·7%)	14 (0·6%)	26 (0·8%)	7 (0·4%)	19 (1·6%)
Difficulty in breathing	3 (0·9%)	29 (0·5%)	17 (0·5%)	12 (0·5%)	17 (0·5%)	5 (0·3%)	12 (1·0%)
Cough	2 (0·6%)	27 (0·5%)	19 (0·6%)	8 (0·4%)	15 (0·5%)	8 (0·4%)	7 (0·6%)
Chest tightness	0	20 (0·4%)	13 (0·4%)	7 (0·3%)	17 (0·5%)	6 (0·3%)	11 (0·9%)
Allergic reactions							
Hives	1 (0·3%)	14 (0·3%)	8 (0·2%)	6 (0·3%)	10 (0·3%)	5 (0·3%)	5 (0·4%)
Itchy eyes	0	10 (0·2%)	5 (0·1%)	5 (0·2%)	8 (0·3%)	2 (0·1%)	6 (0·5%)
Throat swelling	0	6 (0·1%)	3 (0·1%)	3 (0·1%)	2 (0·1%)	1 (0·1%)	1 (0·1%)
Redness of both eyes	0	3 (0·1%)	1 (<0·1%)	2 (0·1%)	2 (0·1%)	0	2 (0·2%)
Facial swelling	0	2 (<0·1%)	1 (<0·1%)	1 (<0·1%)	3 (0·1%)	0	3 (0·2%)
Eyelid swelling	0	2 (<0·1%)	1 (<0·1%)	1 (<0·1%)	1 (<0·1%)	0	1 (0·1%)
Anaphylaxis	0	1 (<0·1%)	0	1 (<0·1%)	0	0	0
Coagulation symptoms‡							
Total number	0	6 (0·1%)	3 (0·1%)	3 (0·1%)	4 (0·1%)	1 (0·1%)	3 (0·2%)

Data are n (%). *All participants were asked about injection site reactions; only those who indicated a significant health event were further asked to provide details and participants were able to select multiple symptoms. †Weakness or paralysis of the arms or legs, confusion, change in personality or behaviour, or difficulty with urination or defecation. ‡Symptoms of blood clot or bleeding, including swelling, pain in legs, or bruising or pinpoint dark rash

Table 2: **Injection site reactions and details of significant health events reported in the 7 days following COVID-19 vaccination in vaccinated pregnant females and unvaccinated controls**

Injection site reactions such as redness, pain, or swelling were reported in between 1430 (75·6%) of 1892 (dose two of BNT162b2) and 1884 (86·3%) of 2183 (dose one of mRNA-1273) vaccine recipients. The most frequently reported significant health events within 7 days of each vaccine dose were feeling unwell or

malaise or myalgia (between 64 [2·9%] of 2183 for dose one of mRNA-1273 and 139 [11·4%] of 1216 for dose two of mRNA-1273) and headache (between 46 [2·1%] of 2183 for dose one of mRNA-1273 and 103 [8·5%] of 1216 for dose two of mRNA-1273]; table 2). When comparing vaccinated pregnant and vaccinated non-pregnant people, significant adverse events following immunisation rates (ie, excluding injection site reactions) were consistently lower among pregnant people across all mRNA vaccine types and doses (table 1). Overall, 226 (4·0%) of 5597 pregnant people reported a significant adverse event following immunisation after dose one and 227 (7·3%) of 3108 reported one after dose two, compared with 10 950 (6·3%) of 174 765 after dose one and 10 254 (11·3%) of 91 131 after dose two for non-pregnant people. Similar differences were seen for both BNT162b2 and mRNA-1273 after both dose one and dose two. The reported rates of serious health events were low (<1%) and similar in vaccinated pregnant people compared with vaccinated non-pregnant controls (table 1).

The multivariable models revealed that pregnancy was associated with a decreased risk of significant health events for any mRNA vaccine for both dose one (any mRNA: aOR 0·63 [95% CI 0·55–0·72]; BNT162b2: aOR 0·63 [0·53–0·75]; mRNA-1273: aOR 0·62 [0·5–0·77]) and dose two (any mRNA: aOR 0·62 [0·54–0·71]; BNT162b2: aOR 0·52 [0·41–0·65]; mRNA-1273: aOR 0·72 [0·6–0·85]; figure 2B). However, for the secondary endpoint of serious adverse events following immunisation, we found the second dose of mRNA-1273 was associated with a higher risk of serious adverse events (aOR 2·3 [95% CI 1·2–4·2]) in pregnant individuals compared with non-pregnant individuals. The second dose of any mRNA vaccine was also associated with a higher risk of serious adverse events (aOR 1·6 [95% CI 1·0–2·6]. This association was not observed in individuals who received BNT162b2 for dose two or with any vaccine groups for dose one. However, a sensitivity analysis that restricted our primary end point (significant health event) to those who sought medical care 7 seven days following each vaccine dose yielded no significant association between any mRNA vaccine and pregnancy status among vaccinated individuals (appendix p 5).

	Control (n=339)	Any mRNA (n=5597)	BNT162b2 (n=3414)	mRNA-1273 (n=2183)
Miscarriage or still birth				
Overall	7 (2·1%)	83 (1·5%)	51 (1·5%)	32 (1·5%)
1st trimester	7/7 (100·0%)	73/83 (88·0%)	47/51 (92·2%)	26/32 (81·3%)
2nd trimester	0	7/83 (8·4%)	4/51 (7·8%)	3/32 (9·4%)
3rd trimester	0	1/83 (1·2%)	0	1/32 (3·1%)
Unknown	0	2/83 (2·4%)	0	2/32 (6·3%)
Adverse pregnancy outcomes				
Any adverse outcome	2 (0·6%)	50 (0·9%)	31 (0·9%)	19 (0·9%)
Preterm labour	0	3 (0·1%)	1 (<0·1%)	2 (0·1%)
High blood pressure	0	6 (0·1%)	4 (0·1%)	2 (0·1%)
Vaginal spotting or vaginal bleeding	1 (0·3%)	21 (0·4%)	10 (0·3%)	11 (0·5%)
Abnormal fetal heart rate	0	2 (<0·1%)	1 (<0·1%)	1 (<0·1%)
Other pregnancy complications*	1 (0·3%)	30 (0·5%)	17 (0·5%)	13 (0·6%)

Data are n (%) or n/N (%). Participants were able to report multiple outcomes. *Included lower abdominal pain, reduced fetal movement, cramp, and vomiting.

Table 3: **Reported pregnancy outcomes in the 7 days following a first dose COVID-19 vaccination in vaccinated pregnant women and unvaccinated pregnant controls**

Discussion

In our prospective study collecting real-time data from pregnant individuals who were both vaccinated and unvaccinated, we found that significant health events—new or worsening health events following vaccination sufficient to cause work or school absenteeism, medical consultation, or prevent daily activities—were lower in pregnant people than in age-matched non-pregnant vaccine recipients. Amongst pregnant individuals, significant adverse events following immunisation were higher in those who received the mRNA-1273 vaccine for their second dose than in unvaccinated pregnant people, with no difference observed for BNT162b2 after either dose. When restricted to events resulting in medical consultation, there was no difference between groups in any of the analyses. These data can be used to appropriately inform pregnant people regarding reactogenicity of COVID-19 vaccines during pregnancy and should be considered alongside effectiveness and immunogenicity data to make appropriate recommendations about best use of COVID-19 vaccines in pregnancy.

The largest study to date of COVID-19 vaccine reactogenicity in pregnancy, which directly collected data from study participants, reported on approximately 30 000 pregnant people in the USA who had received BNT162b2 or mRNA-1273, using data from the v-safe registry.[8] Pregnant people in this study reported high rates of injection site pain (92% after dose two), fatigue (72%), headache (55%), myalgia (54%) and fever or chills (35–37%), with higher rates of adverse events after dose two than after dose one. The data from the v-safe registry suggested an increased rate of these events after mRNA-1273 compared with BNT162b2 after dose two, but no formal comparisons between vaccines was done. Notably, the study collected data on all adverse events following immunisation and specific information regarding severity was not reported, so it is not possible to directly compare results with our study, although if total adverse event rates are higher after dose two, and after mRNA-1273, then rates of significant adverse events would probably follow a similar pattern. A more recent study of 7800 pregnant people compared with 2900 non-pregnant individuals also reported higher rates of adverse events, in pregnant people, after dose two of a

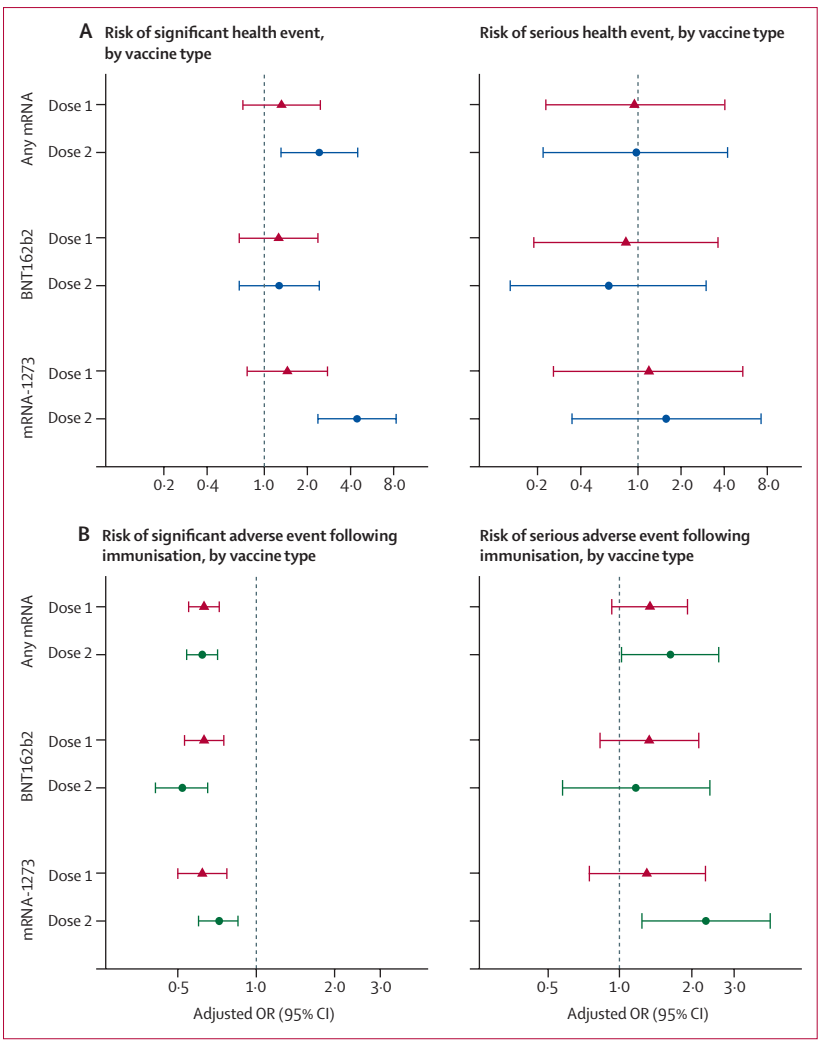


Figure 2: **Multivariable logistic regression analyses comparing significant and serious health events**
(A) Comparison between vaccinated and unvaccinated pregnant females. Red triangles and blue circles represent point estimates of adjusted ORs for vaccine doses one and two, with 95% CIs. The reference group is unvaccinated pregnant people. ORs are adjusted for age group, trimester, and previous SARS-CoV-2 infection. Seven (0·1%) of 5936 pregnant vaccinated plus pregnant unvaccinated cases were not included in the multivariable analysis due to missing data. (B) Comparison between pregnant and non-pregnant vaccinated females. Red triangles and green circles represent point estimates of adjusted ORs for vaccine doses one and two, with 95% CIs. The reference group is vaccinated non-pregnant people. ORs are adjusted for age group and previous SARS-CoV-2 infection. 254 (0·1%) of the 180 362 vaccinated cases were not included in the multivariable analysis due to missing data. The x-axis of each graph is a log scale. OR=odds ratio.

COVID-19 mRNA vaccine.[13] Some adverse events occurred at lower rates in non-pregnant individuals, including fever. Specific data on significant adverse events following immunisation were not comprehensively reported, although 156 pregnant individuals (2·5%) sought medical care after their second vaccine dose, compared with only 1·5% in our cohort. A systematic review including Shimabukuro and colleague's study[8] and multiple other smaller studies reported similarly higher rates of adverse events following immunisation after dose two of a COVID-19 vaccine, but no differences between pregnant and non-pregnant controls.[6]

Initial clinical trials of mRNA-1273 and BNT162b2 reported relatively high rates of adverse events following immunisation compared with most routinely administered vaccines, including higher rates for dose two than dose one.[14,15] Therefore, the fact that our analysis revealed similar patterns among pregnant individuals was unsurprising—although we have been able to specifically quantify the significant and serious adverse event rates in this population for each of the mRNA vaccines. Previous studies of influenza vaccines done using the same CANVAS methodology similarly reported higher rates of adverse events following immunisation among vaccinated than among unvaccinated control participants.[9]

The lower rate of significant adverse events following immunisation among pregnant people than among vaccinated non-pregnant individuals is important. Before the COVID-19 pandemic, influenza and tetanus-diphtheria-pertussis (Tdap) vaccines had been routinely recommended for pregnant people in many countries. Previous studies have mostly reported no significant differences in adverse events following immunisation between pregnant and non-pregnant individuals,[16–19] or higher rates in pregnancy—for example, one study reported increased moderate to severe injection-site pain in pregnant (17·9%) compared with non-pregnant (11·1%) women after Tdap vaccination.[17] Several highly dynamic immunological adaptations occur during pregnancy, including a skew towards a T-helper-2 dominant state.[20] Because mRNA vaccines have been specifically designed to elicit a Th1-biased immune response,[21] it is possible that the Th2-bias during pregnancy is partly responsible for this lower rate of significant adverse events following immunisation.

Our study has several strengths and limitations. It is a multicentre study across Canada and thus includes broad representation of people within Canada, although most participants who reported ethnicity were White and these data therefore might not be fully generalisable to other populations. Overall, the pregnant people in our study had similar characteristics (age, residence, health status) to the pregnant population in Canada.[22–24] Specifically, most of our participants were aged 30–49 years (74·7% versus 61·5% of pregnant people in Canada);[24] most participants were from Ontario (37·2%), Quebec (26·2%), British Columbia/Yukon (20·2%), and Alberta (13·9%), regions which represent 37·9%, 22·8%, 11·8%, and 13·7% of live births in Canada in 2020;[24] 89·9% described their health as excellent, very good, or good—across Canada, severe maternal morbidity has been described in 1·3–1·6% of pregnancies[22] and 27% of pregnant people have chronic conditions (although the severity is variable and some will have a good or better than good health status).[23] Participants were enrolled from all trimesters in pregnancy and this was included as a co-variate in the multivariable models. An important advantage over many other similar studies is the contemporaneous recruitment of non-pregnant

vaccinated individuals, enabling a robust direct comparison in significant adverse events following immunisation between pregnant and non-pregnant individuals. We focused on events occurring within the first 7 days following vaccination and thus acute and local reactions. Longer-term follow-up of this cohort is ongoing, and we will be able to comment on health events that occur over a longer time frame after vaccination once these data are available.

Furthermore, CANVAS is based on self-reports from study participants, without verification from medical records. This method of reporting is subjective and might be subject to recall bias, but has been shown to be reliable for short time periods, such as in this study.[25,26] The study relied on individuals having an email address and actively enrolling. Such individuals might differ in health-seeking behaviour from the rest of the population because they might represent a different socio-economic status, but at least for our comparisons between groups it would be expected that they would be similarly affected by any bias as recruitment required an email address. Study participants were asked their age within prespecified age groups, and we therefore do not know the specific age of each participant. Pregnant participants reported trimester of pregnancy rather than weeks' gestation. Finally, our sample size precludes detection of very rare adverse events, which can be identified in the general population from the passive surveillance systems in place across Canada and in other countries.

Our data provide reassuring evidence that COVID-19 mRNA vaccines are safe in pregnancy, with lower rates of significant adverse events following immunisation in pregnant people than in non-pregnant vaccine recipients for both mRNA vaccines used in Canada, after dose one and dose two. Although rates of significant adverse events following immunisation were highest after dose two for mRNA-1273 recipients, both mRNA vaccines are highly immunogenic and effective in pregnancy.[6] Given the increased rate of significant complications associated with COVID-19 in pregnancy, high vaccine coverage in this group is important for protection of the pregnant individual and young infant,[27] via passive transplacental transfer of antigen-specific IgG antibody and protection via breast milk.[28,29] These data can be used to inform pregnant individuals of the expected adverse events following vaccination. Further studies of non-COVID-19 mRNA vaccines are required to identify if the reduced reactogenicity observed in pregnant people in this study is a feature of the mRNA vaccine platform, or of these specific vaccines. Further long-term data are awaited from this cohort following a 6-month follow-up. The number of pregnant individuals receiving the ChAdOx-S vaccine in our population was very low and data for this vaccine in countries where it has been more widely used are important to provide a more complete overview of the safety of COVID-19 vaccines in pregnancy.

Contributors

JAB conceived and obtained funding for the study. MS, LV, OGV, JDK, MPM, KAT, JEI, AM, GDS, and JAB collected data and contributed to study design. KM contributed to study design. PS, HPS, and MI analysed the data. MS, PS, HPS, MI, and JAB accessed and verified the data. MS and PS drafted the original version of the manuscript. All authors had full access to the data, reviewed the manuscript, contributed to data interpretation, approved the final version and accept responsibility to submit for publication.

Declaration of interests

MS has been an investigator on projects funded by GlaxoSmithKline, Merck, Moderna, Pfizer, Sanofi-Pasteur, Seqirus, Symvivo, and VBI Vaccines. All funds have been paid to his institute, and he has not received any personal payments. OGV has been an investigator, coinvestigator, or expert panelist on projects funded by GlaxoSmithKline, Merck, Pfizer, and Seqirus, outside of the submitted work. JDK has been an investigator on projects funded by GlaxoSmithKline, Merck, Moderna, and Pfizer. All funds have been paid to his institute, and he has not received any personal payments. KAT has been an investigator on projects funded by GlaxoSmithKline. All funds have been paid to her institute, and she has not received any personal payments. JEI has been an investigator on projects funded by GlaxoSmithKline, and Sanofi-Pasteur. All funds have been paid to her institute, and she has not received any personal payments. AJM has been an investigator on projects funded by GlaxoSmithKline, Merck, Pfizer, Sanofi-Pasteur, and Seqirus, with funds paid to her institution, and has received honoraria for participation in advisory boards from Astra-Zeneca, GlaxoSmithKline, Medicago, Merck, Moderna, Pfizer, Sanofi-Pasteur, Seqirus, and for presentations from Astra-Zeneca, and Moderna. GDS has been an investigator on a project funded by Pfizer. All funds have been paid to his institute, and he has not received any personal payments. All other authors declare no competing interests.

Data sharing statement

De-identified data collected for the study (with data dictionary) might be made available upon approval by the study investigators, with relevant agreements (eg, data sharing agreement) and approvals (eg, relevant ethics approvals). Requests should be directed to the corresponding author in the first instance.

Acknowledgements

This work was supported by the COVID-19 Vaccine Readiness funding from the Canadian Institutes of Health Research and the Public Health Agency of Canada CANVAS (grant number CVV-450980) and by funding from the Public Health Agency of Canada, through the Vaccine Surveillance Reference Group and the COVID-19 Immunity Task Force. MS is supported via salary awards from the BC Children's Hospital Foundation, the Canadian Child Health Clinician Scientist Program, and the Michael Smith Foundation for Health Research.

References

1 Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ* 2020; **370:** m3320.

2 Cojocaru L, Noe M, Pahlavan A, et al. Increased risk of severe COVID-19 disease in pregnancy in a multicenter propensity score-matched study. *medRxiv* 2021; published online June 21. https://doi.org/10.1101/2021.06.18.21258899 (preprint).

3 National Advisory Committee on Immunization. Recommendations on the use of COVID-19 vaccines. 2020. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines.html#a8 (accessed June 6, 2022).

4 Poliquin V, Castillo E, Boucoiran I, et al. SOGC statement on COVID-19 vaccination in pregnancy. Ottawa, ON, Canada: Society of Obstetricians and Gynecologists of Canada, 2020.

5 The American College of Obstetricians and Gynecologists. COVID-19 vaccination considerations for obstetric-gynecologic care. 2020. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/covid-19-vaccination-considerations-for-obstetric-gynecologic-care (accessed June 6, 2022).

6 Fu W, Sivajohan B, McClymont E, et al. Systematic review of the safety, immunogenicity, and effectiveness of COVID-19 vaccines in pregnant and lactating individuals and their infants. *Int J Gynaecol Obstet* 2021; **156:** 406–17.

7 Delara M, Sadarangani M. Immunization in pregnancy to protect pregnant people and their newborns against COVID-19. *Expert Rev Vaccines* 2022; 1–3.

8 Shimabukuro TT, Nguyen M, Martin D, DeStefano F. Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS). *Vaccine* 2015; **33:** 4398–405.

9 Bettinger JA, De Serres G, Valiquette L, et al. 2017/18 and 2018/19 seasonal influenza vaccine safety surveillance, Canadian National Vaccine Safety (CANVAS) Network. *Euro Surveill* 2020; **25**: 22.

10 Bettinger JA, Sadarangani M, De Serres G, et al. The Canadian National Vaccine Safety Network: surveillance of adverse events following immunisation among individuals immunised with the COVID-19 vaccine, a cohort study in Canada. *BMJ Open* 2022; **12:** e051254.

11 Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)-A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009; **42:** 377–81.

12 Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform* 2019; **95:** 103208.

13 Kachikis A, Englund JA, Singleton M, Covelli I, Drake AL, Eckert LO. Short-term reactions among pregnant and lactating individuals in the first wave of the COVID-19 vaccine rollout. *JAMA Netw Open* 2021; **4:** e2121310.

14 Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. *N Engl J Med* 2020; **383:** 2603–15.

15 Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2021; **384:** 403–16.

16 Munoz FM, Englund JA. Vaccines in pregnancy. *Infect Dis Clin North Am* 2001; **15:** 253–71.

17 Fortner KB, Swamy GK, Broder KR, et al. Reactogenicity and immunogenicity of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) in pregnant and nonpregnant women. *Vaccine* 2018; **36:** 6354–60.

18 Munoz FM, Patel SM, Jackson LA, et al. Safety and immunogenicity of three seasonal inactivated influenza vaccines among pregnant women and antibody persistence in their infants. *Vaccine* 2020; **38:** 5355–63.

19 Sullivan SG, Price OH, Regan AK. Burden, effectiveness and safety of influenza vaccines in elderly, paediatric and pregnant populations. *Ther Adv Vaccines Immunother* 2019; **7:** 2515135519826481.

20 Abu-Raya B, Michalski C, Sadarangani M, Lavoie PM. Maternal immunological adaptation during normal pregnancy. *Front Immunol* 2020; **11:** 575197.

21 Sadarangani M, Marchant A, Kollmann TR. Immunological mechanisms of vaccine-induced protection against COVID-19 in humans. *Nat Rev Immunology* 2021; **21:** 475–84.

22 Public Health Agency of Canada. Perinatal Health Indicators for Canada 2017. Ottawa, ON, Canada: Government of Canada, 2019.

23 Public Health Agency of Canada. Pregnancy in Canada. 2020. https://www.canada.ca/en/public-health/services/publications/healthy-living/pregnancy-canada-infographic.html (accessed June 6, 2022).

24 Statistics Canada. Births, 2020. 2021. https://www150.statcan.gc.ca/n1/daily-quotidien/210928/dq210928d-cansim-eng.htm (accessed June 3, 2022).

25 Short ME, Goetzel RZ, Pei X, et al. How accurate are self-reports? Analysis of self-reported health care utilization and absence when compared with administrative data. *J Occup Environ Med* 2009; **51:** 786–96.

26 Clothier HJ, Selvaraj G, Easton ML, Lewis G, Crawford NW, Buttery JP. Consumer reporting of adverse events following immunization. *Hum Vaccin Immunother* 2014; **10:** 3726–30.

27 Halasa NB, Olson SM, Staat MA, et al. Effectiveness of maternal vaccination with mRNA COVID-19 vaccine during pregnancy against COVID-19-associated hospitalization in infants aged <6 months—17 States, July 2021–January 2022. *MMWR Morb Mortal Wkly Rep* 2022; **71:** 264–70.

28 Yang YJ, Murphy EA, Singh S, et al. Association of gestational age at coronavirus disease 2019 (COVID-19) vaccination, history of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection, and a vaccine booster dose with maternal and umbilical cord antibody levels at delivery. *Obstet Gynecol* 2022; **139:** 373–80.

29 Shook LL, Atyeo CG, Yonker LM, et al. Durability of anti-spike antibodies in infants after maternal COVID-19 vaccination or natural infection. *JAMA* 2022; **327:** 1087–89.

THE LANCET
Infectious Diseases

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Sadarangani M, Soe P, Shulha HP, et al. Safety of COVID-19 vaccines in pregnancy: a Canadian National Vaccine Safety (CANVAS) network cohort study. *Lancet Infect Dis* 2022; published online Aug 11. https://doi.org/10.1016/S1473-3099(22)00426-1.

Appendix

Supplementary Table 1. Characteristics of females aged 15-49 years in the CANVAS-COVID-19 study

		Dose 1*				Dose 2*			
	Control N (%)	All vaccine type N (%)	BNT162b2 N (%)	mRNA-1273 N(%)	ChAdOx1-S N(%)	All vaccine type N(%)	BNT162b2 N (%)	mRNA-1273 N(%)	ChAdOx1-S N(%)
Total N	6,179(100)	191,360(100)	110,535(100)	69,827(100)	10,857(100)	94,937(100)	54,969(100)	39,270(100)	631(100)
Non-pregnant	5840(94·5)	185,735(97·1)	107,121(96·9)	67,644(96·9)	10,832(99·8)	91,823(96·7)	53,077(96·6)	38,054(96·9)	625(99·2)
Pregnant	339(5·5)	5,625(2·9)	3,414(3·1)	2,183(3·1)	25(0·2)	3,114(3·3)	1,892(3·4)	1,216(3·1)	6(0·8)
Trimester									
First	105(1·7)	1,297(0·7)	802(0·8)	487(0·7)	7 (0·1)	956(1·0)	568(1·0)	385(1·0)	3(0·3)
Second	144(2·3)	2,409(1·3)	1,473(1·3)	924(1·3)	11(0·1)	1,037(1·1)	636(1·2)	399(1·0)	2(0·3)
Third	90(1·5)	1,917(1·0)	1,139(1·0)	770(1·1)	7(0·1)	1,119(1·2)	687(1·2)	431(1·1)	1(0·1)
Unknown	0	2(0·0)	0	2(0·0)	0	2(0·0)	1(0·0)	1(0·0)	0

*There were 141 females with unknown vaccine type in dose one and 67 females in dose two.

Supplementary Table 2. Significant and serious health event rates by vaccine type among vaccinated and unvaccinated (controls) pregnant females, and onset and duration of significant health events

		Dose 1			Dose 2		
	Control N (%)	Any mRNA N (%)	BNT162b2 N (%)	mRNA-1273 N (%)	Any mRNA N (%)	BNT162b2 N (%)	mRNA-1273 N (%)
Sample size	339	5597	3414	2183	3108	1892	1216
Significant health events	11(3·2)	226(4·0)	137(4·0)	89(4·1)	227(7·3)	80(4·2)	147(12·1)
Onset of significant health events							
Within 60 minutes	0(0·0)	12(5·3)	8(5·8)	4(4·5)	4(1·8)	1(1·3)	3(2·0)
1-24 hours	2(18·2)	118(52·2)	69(50·4)	49(55·1)	183(80·6)	55(68·8)	128(87·1)
2-3 days	0(0·0)	55(24·3)	34(24·8)	21(23·6)	26(11·5)	14(17·5)	12(8·2)
4-5 days	3(27·3)	22(9·7)	12(8·8)	10(11·2)	5(2·2)	3(3·8)	2(1·4)
6-7 days	4(36·4)	11(4·9)	9(6·6)	2(2·2)	4(1·8)	4(5·0)	0(0·0)
8+ days	2(18·2)	7(3·1)	4(2·9)	3(3·4)	5(2·2)	3(3·8)	2(1·4)
Duration of significant health events							
Within 60 minutes	0(0·0)	6(2·7)	4(2·9)	2(2·2)	2(0·9)	1(1·3)	1(0·7)
1-10 hours	0(0·0)	17(7·5)	14(10·2)	3(3·4)	15(6·6)	6(7·5)	9(6·1)
11-24 hours	0(0·0)	46(20·4)	29(21·2)	17(19·1)	84(37·0)	29(36·3)	55(37·4)
2-3 days	1(9·1)	55(24·3)	32(23·4)	23(25·8)	67(29·5)	19(23·8)	48(32·7)
4-5 days	1(9·1)	33(14·6)	17(12·4)	16(18·0)	18(7·9)	6(7·5)	12(8·2)
6+ days	0(0·0)	17(7·5)	12(8·8)	5(5·6)	25(11·0)	11(13·8)	14(9·5)
Ongoing	9(81·8)	51(22·6)	28(20·4)	23(25·8)	16(7·0)	8(10·0)	8(5·4)

Supplementary Table 3. Reported diagnosis for serious health event rates by vaccine type among vaccinated and unvaccinated pregnant females

		Dose 1			Dose 2		
	Control N (%)	**Any mRNA N (%)**	**BNT162b2 N (%)**	**mRNA-1273 N (%)**	**Any mRNA N (%)**	**BNT162b2 N (%)**	**mRNA-1273 N (%)**
Sample size	339	5597	3414	2183	3108	1892	1216
Serious health events	2(0·6)	31(0·6)	18(0·5)	13(0·6)	19(0·6)	8(0·4)	11(0·9)
Reported diagnosis							
Anaphylaxis	0	5(16·1)	3(16·7)	2(15·4)	2(10·5)	0	2(18·2)
Sepsis	0	0	0	0	1(5·3)	0	1(9·1)
Coagulation	0	1(3·2)	0	1(7·7)	0	0	0
Pulmonary Embolism	0	1(3·2)	0	1(7·7)	0	0	0
Bell's Palsy	0	0	0	0	1(5·3)	1(12·5)	0
Severe Morning sickness	0	1(3·2)	0	1(7·7)	0	0	0
Pre-term labor	0	1(3·2)	1(5·6)	0	2(10·5)	1(12·5)	1(9·1)
Still birth	0	0	0	0	1(5·3)	1(12·5)	0
Miscarriage	0	1(3·2)	0	1(7·7)	3(15·8)	0	3(27·3)
Abruptio placenta	0	2(6·5)	2(11·1)	0	2(10·5)	2(25·0)	0
Fibroid pain	0	2(6·5)	2(11·1)	0	0	0	0
COVID-19 infection	1(50·0)	1(3·2)	1(5·6)	0	0	0	0
Oral Thrush	0	0	0	0	1(5·3)	1(12·5)	0
Muscle soreness	0	0	0	0	1(5·3)	1(12·5)	0
Kidney stones/Cholestasis	0	2(6·5)	2(11·1)	0	0	0	0
Anxiety attack	0	1(3·2)	0	1(7·7)	0	0	0
No diagnosis	1(50·0)	12(38·7)	7(38·9)	5(38·5)	5(26·3)	1(12·5)	4(36·4)
Prefer not to answer	0	1(3·2)	0	1(7·7)	0	0	0

Serious health event: any event resulting in emergency department visit and/or hospitalization in the previous seven days

Supplementary Table 4. Results of primary and sensitivity analyses assessing the relationship between vaccination status and significant health events among pregnant people

	Dose 1		Dose 2	
	Unadjusted OR (95% CI)	**Adjusted aOR*(95% CI)**	**Unadjusted OR (95% CI)**	**Adjusted aOR*(95% CI)**
Primary analysis[a]:				
Any mRNA	1·25[0·68 – 2·32]	1·32[0·71 – 2·46]	2·35[1·27 – 4·35]	2·42[1·31 – 4·49]
BNT162b2	1·25[0·67 – 2·33]	1·26[0·67 – 2·37]	1·32[0·69 – 2·50]	1·27[0·67 – 2·42]
mRNA-1273	1·27[0·67 – 2·40]	1·45[0·76 – 2·76]	4·10[2·19 – 7·66]	4·44[2·37 – 8·31]
Sensitivity analysis[b]				
Any mRNA	1·18 [0·43 -3·25]	1·22[0·44 – 3·36]	1·29[0·46 – 3·59]	1·26[0·45 – 3·52]
BNT162b2	1·12[0·40 – 3·13]	1·11[0·39 – 3·12]	0·99[0·34 – 2·88]	0·90[0·31 – 2·64]
mRNA-1273	1·29[0·45 – 3·65]	1·41[0·49 – 4·07]	1·76[0·61 – 5·09]	1·81[0·62 – 5·28]

[a]Primary end point (significant health event): a new or worsening of a health event sufficient to cause work/school absenteeism, medical consultation and/or prevent daily activities in the previous seven days

[b]Severe health event: a new or worsening of a health event resulting medical consultation in the previous seven days

*Reference: unvaccinated pregnant control; adjusted for age groups, trimester and previous COVID-19 infection

Supplementary Table 5. Results of primary and sensitivity analyses assessing the relationship between pregnancy status and significant health events among vaccinated people

	Dose 1		Dose 2	
	Unadjusted OR (95% CI)	**Adjusted aOR*(95% CI)**	**Unadjusted OR (95% CI)**	**Adjusted aOR*(95% CI)**
Primary analysis[a]:				
Any mRNA	0·63[0·55 – 0·72]	0·63[0·55 – 0·72]	0·62[0·54 – 0·71]	0·62[0·54 – 0·71]
BNT162b2	0·65[0·54 – 0·77]	0·63[0·53 – 0·75]	0·52[0·42 – 0·66]	0·52[0·41 – 0·65]
mRNA-1273	0·60[0·49 – 0·75]	0·62[0·50 – 0·77]	0·72[0·60 – 0·85]	0·72[0·60 – 0·85]
Sensitivity analysis[b]				
Any mRNA	1·00[0·80 – 1·25]	1·01[0·80 – 1·27]	1·10[0·82 – 1·47]	1·10[0·82 – 1·47]
BNT162b2	1·01[0·75 – 1·37]	1·00[0·74 – 1·35]	0·93[0·61 – 1·43]	0·91[0·59 – 1·39]
mRNA-1273	0·98[0·69 – 1·38]	1·01[0·71 – 1·43]	1·32[0·88 – 1·98]	1·35[0·90 – 2·02]

[a]Primary end point (significant health event): a new or worsening of a health event sufficient to cause work/school absenteeism, medical consultation and/or prevent daily activities in the previous seven days following each dose of vaccine

[b]Severe health event: a new or worsening of a health event resulting medical consultation in the previous seven days following each dose of vaccine

*Reference: vaccinated non-pregnant women; adjusted for age groups and previous COVID-19 infection

Vaccine 41 (2023) 1716–1725

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Temporal trends and determinants of COVID-19 vaccine coverage and series initiation during pregnancy in Ontario, Canada, December 2020 to December 2021: A population-based retrospective cohort study

Deshayne B. Fell [a,b,*], Eszter Török [a,c], Ann E. Sprague [a,c], Annette K. Regan [d,e], Tavleen Dhinsa [c], Gillian D. Alton [a,c], Sheryll Dimanlig-Cruz [b,c], Shannon E. MacDonald [f,g,h], Sarah A. Buchan [i,j], Jeffrey C. Kwong [i,j,k,l], Sarah E. Wilson [i,j], Siri E. Håberg [m], Christopher A. Gravel [b,n], Kumanan Wilson [o,p,q], Sandra I. Dunn [a,r], Prakesh S. Shah [s,t,u,v], Darine El-Chaâr [b,o,w], Jon Barrett [x], Mark C. Walker [a,b,c,o,w], Nannette Okun [y], Shelley D. Dougan [a,c]

[a] Children's Hospital of Eastern Ontario (CHEO) Research Institute, Ottawa, ON, Canada
[b] School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON, Canada
[c] Better Outcomes Registry & Network (BORN) Ontario, Ottawa, Ontario, ON, Canada
[d] School of Nursing and Health Professions, University of San Francisco, San Francisco, CA, USA
[e] Department of Epidemiology, UCLA Fielding School of Public Health, Los Angeles, CA, USA
[f] Faculty of Nursing, University of Alberta, Edmonton, AB, Canada
[g] School of Public Health, University of Alberta, Edmonton, AB, Canada
[h] Department of Pediatrics, University of Calgary, Calgary, AB, Canada
[i] Public Health Ontario, Toronto, ON, Canada
[j] Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada
[k] ICES, Toronto, ON, Canada
[l] Department of Family and Community Medicine, University of Toronto, Toronto, ON, Canada
[m] Centre for Fertility and Health, Norwegian Institute of Public Health, Oslo, Norway
[n] Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, QC, Canada
[o] Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, ON, Canada
[p] Department of Medicine, University of Ottawa, Ottawa, ON, Canada
[q] Bruyère Research Institute, Ottawa, ON, Canada
[r] School of Nursing, University of Ottawa, Ottawa, ON, Canada
[s] Department of Pediatrics, Mount Sinai Hospital, Toronto, ON, Canada
[t] Department of Pediatrics, University of Toronto, Toronto, ON, Canada
[u] Maternal-infant Care Research Centre, Department of Pediatrics, Mount Sinai Hospital, Toronto, ON, Canada
[v] Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada
[w] Department of Obstetrics and Gynecology, University of Ottawa, Ottawa, ON, Canada
[x] Department of Obstetrics and Gynecology, McMaster University, Hamilton, ON, Canada
[y] Department of Obstetrics and Gynaecology, University of Toronto, Toronto, ON, Canada

ARTICLE INFO

Article history:
Received 29 September 2022
Received in revised form 24 January 2023
Accepted 27 January 2023
Available online 3 February 2023

Keywords:
COVID-19
COVID-19 vaccination
Pregnancy
Vaccine coverage
Vaccine series initiation

ABSTRACT

Background: Population-based COVID-19 vaccine coverage estimates among pregnant individuals are limited. We assessed temporal patterns in vaccine coverage (≥1 dose before or during pregnancy) and evaluated factors associated with vaccine series initiation (receiving dose 1 during pregnancy) in Ontario, Canada.

Methods: We linked the provincial birth registry with COVID-19 vaccination records from December 14, 2020 to December 31, 2021 and assessed coverage rates among all pregnant individuals by month, age, and neighborhood sociodemographic characteristics. Among individuals who gave birth since April 2021—when pregnant people were prioritized for vaccination—we assessed associations between sociodemographic, behavioral, and pregnancy-related factors with vaccine series initiation using multivariable regression to estimate adjusted risk ratios (aRR) and risk differences (aRD) with 95% confidence intervals (CI).

Results: Among 221,190 pregnant individuals, vaccine coverage increased to 71.2% by December 2021. Gaps in coverage across categories of age and sociodemographic characteristics decreased over time,

* Corresponding author at: 401 Smyth Road, Centre for Practice Changing Research, Room L1154, Ottawa, Ontario K1H 8L1, Canada.
E-mail address: dfell@cheo.on.ca (D.B. Fell).

https://doi.org/10.1016/j.vaccine.2023.01.073
0264-410X/© 2023 The Author(s). Published by Elsevier Ltd.
This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

but did not disappear. Lower vaccine series initiation was associated with lower age (<25 vs. 30–34 years: aRR 0.53, 95%CI 0.51–0.56), smoking (vs. non-smoking: 0.64, 0.61–0.67), no first trimester prenatal care visit (vs. visit: 0.80, 0.77–0.84), and residing in neighborhoods with the lowest income (vs. highest: 0.69, 0.67–0.71). Vaccine series initiation was marginally higher among individuals with pre-existing medical conditions (vs. no conditions: 1.07, 1.04–1.10).

Conclusions: COVID-19 vaccine coverage among pregnant individuals remained lower than in the general population, and there was lower vaccine initiation by multiple characteristics.

© 2023 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

1. Introduction

COVID-19 is associated with a higher risk of severe illness in pregnant individuals than in similarly aged non-pregnant females [1], and with a higher risk of adverse birth outcomes, compared with uninfected pregnant individuals [2]. After COVID-19 vaccines became available in late 2020, many countries adopted recommendations for COVID-19 vaccination during pregnancy [3]. Vaccination during pregnancy has been found to provide similarly effective protection against COVID-19 as in non-pregnant people [4,5], and reduce the risk of COVID-19 infection and hospitalization in young infants [6–8]. Despite these benefits, and increasing evidence that COVID-19 vaccination during pregnancy is not associated with increased risk of adverse outcomes such as spontaneous abortion, preterm birth, stillbirth, postpartum hemorrhage, low neonatal Apgar scores, or neonatal intensive care unit admission [9–15], vaccine coverage has been lower in pregnant individuals in some (e.g., United States [U.S.] [16] and Scotland [17]), but not all (e.g., Sweden and Norway [18]), countries compared to the female population of reproductive age.

Similar to other countries [3], recommendations for COVID-19 vaccination during pregnancy in Canada have changed over time. Initially in late 2020, the National Advisory Committee on Immunization (NACI) advised that pregnant people could be offered COVID-19 vaccination—with informed consent—if they were in an eligible priority group, but otherwise it was not recommended [19] due to the lack of pregnancy-specific safety data resulting from exclusion of pregnant individuals from pre-licensure clinical trials of COVID-19 vaccines [20]. This policy became more permissive over the ensuing months and by May 28, 2021, NACI recommended that a COVID-19 vaccine series should be offered to pregnant people in the authorized age group [21]. In Ontario, Canada, pregnant people were prioritized for vaccination in late April 2021 [22]; due to a limited supply of vaccines through the first 3–4 months of 2021, the vaccination program had not yet expanded to the general adult population by that time. On December 15, 2021, all adults over 18 years of age, including pregnant people, became eligible for a COVID-19 booster dose [23]. In this population-based study in Ontario, we assessed temporal patterns in COVID-19 vaccine coverage among all pregnant people over the first year of the COVID-19 vaccination program, and evaluated factors associated with COVID-19 vaccine series initiation during pregnancy from April 2021, when pregnant people were prioritized for COVID-19 vaccination in the province [22].

2. Methods

2.1. Study design and data sources

We conducted a population-based retrospective cohort study of all pregnant individuals in Ontario, Canada between December 14, 2020 (when the provincial COVID-19 vaccination program began) and December 31, 2021. Data from Ontario's birth registry (https://www.bornontario.ca) were used to identify the study population—the registry collects information on the maternal-newborn population from hospitals, midwifery practice groups, and prenatal screening laboratories across the province [24]. Prenatal screening records from hospital- and community-based laboratories and ultrasound clinics are received on a weekly basis; approximately 70% of pregnant individuals in Ontario undergo prenatal screening [25]. After pregnancy completion, integrated maternal-newborn records for births of at least 500 g or ≥20 weeks' gestation are transferred to the registry where they are automatically linked with any corresponding prenatal screening records for the index pregnancy [24]. Limited information is available from prenatal screening records alone (maternal age, estimated date of birth, and postal code which is used to obtain area-based socioeconomic variables), while detailed information on maternal demographics, health behaviors, pre-existing health conditions, obstetric complications, and birth outcomes is available from completed birth records.

We deterministically linked birth records for completed pregnancies during the study period with the provincial COVID-19 immunization database, COVaxON, which contains information for all COVID-19 vaccines administered, regardless of delivery site or provider. We additionally linked prenatal screening records for individuals still pregnant as of December 31, 2021 to the COVaxON database, so that ongoing pregnancies could be used for coverage estimates among all pregnant people. Residential postal codes were used to link the study population to area-based socioeconomic information from Statistics Canada's 2016 Census (the most recent Census data available when this study was conducted) and the Ontario Marginalization Index [26]. Additional information on data sources is provided in Table S1.

2.2. Study population

Ontario is Canada's largest province with publicly-funded health care and approximately 140,000 births each year. To assess temporal patterns in COVID-19 vaccine coverage (i.e., having received at least one dose of a COVID-19 vaccine before or during pregnancy) among all individuals who were pregnant at any point during the study period, we included all completed pregnancies from December 14, 2020 to December 31, 2021, and those pregnancies still ongoing as of December 31, 2021.

To evaluate factors associated with COVID-19 vaccine series initiation during pregnancy, we excluded ongoing pregnancies due to limited information available on the prenatal screening records from which the ongoing pregnancies are identified. We also excluded births prior to April 1, 2021 because vaccination during pregnancy was limited before that time due to eligibility criteria in Ontario's vaccination program [22]. Records with documented gestational age <20 weeks and birth weight <500 g, or pregnancy termination were also excluded, as these events are not systematically captured in the registry. Finally, we excluded individuals who had received ≥1 dose of COVID-19 vaccine before pregnancy, since they were few in number during the study period (most individuals vaccinated prior to conception gave birth in 2022) and we

were specifically interested in vaccine series initiation during pregnancy.

2.3. Measures

2.3.1. Vaccination status and timing

Information on COVID-19 vaccine doses and dates of administration were obtained from the COVaxON database. We used date of birth combined with gestational age to estimate the date of conception for completed pregnancies, and used the estimated date of birth (predominantly from early ultrasound assessment) from prenatal screening records to derive the date of conception for ongoing pregnancies. We considered a vaccine dose to have been received during pregnancy if administered between the date of conception up to 1 day before birth, inclusive.

- COVID-19 vaccine coverage was defined as the proportion of all pregnant individuals in any given time interval who had received at least one dose of any COVID-19 vaccine by that point in time (dose 1, dose 2, or dose 3 [i.e., first booster dose]), either before or during pregnancy (i.e., to evaluate the proportion of individuals who were protected while pregnant).
- COVID-19 vaccine series initiation during pregnancy was defined as having received dose 1 of COVID-19 vaccine during pregnancy (i.e., to explore factors associated with initiating their vaccine series when pregnant).

2.3.2. Sociodemographic and pregnancy characteristics

The following information from the prenatal screening records was available for the entire study population (completed pregnancies and those still ongoing at the end of the study period): maternal age (<25, 25–29, 30–34, 35–39, ≥40 years), calendar timing of conception (before July 2020, August-September 2020, October-November 2020, December 2020 or later), and area-based measures from Statistics Canada's 2016 Census (rural/urban residence; neighborhood income quintile) and the Ontario Marginalization Index, which provides measures of social and economic marginalization in four dimensions represented by quintiles (residential instability, material deprivation, dependency, ethnic concentration) [26]. See Table S1 for additional information on study variables.

Additional variables from birth records were available for completed pregnancies: pre-pregnancy body mass index (<30/≥30 kg/m^2); first prenatal visit in the first trimester (yes/no); self-reported smoking (yes/no) or substance use (yes/no) during pregnancy; public health unit region of residence (seven regions); pre-existing maternal health conditions (asthma, chronic hypertension, diabetes, heart disease, thyroid disease); parity (number of previous live and stillbirths: 0, 1 ≥ 2); and multiple birth (yes/no).

2.4. Statistical analysis

2.4.1. Temporal patterns in COVID-19 vaccine coverage among all pregnant individuals

We used heat maps to visually display calendar and gestational timing of COVID-19 vaccine doses received during pregnancy. Rates of COVID-19 vaccine coverage (≥1 dose of COVID-19 vaccine before or during pregnancy) among pregnant individuals—completed and ongoing pregnancies—were calculated by month. The denominator for each month was the number of individuals who were pregnant at any point during the month (i.e., any birth during the month or ongoing pregnancy as of the last day of the month). From April 1, 2021 to the end of the study—the time period reflecting widespread availability of COVID-19 vaccines to pregnant people—we further stratified monthly coverage rates by maternal age and neighborhood quintiles for household income and material deprivation. We quantified gradients in coverage over time across these characteristics using unadjusted rate differences, with corresponding 95% confidence intervals (CI), contrasting <25 years of age vs. ≥40, lowest neighborhood income vs. highest, and highest material deprivation vs. lowest.

2.4.2. Factors associated with COVID-19 vaccine series initiation during pregnancy

Among individuals who gave birth between April 1 and December 31, 2021 and had not received any vaccine doses prior to pregnancy, we computed unadjusted rates of COVID-19 vaccine series initiation during pregnancy by maternal sociodemographic factors, health behaviors, pre-existing health conditions, and pregnancy characteristics. Associations between these factors and vaccine series initiation were assessed using log Poisson generalized linear models with robust error estimation to produce rate ratios (RR) with 95% confidence intervals (CI). To compute rate differences (RD), we used a modified least squares approach with a robust variance estimator, implemented using the 'GLIMMIX' procedure in SAS Version 9.4 (SAS Institute Inc, Cary, NC). Adjusted models included maternal age (continuous), week of conception (categorical), neighborhood income quintile (quintiles 1–5), rural vs. urban residence, and public health unit region of residence. Multiple imputation was used to address missing covariate values (variables with missing information are shown in Table S2). We used a fully conditional specification to generate five multiple imputation datasets using the 'MI' procedure; these datasets were used in all regression models to produce coefficients and standard errors, which were combined using the 'MIANALYZE' procedure.

2.5. Ethical approval.

This study received ethical approval from the Children's Hospital of Eastern Ontario Research Ethics Board.

3. Results

There were 143,133 completed pregnancies and 78,057 ongoing pregnancies (still pregnant as of December 31, 2021 or birth record not yet transferred to the birth registry), for a total of 221,190 individuals who were pregnant during the study period (Fig. 1). Across the entire time period, 81,104 (36.7%) individuals received at least one dose of COVID-19 vaccine during pregnancy (Table S3). Fig. 2 displays the temporal and gestational timing of the first COVID-19 vaccination received during pregnancy (i.e., dose 1, dose 2, or dose 3). Following an initial cluster of vaccinations among pregnant individuals in January 2021, the most intense periods of vaccinations during pregnancy occurred from late April to early June 2021, after pregnancy was prioritized, and in December 2021, when all adults ≥18 years became eligible for a booster dose. Among completed pregnancies, the majority of first doses received during pregnancy (whether dose 1, dose 2, or dose 3) occurred in the second and third trimester, whereas among ongoing pregnancies, the largest number of first doses was administered at earlier gestational ages, especially during the first trimester (Figure S1).

3.1. Temporal patterns in COVID-19 vaccine coverage

Among all 221,190 individuals who were pregnant at any point between December 14, 2020 and December 31, 2021, vaccine coverage (≥1 dose before or during pregnancy) increased from 0.03% to 71.2% by December 2021 (Fig. 3 and Table S4). Among pregnant individuals in the month of December 2021, 2.8% had only received

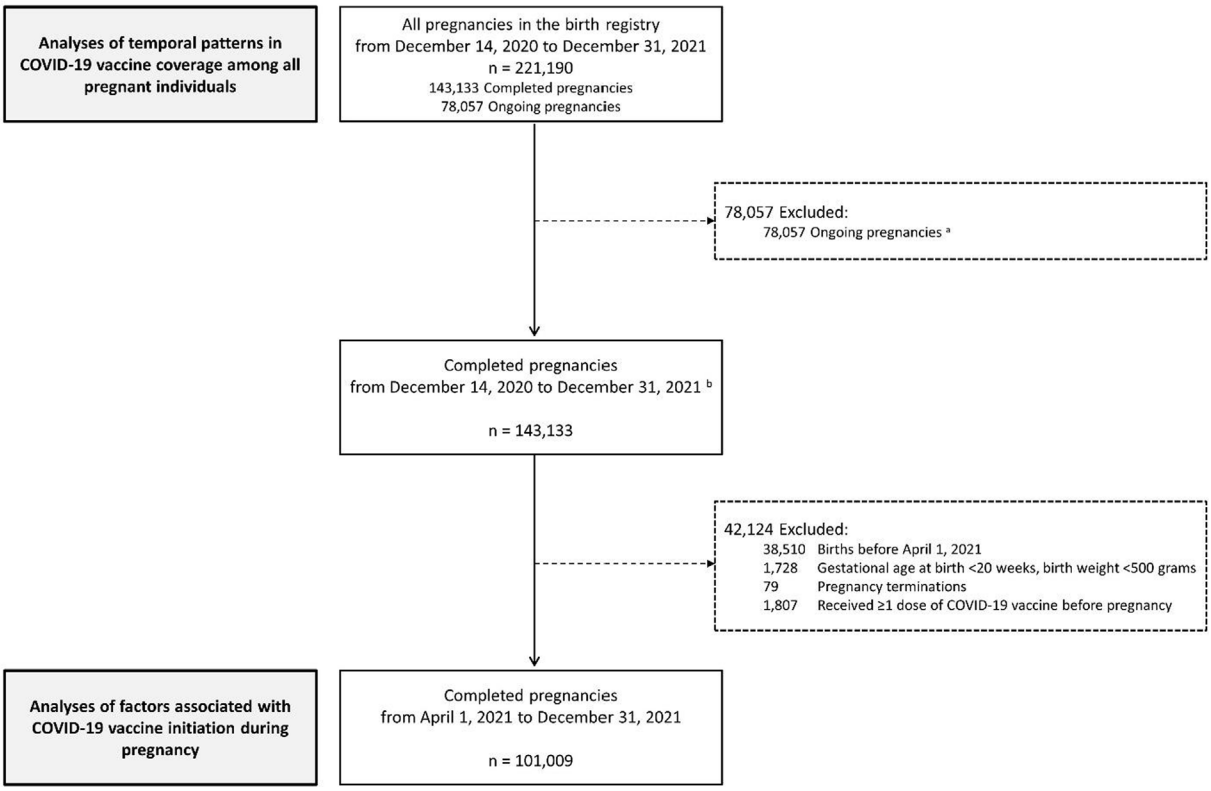


Fig. 1. Study flow diagram. [a]Ongoing pregnancies comprised those that were ongoing as of December 31, 2021 (n = 56,163) and those with an estimated date of birth before December 31, 2021, but the birth record had not yet been transferred to the birth registry (n = 21,894). [b]Births that already occurred and the birth record had been transferred to the birth registry.

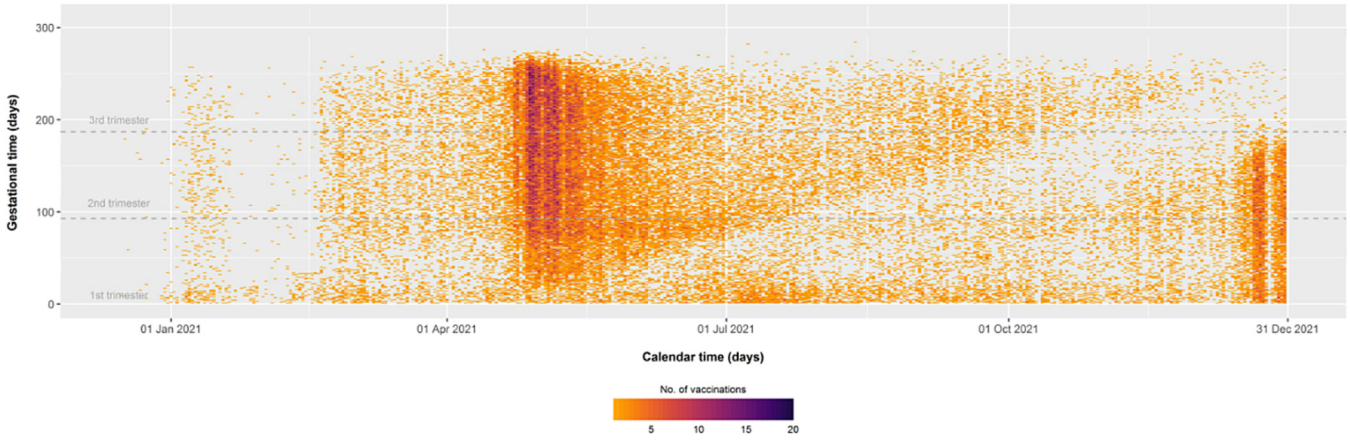


Fig. 2. Heat map of daily number of first COVID-19 vaccine doses administered during pregnancy by calendar time (x-axis) and gestational time (y-axis), December 14, 2020 to December 31, 2021 [a, b, c]

[a]Includes vaccinations administered during pregnancy among all pregnant individuals (i.e., completed pregnancies, as well as those that were still ongoing as of December 31, 2021; records with an estimated date of birth before December 31, 2021 for which the birth record had not yet been transferred to the birth registry were grouped with the completed pregnancies in the heat map). Individual heat maps for completed pregnancies and ongoing pregnancies can be found in Figure S1.[b]Heat map displays the first dose of COVID-19 vaccine that was received during pregnancy (i.e., dose 1, dose 2, or dose 3); 81,104 individuals received ≥1 dose of COVID-19 vaccine during pregnancy. Individual heat maps for each dose received during pregnancy can be found in Figure S1.[c]On December 14, 2020 (beginning of Ontario's COVID-19 vaccination program), pregnant people could be offered COVID-19 vaccination—with informed consent—if they were in an eligible early priority group, but otherwise it was initially not recommended during pregnancy. Pregnant people were prioritized within Ontario's vaccination program in late April 2021. On December 15, 2021, all adults over 18 years of age, including pregnant people, became eligible to receive a COVID-19 booster dose.

dose 1 by that point, 55.9% had received doses 1 and 2, and 12.5% had received three doses.

Between April and December 2021, large differences in vaccine coverage were noted by maternal age, neighborhood income quintile, and neighborhood quintile of material deprivation (Fig. 4). Among individuals who were pregnant in April 2021, coverage was initially 13 percentage points lower among those <25 years of age compared with those ≥40 years of age (5.1% vs. 18.3%, respectively; Fig. 4A and B, Table S5), but the gap increased to 26 percentage points in May. The difference in coverage between

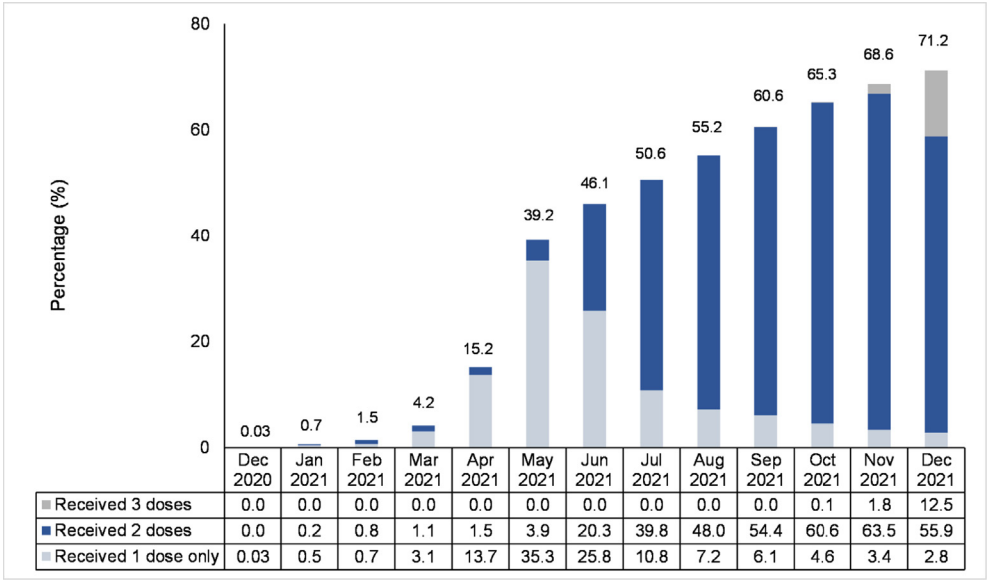


Fig. 3. Temporal trends in rates of COVID-19 vaccine coverage (≥1 dose of COVID-19 vaccine before or during pregnancy) among all pregnant individuals by month, December 14, 2020 to December 31, 2021 [a, b, c, d]

[a]Coverage was calculated among all completed and ongoing pregnancies in each calendar month (i.e., any birth during the month or ongoing pregnancy as of the last day of the month).[b]Doses received either before or during pregnancy.[c]Data for estimates displayed in plot can be found in Table S4.[d]On December 14, 2020 (beginning of Ontario's COVID-19 vaccination program), pregnant people could be offered COVID-19 vaccination—with informed consent—if they were in an eligible early priority group, but otherwise it was not recommended during pregnancy. Pregnant people were prioritized within Ontario's vaccination program in late April 2021. On December 15, 2021, all adults over 18 years of age, including pregnant people, became eligible to receive a COVID-19 booster dose.

these two age groups decreased over time after August, but remained 20 percentage points lower by December 2021 (53.1% vs. 73.5%, respectively). The differences between the lowest and highest quintiles of neighborhood income (Fig. 4C and D) and material deprivation (Fig. 4E and F) were less pronounced, and also decreased over time.

3.2. Factors associated with COVID-19 vaccine series initiation during pregnancy

Among 101,009 individuals who gave birth between April 1 and December 31, 2021, 45.7% of individuals initiated their COVID-19 vaccine series, but there was substantial variation by sociodemographic and pregnancy-related characteristics (Table 1). Across maternal age groups, vaccine initiation during pregnancy was lowest among individuals <25 years of age (24.8%), compared with those 30–34 years of age (50.2%); the corresponding adjusted RR (aRR) was 0.53 (95% CI 0.51–0.56) and was 21 percentage points lower (aRD −21.9, 95% CI −23.0 to −20.9). Vaccine initiation during pregnancy was also lower among smokers compared with non-smokers (26.4% vs. 47.1%; aRR 0.64, 95% CI 0.61–0.67; aRD −14.8, 95% CI −15.9 to −13.7), among those who reported substance use during pregnancy compared with non-use (29.2% vs. 46.6%; aRR 0.72, 95% CI 0.69–0.76; aRD −11.0, 95% CI −12.2 to −9.7), among those with no prenatal care visit in the first trimester compared with having a first trimester visit (35.4% vs. 46.4; aRR 0.80, 95% CI 0.77–0.84; aRD −8.8, 95% CI −10.0 to −7.6), and among individuals living in rural compared with urban areas (38.6% vs. 46.9%; aRR 0.86, 95% CI 0.83–0.88; aRD −6.6, 95% CI −7.4 to −5.7). Vaccine series initiation was lowest among those in the lowest neighborhood income quintile compared with the highest (37.3% vs. 54.1%; aRR 0.69, 95% CI 0.67–0.71; aRD −16.9, 95% CI: −17.9 to −15.9), and among individuals in the highest material deprivation quintile compared with the lowest (34.9% vs. 55.5%; aRR 0.70, 95% CI 0.67–0.73; aRD −15.6, 95% CI −17.0 to −14.3). Vaccine series initiation was marginally higher among those with a pre-existing medical condition compared with no pre-existing condition (50.3% vs. 45.2%, aRR 1.07, 95% CI 1.04–1.10; aRD 3.5, 95% CI 2.5 to 4.4) but there was no difference by maternal pre-pregnancy body mass index ≥30.0 kg/m^2, compared with <30.

4. Discussion

In this population-wide study of over 200,000 individuals who were pregnant during the first year of Ontario's COVID-19 vaccination program, coverage with at least one dose (before or during pregnancy) increased to 71.2% among those pregnant in December 2021—this included 12.5% that had received a third dose. Despite prioritization of pregnant individuals for vaccination in late April 2021 [22], coverage with at least one dose remained lower than in the general population of females aged 18–49 years, among whom it was approximately 88% by the end of 2021 (Figure S2). Gradients in 1-dose vaccine coverage among pregnant individuals across categories of maternal age, neighborhood income, and material deprivation decreased by the end of 2021, but did not disappear.

Lower vaccine coverage among pregnant individuals, compared with the general population of reproductive-age females, is a concern given the higher risk of adverse outcomes following COVID-19 during pregnancy [1,2]. Other countries have noted similar gaps early in their COVID-19 vaccination programs—by May 8, 2021, 16.3% of 135,968 pregnant individuals in seven U.S. states (Vaccine Safety Datalink sites) had received at least one dose of COVID-19 vaccine during pregnancy, and 11.1% had completed their primary series, while 24.9% of non-pregnant females of similar age had completed their primary series [16]. A population-based study in Scotland estimated that 32.3% of those who gave birth in October 2021 had received two doses of COVID-19 vaccine, whereas 77.4% of females 18–44 years in the general population had received two doses by that time [17]. In contrast, a population-based cohort study of 164,560 women who gave birth from May 2021 through May 2022 in Sweden and Norway found that vaccine uptake by pregnant women was comparable to vaccination rates in

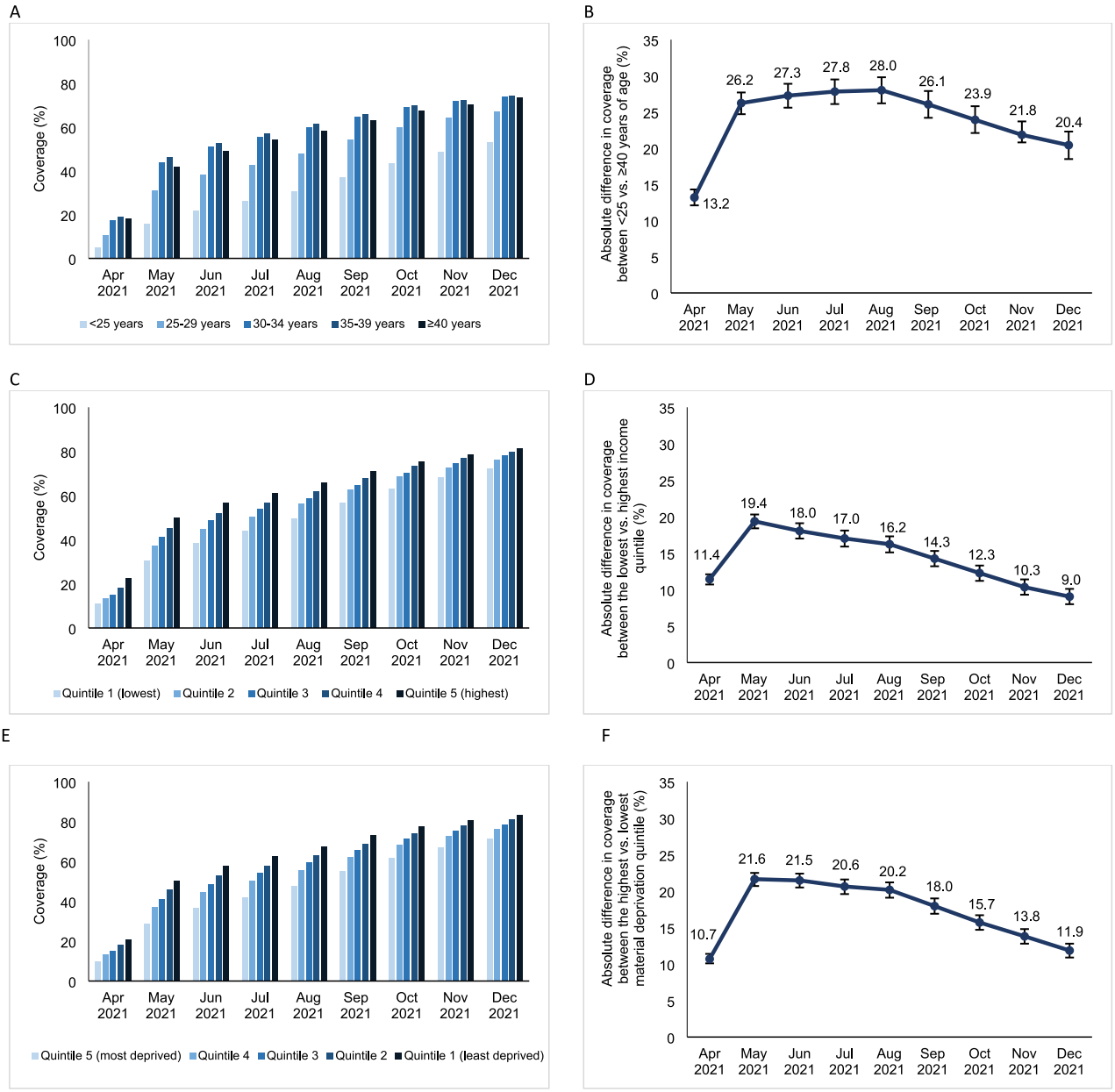


Fig. 4. Temporal trends in rates of COVID-19 vaccine coverage (≥1 dose of COVID-19 vaccine before or during pregnancy) among all pregnant individuals by month from April 1, 2021 to December 31, 2021, stratified by maternal age (A, B), neighborhood income quintile (C, D), and neighborhood quintile of material deprivation (E, F)
Panels A, C, and E display coverage estimates (≥1 dose of COVID-19 vaccine during pregnancy). Panels B, D, and F display the absolute differences in coverage between the lowest and highest category. Coverage was calculated among all completed and ongoing pregnancies in each calendar month (i.e., any birth during the month or ongoing pregnancy as of the last day of the month). Data for estimates displayed in plot can be found in Table S5.

the general female population of reproductive age [18]. It was reported that 78% and 87% of women giving birth in Sweden and Norway, respectively, were vaccinated with at least one dose of COVID-19 prior to delivery, which was similar to the overall vaccination coverage in these countries (i.e., 77% in Sweden, 85% in Norway) [18].

Several studies have sought to identify factors associated with COVID-19 vaccination during pregnancy—being younger, not having sufficient prenatal care, living in areas with higher socioeconomic deprivation, and being a smoker during pregnancy were among the factors found to be associated with lower likelihood of getting vaccinated against COVID-19 during pregnancy [16–18,27,28]. Our results are very comparable to these earlier findings. In addition, although obesity and chronic medical conditions are known risk factors for severe COVID-19 [29], we found that COVID-19 vaccine series initiation was not higher among those with a high pre-pregnancy body mass index and only marginally higher among pregnant individuals with pre-existing chronic medical conditions. Higher pre-pregnancy body mass index was found to be associated with lower uptake of COVID-19 vaccination during pregnancy in Sweden, but not Norway, and uptake was higher among those with pre-existing chronic medical conditions in both countries [18].

Unsurprisingly, the factors associated with COVID-19 vaccine series initiation in Ontario were also similar to those observed in Ontario during the 2009–2010 A/H1N1 influenza pandemic, when 42.6% of people who gave birth between November 2009 and April 2010 received the pandemic monovalent A/H1N1 influenza vaccine

Table 1
Factors associated with COVID-19 vaccine series initiation during pregnancy, among completed pregnancies from April 1, 2021 to December 31, 2021.

Characteristic	All completed pregnancies, April 1, 2021 to December 31, 2021		Received dose 1 of COVID-19 vaccine during pregnancy					
	N(101,009) [a]	%	Yes (n = 46,196)	Vaccine initiation rate per 100	Unadjusted rate ratio (95% CI)	Adjusted rate ratio(95% CI) [b]	Unadjusted rate difference per 100 (95% CI)	Adjusted rate difference per 100 (95% CI) [b]
Overall	101,009	100	46,196	45.7				
Maternal age (years)								
<25	8,214	8.1	2,040	24.8	0.49 (0.47 to 0.52)	0.53 (0.51 to 0.56)	−25.3 (−26.4 to −24.3)	−21.9 (−23.0 to −20.9)
25–29	24,291	24.0	9,290	38.2	0.76 (0.74 to 0.78)	0.80 (0.78 to 0.82)	−12.0 (−12.7 to −11.2)	−10.0 (−10.8 to −9.3)
30–34	40,480	40.1	20,324	50.2	1 (ref)	1 (ref)	0.0	0.0
35–39	23,035	22.8	12,177	52.9	1.05 (1.03 to 1.08)	1.02 (1.00 to 1.04)	2.7 (1.8 to 3.5)	1.3 (0.5 to 2.0)
≥40	4,989	4.9	2,365	47.4	0.94 (0.90 to 0.99)	0.92 (0.88 to 0.96)	−2.8 (−4.3 to −1.3)	−4.1 (−5.5 to −2.7)
Mean age (SD)	32 (4.9)	–	33 (4.4)	–	–	–	–	–
Parity								
0 (nulliparous)	43,933	43.5	21,181	48.2	0.99 (0.97 to 1.01)	1.05 (1.03 to 1.08)	−0.4 (−1.1 to 0.3)	2.4 (1.8 to 3.1)
1 (primiparous)	35,697	35.3	17,359	48.6	1 (ref)	1 (ref)	0.0	0.0
≥2 (multiparous)	21,379	21.2	7,656	35.8	0.74 (0.72 to 0.76)	0.72 (0.71 to 0.74)	−12.9 (−13.7 to −12.0)	−13.6 (−14.4 to −12.8)
Multiple birth								
No	99,503	98.5	45,485	45.7	1 (ref)	1 (ref)	0.0	0.0
Yes	1,506	1.5	711	47.2	1.03 (0.96 to 1.11)	0.95 (0.89 to 1.03)	1.5 (−1.0 to 4.0)	−2.1 (−4.5 to 0.3)
Any pre-existing maternal medical condition [c]								
No	89,657	88.8	40,491	45.2	1 (ref)	1 (ref)	0.0	0.0
Yes	11,352	11.2	5,705	50.3	1.11 (1.08 to 1.14)	1.07 (1.04 to 1.10)	5.1 (4.1 to 6.1)	3.5 (2.5 to 4.4)
Thyroid disease	5,998	5.9	3,213	53.6	1.18 (1.14 to 1.23)	1.11 (1.07 to 1.15)	8.3 (7.0 to 9.6)	5.4 (4.2 to 6.7)
Asthma	3,897	3.9	1,799	46.2	1.01 (0.96 to 1.06)	1.03 (0.98 to 1.08)	0.45 (−1.1 to 2.0)	1.5 (−0.03 to 3.0)
Diabetes	1,120	1.1	552	49.3	1.08 (0.99 to 1.17)	1.03 (0.94 to 1.12)	3.6 (0.6 to 6.5)	1.3 (−1.5 to 4.2)
Chronic hypertension	936	0.9	456	48.7	1.07 (0.97 to 1.17)	0.98 (0.89 to 1.07)	3.0 (−0.2 to 6.2)	−0.9 (−4.0 to 2.2)
Heart disease	124	0.1	65	52.4	1.15 (0.90 to 1.46)	1.09 (0.86 to 1.39)	6.7 (−2.1 to 15.5)	4.8 (−3.7 to 13.3)
Smoked during pregnancy								
Yes	6,518	6.5	1,721	26.4	0.56 (0.54 to 0.59)	0.64 (0.61 to 0.67)	−20.6 (−21.8 to −19.5)	−14.8 (−15.9 to −13.7)
No	94,491	93.5	44,475	47.1	1 (ref)	1 (ref)	0.0	0.0
Substance use during pregnancy [d]								
Yes	5,175	5.1	1,509	29.2	0.63 (0.60 to 0.66)	0.72 (0.69 to 0.76)	−17.3 (−18.6 to −16.1)	−11.0 (−12.2 to −9.7)
No	95,834	94.9	44,687	46.6	1 (ref)	1 (ref)	0.0	0.0
First prenatal care visit in the first trimester								
No	5,887	5.8	2,084	35.4	0.76 (0.73 to 0.80)	0.80 (0.77 to 0.84)	−11.1 (−12.3 to −9.8)	−8.8 (−10.0 to −7.6)
Yes	95,122	94.2	44,112	46.4	1 (ref)	1 (ref)	0.0	0.0
Maternal BMI (kg/m^2)								
≥30.0 (obese)	21,409	21.2	9,524	44.5	0.96 (0.94 to 0.99)	0.98 (0.96 to 1.01)	−1.7 (−2.5 to −0.8)	−0.7 (−1.5 to 0.04)
<30.0	79,600	78.8	36,672	46.1	1 (ref)	1 (ref)	0.0	0.0
Neighborhood median family income quintiles								
1 (Lowest)	20,700	20.5	7,716	37.3	0.69 (0.67 to 0.71)	0.69 (0.67 to 0.71)	−16.8 (−17.8 to −15.8)	−16.9 (−17.9 to −15.9)
2	20,471	20.3	8,748	42.7	0.79 (0.77 to 0.81)	0.81 (0.78 to 0.83)	−11.4 (−12.5 to −10.4)	−10.5 (−11.5 to −9.5)
3	21,581	21.4	9,899	45.9	0.85 (0.82 to 0.87)	0.87 (0.84 to 0.89)	−8.3 (−9.3 to −7.2)	−7.2 (−8.2 to −6.3)
4	21,372	21.2	10,691	50.0	0.92 (0.90 to 0.95)	0.94 (0.92 to 0.97)	−4.1 (−5.1 to −3.1)	−3.1 (−4.1 to −2.2)
5 (Highest)	16,885	16.7	9,142	54.1	1 (ref)	1 (ref)	0.0	0.0

Table 1 (*continued*)

Characteristic	All completed pregnancies, April 1, 2021 to December 31, 2021		Received dose 1 of COVID-19 vaccine during pregnancy					
	N(101,009) [a]	%	Yes (n = 46,196)	Vaccine initiation rate per 100	Unadjusted rate ratio (95% CI)	Adjusted rate ratio(95% CI) [b]	Unadjusted rate difference per 100 (95% CI)	Adjusted rate difference per 100 (95% CI) [b]
Rural residence								
No	86,419	85.6	40,568	46.9	1 (ref)	1 (ref)	0.0	0.0
Yes	14,590	14.4	5,628	38.6	0.82 (0.80 to 0.85)	0.86 (0.83 to 0.88)	−8.4 (−9.2 to −7.5)	−6.6 (−7.4 to −5.7)
Public health unit region of residence [e]								
South West	12,371	12.2	4,769	38.6	0.75 (0.72 to 0.78)	0.78 (0.76 to 0.81)	−12.9 (−14.1 to −11.8)	−10.8 (−11.9 to −9.7)
Central West	21,508	21.3	9,553	44.2	0.86 (0.84 to 0.89)	0.86 (0.83 to 0.88)	−7.1 (−8.1 to −6.2)	−7.4 (−8.4 to −6.5)
Central East	28,455	28.2	12,619	44.4	0.86 (0.84 to 0.88)	0.85 (0.82 to 0.87)	−7.2 (−8.1 to −6.3)	−7.9 (−8.8 to −7.0)
Greater Toronto Area	19,904	19.7	10,266	51.6	1 (ref)	1 (ref)	0.0	0.0
Eastern	13,610	13.5	6,925	50.9	0.99 (0.96 to 1.02)	1.00 (0.97 to 1.03)	−0.6 (−1.7 to 0.5)	0.08 (−1.0 to 1.2)
North West	1,700	1.7	709	41.7	0.81 (0.75 to 0.88)	0.92 (0.85 to 0.99)	−9.8 (−12.2 to −7.3)	−3.8 (−6.2 to −1.4)
North East	3,461	3.4	1,355	39.2	0.76 (0.72 to 0.80)	0.86 (0.81 to 0.91)	−12.6 (−14.4 to −10.8)	−6.8 (−8.6 to −5.0)
Marginalization Indices Residential instability quintile								
1 (least unstable)	20,305	20.1	9,433	46.5	1 (ref)	1 (ref)	0.0	0.0
2	18,981	18.8	8,796	46.3	1.00 (0.97 to 1.03)	1.01 (0.98 to 1.04)	−0.2 (−1.2 to 0.8)	0.2 (−0.8 to 1.1)
3	19,248	19.1	8,841	45.9	0.99 (0.96 to 1.02)	1.05 (1.02 to 1.08)	−0.6 (−1.5 to 0.5)	2.5 (1.5 to 3.4)
4	18,932	18.7	8,431	44.5	0.96 (0.93 to 0.99)	1.11 (1.07 to 1.14)	−1.9 (−2.9 to −0.9)	5.2 (4.2 to 6.3)
5 (most unstable)	23,543	23.3	10,695	45.4	0.98 (0.95 to 1.01)	1.18 (1.14 to 1.22)	−1.1 (−2.0 to −0.1)	7.9 (6.7 to 9.0)
Material deprivation quintile								
1 (least deprived)	22,946	22.7	12,728	55.5	1 (ref)	1 (ref)	0.0	0.0
2	20,529	20.3	10,206	49.7	0.90 (0.87 to 0.92)	0.95 (0.93 to 0.98)	−5.7 (−6.6 to −4.7)	−2.9 (−3.8 to −1.9)
3	18,710	18.5	8,438	45.1	0.81 (0.79 to 0.84)	0.89 (0.86 to 0.91)	−10.4 (−11.3 to −9.4)	−6.4 (−7.5 to −5.3)
4	18,388	18.2	7,695	41.9	0.76 (0.74 to 0.78)	0.83 (0.80 to 0.86)	−13.5 (−14.5 to −12.5)	−9.4 (−10.6 to −8.2)
5 (most deprived)	20,436	20.2	7,129	34.9	0.63 (0.61 to 0.65)	0.70 (0.67 to 0.73)	−20.6 (−21.5 to −19.7)	−15.6 (−17.0 to −14.3)
Dependency quintile								
1 (least dependent)	33,054	32.7	15,943	48.2	1 (ref)	1 (ref)	0.0	0.0
2	21,133	20.9	9,655	45.7	0.95 (0.92 to 0.97)	1.00 (0.97 to 1.02)	−2.6 (−3.5 to −1.7)	−0.3 (−1.1 to 0.5)
3	17,021	16.9	7,728	45.4	0.94 (0.91 to 0.96)	1.00 (0.97 to 1.02)	−3.0 (−3.9 to −2.0)	−0.3 (−1.2 to 0.7)
4	15,492	15.3	6,762	43.7	0.91 (0.88 to 0.93)	0.97 (0.95 to 1.00)	−4.5 (−5.5 to −3.5)	−1.1 (−2.1 to −0.2)
5 (most dependent)	14,309	14.2	6,108	42.7	0.88 (0.86 to 0.91)	0.98 (0.95 to 1.01)	−5.6 (−6.7 to −4.6)	−0.9 (−1.9 to 0.2)
Ethnic concentration quintile								
1 (lowest concentration)	14,458	14.3	5,997	41.5	1 (ref)	1 (ref)	0.0	0.0
2	16,410	16.2	7,433	45.3	1.10 (1.06 to 1.13)	1.01 (0.97 to 1.05)	4.0 (2.9 to 5.1)	0.4 (−0.7 to 1.5)
3	18,268	18.1	8,940	48.9	1.18 (1.14 to 1.22)	1.01 (0.97 to 1.04)	7.6 (6.5 to 8.7)	0.5 (−0.7 to 1.7)
4	22,102	21.9	10,725	48.5	1.17 (1.13 to 1.21)	0.97 (0.94 to 1.01)	7.2 (6.1 to 8.2)	−1.3 (−2.4 to −0.1)
5 (highest concentration)	29,771	29.5	13,101	44.0	1.06 (1.03 to 1.10)	0.95 (0.91 to 0.98)	2.6 (1.6 to 3.6)	−2.9 (−4.1 to −1.7)

Abbreviations: BMI, body mass index.

[a] Counts and column percentages from imputation dataset #1 were used for variables with missing information (see Table S2).

[b] Models were adjusted for maternal age, estimated date of conception, neighborhood income quintile, rural residence, and public health unit region.

[c] Composite of: asthma, chronic hypertension, diabetes, heart disease, thyroid disease. Sum of individual conditions does not equal the total number of individuals with any condition, as categories were not mutually exclusive.

[d] Self-reported cannabis, opioid or alcohol use during pregnancy.

[e] Public health units within each region are provided in Table S1.

during pregnancy [30]. While lower maternal age, smoking, and lower neighborhood income were associated with lower vaccine initiation during the A/H1N1 influenza pandemic [30], the associations were generally smaller in magnitude than what we observed in the COVID-19 pandemic in Ontario. Other studies from the 2009 A/H1N1 influenza pandemic documented significantly lower vaccination rates among pregnant individuals who smoked during pregnancy [31] and lived in rural settings [32], and higher vaccination rates among those with chronic medical conditions [31,32]. These findings are also congruent with patterns generally observed for seasonal influenza and pertussis vaccine coverage during pregnancy, which also vary considerably between individuals of higher and lower socioeconomic status [33,34].

When COVID-19 vaccination was initially recommended for pregnant individuals, it was unclear what the uptake would be, especially amid initial concerns about the use of novel vaccine technologies during pregnancy [35]. Surveys of pregnant people reported decreased intention to become vaccinated, largely due to concerns about potential harm to the fetus [36]; this also continues to be the most commonly-cited reason for low uptake of influenza vaccine during pregnancy [33]. Although substantial evidence on safety of COVID-19 vaccination during pregnancy has accumulated [9–15], our results suggest that there is a subgroup of individuals who are less likely to get vaccinated during pregnancy. Previous studies in the general population have shown that lower socioeconomic status (e.g., lower level of education, poverty, lower household income) are risk factors for COVID-19 infection, confirmed diagnosis, and death, and that socioeconomic determinants play an important role in COVID-19 outcomes [37–40]. Moreover, socioeconomic status is also associated with inequalities in perinatal health; for example, lower socioeconomic position is a risk factor for adverse pregnancy outcomes such as low birth weight and preterm birth [41,42]. Thus, to prevent severe COVID-19-related outcomes among higher-risk subgroups of pregnant individuals and decrease disparities in vaccine coverage, interventions specifically targeted for these subgroups may be required.

Strengths of this study include the large birth population and deterministically linked population-based data sources within a publicly-funded health care system providing ascertainment of COVID-19 vaccinations received during pregnancy and comprehensive sociodemographic and pregnancy-related information. Study limitations include potential underestimation of the number of pregnancies in the later months of the study period, due to lag times in receiving completed birth records from some hospitals and because not all pregnant people undergo prenatal screening [25], which we relied on to identify ongoing pregnancies. Although we had information on a wide range of sociodemographic, health-related, and pregnancy-related factors, decisions about vaccination during pregnancy are likely influenced by other factors that we could not measure, such as frequency and method (virtual versus in-person) of prenatal care visits, or individual knowledge, attitudes, and beliefs. Our assessment of factors associated with COVID-19 vaccine series initiation during pregnancy—which relied on completed pregnancies after April 1, 2021—likely predominantly reflects associations with vaccination during the second and third trimesters of pregnancy; it is possible that some patterns of association may differ for early pregnancy vaccination.

5. Conclusions

Our population-based study in Ontario, Canada found that COVID-19 vaccine coverage with at least one dose remained substantially lower among pregnant individuals than among similarly-aged females in the general population in 2021. Although disparities in coverage across categories of maternal age and socioeconomic status showed some diminution by the end of 2021, at the population level, persistent gaps could translate into thousands fewer pregnant individuals in specific subgroups not having been vaccinated. We identified several sociodemographic, health-related, and pregnancy-related factors that were associated with initiating COVID-19 vaccination during pregnancy—combined with the growing body of evidence supporting safety of COVID-19 vaccination during pregnancy, these findings can help inform public health strategies to increase COVID-19 vaccine acceptance and coverage in the pregnant population.

6. Funding

This study was supported by funding from the Public Health Agency of Canada, through the Vaccine Surveillance Reference Group and the COVID-19 Immunity Task Force; S. Håberg was partly supported by the Research Council of Norway (project number, 324312) and through its Centers of Excellence funding scheme (project number, 262700) and by NordForsk (project number, 105545).

7. Disclaimer

The study sponsors did not participate in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication. Parts of this material are based on data and information compiled and provided by BORN Ontario and the Ontario Ministry of Health; however, the analyses, conclusions, opinions and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

8. Data sharing

The dataset from this study is held securely by BORN Ontario. Although the dataset cannot be made publicly available, the analytic code may be available on request.

Data availability

The dataset from this study is held securely by BORN Ontario. Although the dataset cannot be made publicly available, the analytic code may be available on request.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: K. Wilson is CEO of CANImmunize Inc, which hosts a national digital immunization record, and is a member of the independent data safety board for the Medicago COVID-19 vaccine trial; there were no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

The authors thank the Ontario Ministry of Health for granting access to the COVaxON database and the Public Health Case and Contact Management Solution (CCM). The authors also thank maternal-newborn hospitals and midwifery practice groups in Ontario for providing maternal-newborn data to BORN Ontario.

Finally, the authors thank BORN Ontario staff for their assistance with data extraction, linkage, code review, and results review.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2023.01.073.

References

[1] Centers for Disease Control and Prevention. Precautions for people with certain medical conditions. Accessed January 24, 2023. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html.

[2] Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: The INTERCOVID Multinational Cohort Study. JAMA Pediatr 2021;175:817–26.

[3] Zavala E, Krubiner CB, Jaffe EF, Nicklin A, Gur-Arie R, Wonodi C, et al. Global disparities in public health guidance for the use of COVID-19 vaccines in pregnancy. BMJ Glob Health 2022;7:e007730.

[4] Dagan N, Barda N, Biron-Shental T, Makov-Assif M, Key C, Kohane IS, et al. Effectiveness of the BNT162b2 mRNA COVID-19 vaccine in pregnancy. Nat Med 2021;27:1693–5.

[5] Magnus MC, Håberg SE, Carlsen EØ, Kwong JC, Buchan SA, Fell DB. Pregnancy status at the time of COVID-19 vaccination and incidence of SARS-CoV-2 infection. Clin Infect Dis 2023;76:57–65.

[6] Halasa NB, Olson SM, Staat MA, Newhams MM, Price AM, Pannaraj PS, et al. Maternal vaccination and risk of hospitalization for Covid-19 among infants. N Engl J Med 2022;387:109–19.

[7] Carlsen EØ, Magnus MC, Oakley L, Fell DB, Greve-Isdahl M, Kinge JM, et al. Association of COVID-19 vaccination during pregnancy with incidence of SARS-CoV-2 infection in infants. JAMA Intern Med 2022;182:825–31.

[8] Jorgensen SCJ, Hernandez A, Fell DB, Austin PC, D'Souza R, Guttmann A, et al. Effectiveness of maternal mRNA COVID-19 vaccination during pregnancy against Delta and Omicron SARS-CoV-2 infection and hospitalization in infants: a test-negative design study. BMJ 2023. In press.

[9] Kharbanda EO, Haapala J, DeSilva M, Vazquez-Benitez G, Vesco KK, Naleway AL, et al. Spontaneous abortion following COVID-19 vaccination during pregnancy. JAMA 2021;326:1629–31.

[10] Magnus MC, Gjessing HK, Eide HN, Wilcox AJ, Fell DB, Håberg SE. Covid-19 vaccination during pregnancy and first-trimester miscarriage. N Engl J Med 2021;385:2008–10.

[11] Lipkind HS, Vazquez-Benitez G, DeSilva M, Vesco KK, Ackerman-Banks C, Zhu J, et al. Receipt of COVID-19 vaccine during pregnancy and preterm or small-for-gestational-age at birth - Eight integrated health care organizations, United States, December 15, 2020-July 22, 2021. MMWR Morb Mortal Wkly Rep 2022;71:26–30.

[12] Magnus MC, Örtqvist AK, Dahlqwist E, Ljung R, Skår F, Oakley L, et al. Association of SARS-CoV-2 vaccination during pregnancy with pregnancy outcomes. JAMA 2022;327:1469–77.

[13] Fell DB, Dhinsa T, Alton GD, Török E, Dimanlig-Cruz S, Regan AK, et al. Association of COVID-19 vaccination in pregnancy with adverse peripartum outcomes. JAMA 2022;327:1478–87.

[14] Fell DB, Dimanlig-Cruz S, Regan AK, Haberg S, Gravel CA, Oakley L, et al. Risk of preterm birth, small for gestational age at birth, and stillbirth after covid-19 vaccination during pregnancy: population based retrospective cohort study. BMJ 2022;378:e071416.

[15] Ibroci E, Liu X, Lieb W, Jessel R, Gigase FAJ, Chung K, et al. Impact of prenatal COVID-19 vaccination on delivery and neonatal outcomes: Results from a New York City cohort. Vaccine 2023;41:649–56.

[16] Razzaghi H, Meghani M, Pingali C, Crane B, Naleway A, Weintraub E, et al. COVID-19 vaccination coverage among pregnant women during pregnancy - Eight integrated health care organizations, United States, December 14, 2020-May 8, 2021. MMWR Morb Mortal Wkly Rep 2021;70:895–9.

[17] Stock SJ, Carruthers J, Calvert C, Denny C, Donaghy J, Goulding A, et al. SARS-CoV-2 infection and COVID-19 vaccination rates in pregnant women in Scotland. Nat Med 2022;28:504–12.

[18] Örtqvist AK, Dahlqwist E, Magnus MC, Ljung R, Jonsson J, Aronsson B, et al. COVID-19 vaccination in pregnant women in Sweden and Norway. Vaccine 2022;40:4686–92.

[19] National Advisory Committee on Immunization. Recommendations on the use of COVID-19 vaccines [2020-12-12]. Accessed January 24, 2023. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines/december-12-2020.html#a7.

[20] Heath PT, Le Doare K, Khalil A. Inclusion of pregnant women in COVID-19 vaccine development. Lancet Infect Dis 2020;20:1007–8.

[21] National Advisory Committee on Immunization. Recommendations on the use of COVID-19 vaccines [2021-05-28]. Accessed January 24, 2023. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines/may-28-2021.html.

[22] COVID-19 vaccination during pregnancy in Ontario - Report #6: December 14, 2020 to September 30, 2022 Accessed February 6, 2023. https://www.bornontario.ca/en/whats-happening/resources/Documents/COVID-19-Vaccination-during-pregnancy-in-Ontario_Report6.pdf, ; 2020.

[23] Ontario Ministry of Health. All Ontarians 18+ eligible for COVID-19 booster appointments at three-month interval. Accessed January 24, 2023. https://news.ontario.ca/en/release/1001352/all-ontarians-18-eligible-for-covid-19-booster-appointments-at-three-month-interval.

[24] Murphy MSQ, Fell DB, Sprague AE, Corsi DJ, Dougan S, Dunn SI, et al. Data Resource Profile: Better Outcomes Registry & Network (BORN) Ontario. Int J Epidemiol 2021;50:1416–1417h.

[25] Huang T, Dougan S, Walker M, Armour CM, Okun N. Trends in the use of prenatal testing services for fetal aneuploidy in Ontario: a descriptive study. CMAJ Open 2018;6:E436–44.

[26] Public Health Ontario. Ontario Marginalization Index (ON-Marg). Accessed January 24, 2023. https://www.publichealthontario.ca/en/data-and-analysis/health-equity/ontario-marginalization-index.

[27] Wainstock T, Yoles I, Sergienko R, Sheiner E. Prenatal maternal COVID-19 vaccination and pregnancy outcomes. Vaccine 2021;39:6037–40.

[28] Blakeway H, Prasad S, Kalafat E, Heath PT, Ladhani SN, Le Doare K, et al. COVID-19 vaccination during pregnancy: coverage and safety. Am J Obstet Gynecol 2022;226:236.e1–236.e14.

[29] Booth A, Reed AB, Ponzo S, Yassaee A, Aral M, Plans D, et al. Population risk factors for severe disease and mortality in COVID-19: A global systematic review and meta-analysis. PLoS One 2021;16:e0247461.

[30] Liu N, Sprague AE, Yasseen ASI, Fell DB, Wen SW, Smith GN, et al. Vaccination patterns in pregnant women during the 2009 H1N1 influenza pandemic: a population-based study in Ontario. Canada Can J Public Health 2012;103:353–8.

[31] Sebghati M, Khalil A. Uptake of vaccination in pregnancy. Best Pract Res Clin Obstet Gynaecol 2021;76:53–65.

[32] Vilca LM, Verma A, Buckeridge D, Campins M. A population-based analysis of predictors of influenza vaccination uptake in pregnant women: The effect of gestational and calendar time. Prev Med 2017;99:111–7.

[33] Yuen CYS, Tarrant M. Determinants of uptake of influenza vaccination among pregnant women - a systematic review. Vaccine 2014;32:4602–13.

[34] Gkentzi D, Katsakiori P, Marangos M, Hsia Y, Amirthalingam G, Heath PT, et al. Maternal vaccination against pertussis: a systematic review of the recent literature. Arch Dis Child - Fetal Neonatal Ed 2017;102:F456–63.

[35] Iacobucci G. Covid-19 and pregnancy: vaccine hesitancy and how to overcome it. BMJ 2021;375:n2862.

[36] Skjefte M, Ngirbabul M, Akeju O, Escudero D, Hernandez-Diaz S, Wyszynski DF, et al. COVID-19 vaccine acceptance among pregnant women and mothers of young children: results of a survey in 16 countries. Eur J Epidemiol 2021;36:197–211.

[37] Khanijahani A, Iezadi S, Gholipour K, Azami-Aghdash S, Naghibi D. A systematic review of racial/ethnic and socioeconomic disparities in COVID-19. Int J Equity Health 2021;20:248.

[38] Mena GE, Martinez PP, Mahmud AS, Marquet PA, Buckee CO, Santillana M. Socioeconomic status determines COVID-19 incidence and related mortality in Santiago, Chile. Science 2021:372.

[39] van Ingen T, Brown KA, Buchan SA, Akingbola S, Daneman N, Warren CM, et al. Neighbourhood-level socio-demographic characteristics and risk of COVID-19 incidence and mortality in Ontario, Canada: A population-based study. PLoS One 2022;17:e0276507.

[40] Wang L, Calzavara A, Baral S, Smylie J, Chan AK, Sander B, et al. Differential patterns by area-level social determinants of health in COVID-19 related mortality and non-COVID-19 mortality: a population-based study of 11.8 million people in Ontario, Canada. Clin Infect Dis 2022;ciac850.

[41] Sow M, Raynault M-F, De Spiegelaere M. Associations between socioeconomic status and pregnancy outcomes: a greater magnitude of inequalities in perinatal health in Montreal than in Brussels. BMC Public Health 2022;22:829.

[42] Simoncic V, Deguen S, Enaux C, Vandentorren S, Kihal-Talantikite W. A Comprehensive review on social inequalities and pregnancy outcome-identification of relevant pathways and mechanisms. Int J Environ Res Public Health 2022;19:16592.

Canadian Immunization Conference 2023 Conférence canadienne sur l'immunisation

Passive surveillance monitoring: what role does it play with respect to the pregnant population in Canada?

Gaston De Serres, MD, PhD

Institut national de santé Publique du Québec

Université Laval

26 April 2023

Canadian Immunization Conference 2023 Conférence canadienne sur l'immunisation

SPEAKER NAME: Gaston De Serres

I have no conflict of interest to declare in relation to this presentation.

Objectives

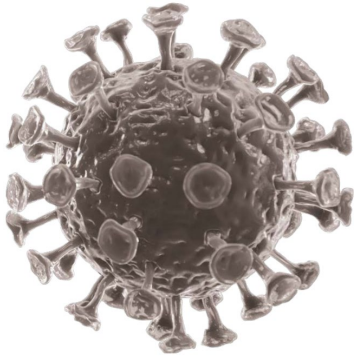
Identify relative strengths and weaknesses of the passive vaccine safety surveillance in Canada for the pregnant population

1. Summarize the current Canadian landscape for vaccine safety passive surveillance during pregnancy
2. Propose enhancements to the current system and approaches to address gaps in vaccine safety surveillance during pregnancy in Canada

COVID-19 VACCINES:

SAFETY SURVEILLANCE MANUAL

MODULE: SAFETY SURVEILLANCE OF COVID-19 VACCINES IN PREGNANT AND BREASTFEEDING WOMEN



World Health Organization

https://apps.who.int/iris/bitstream/handle/10665/342538/WHO-MHP-RPQ-PVG-2021.1-eng.pdf?sequence=1&isAllowed=y

Key points

- Passive surveillance approaches need to take into consideration three potential scenarios:
  - maternal AEFIs not directly related to the pregnancy;
  - obstetric adverse events believed to be linked to COVID-19 vaccination during pregnancy; and
  - adverse events in the fetus (in the case of pregnancy loss), neonate, infant or child suspected to be associated with COVID-19 vaccination during pregnancy.
  - late/delayed adverse event in a child believed to be linked to COVID-19 vaccination during pregnancy.

https://apps.who.int/iris/bitstream/handle/10665/342538/WHO-MHP-RPQ-PVG-2021.1-eng.pdf?sequence=1&isAllowed=y

Maternal and fetal/newborn/infant health needs to be monitored. Exposure to a vaccine can potentially affect both maternal and fetal health. The fetus can be affected:

- indirectly, if an event experienced by the mother, e.g., anaphylaxis, seizures with high fever, has an impact on her health and safety during pregnancy; or
- directly, e.g., theoretical risks of live-attenuated vaccines to the fetus.

Therefore, systematic **reporting of both maternal and neonatal/infant adverse events following immunization (AEFIs)** must be incorporated into surveillance systems.

https://apps.who.int/iris/bitstream/handle/10665/342538/WHO-MHP-RPQ-PVG-2021.1-eng.pdf?sequence=1&isAllowed=y

Table 1: Suggested adverse events of special interest following exposure to COVID-19 vaccines in pregnancy. For standard case definition see the Brighton Collaboration website[16,17,18]

Maternal AESI
— Maternal death
— Maternal hospitalization
— Maternal thrombotic events
— Hypertensive disorders of pregnancy
— Miscarriage/spontaneous abortion
— Stillbirth
— Preterm birth
— Neonatal death
— Microcephaly
— Major congenital anomalies
— Infant death

https://apps.who.int/iris/bitstream/handle/10665/342538/WHO-MHP-RPQ-PVG-2021.1-eng.pdf?sequence=1&isAllowed=y

TABLE 1

Gestational time periods relevant to teratogenesis[6,8]

Period	Gestational age, wk[a]	Events	Potential teratogenic effects
Before implantation	0-2	Fertilization, cell division, blastocyst formation, implantation	Injury to a large number of cells → spontaneous abortion OR injury to a small number of cells → survival without abnormalities
Embryonic	2-9	Organogenesis	Malformations, altered function
			Onset for major defects in organs
			Central nervous system: 3 wk
			Heart: 3 wk
			Sensory organs (eyes, ears): 4 wk
			Limbs: 4 wk
			Palate: 6 wk
			Teeth: 6 wk
			Genitalia: 7 wk
Fetal	9-term	Growth, differentiation, maturation	Small for gestational age/intrauterine growth restriction, fetal death, minor malformations and altered function
			Continued susceptibility period for minor defects in organs
			Central nervous system: to end of period
			Sensory organs: to end of period
			Palate: through 9 wk
			Teeth: to end of period
			Genitalia: to end of period

[a] Gestational age values, as presented, specifically reference embryonic age and not gestational age as determined from last menstrual period dating.

Bednarczyk. Influenza vaccine safety for fetus and neonate. Am J Obstet Gynecol 2012.

Role of Vaccine Safety Passive Surveillance

- To identify safety issues and generate early signals for additionnal investigations as passive surveillance lacks the controls necessary to estimate if the risk is increased compared to unvaccinated individuals

Reported side effects following COVID-19 vaccination in Canada

97,597,702

Total doses administered up to and including March 3, 2023

https://health-infobase.canada.ca/covid-19/vaccine-safety/#a5

Figure 3. Number of adverse event reports received by age group 2023 (n=54,569)

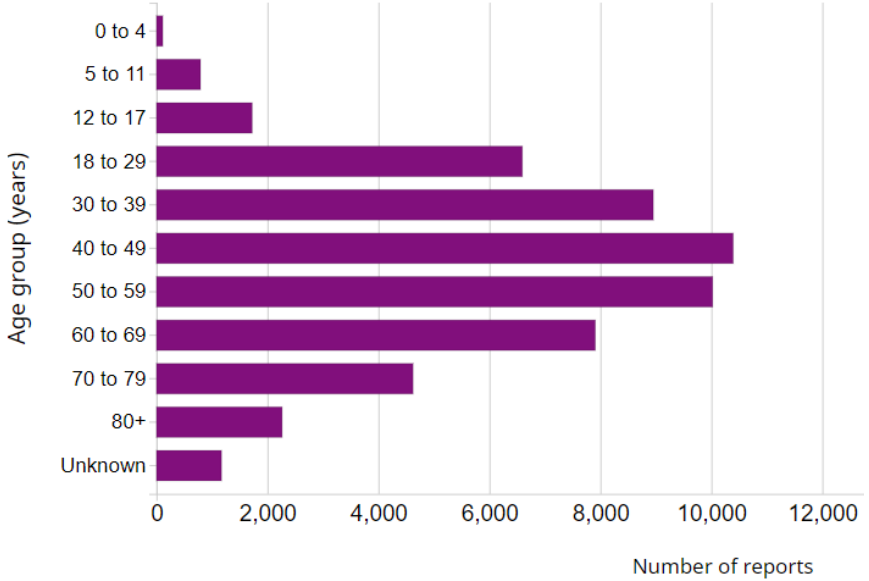
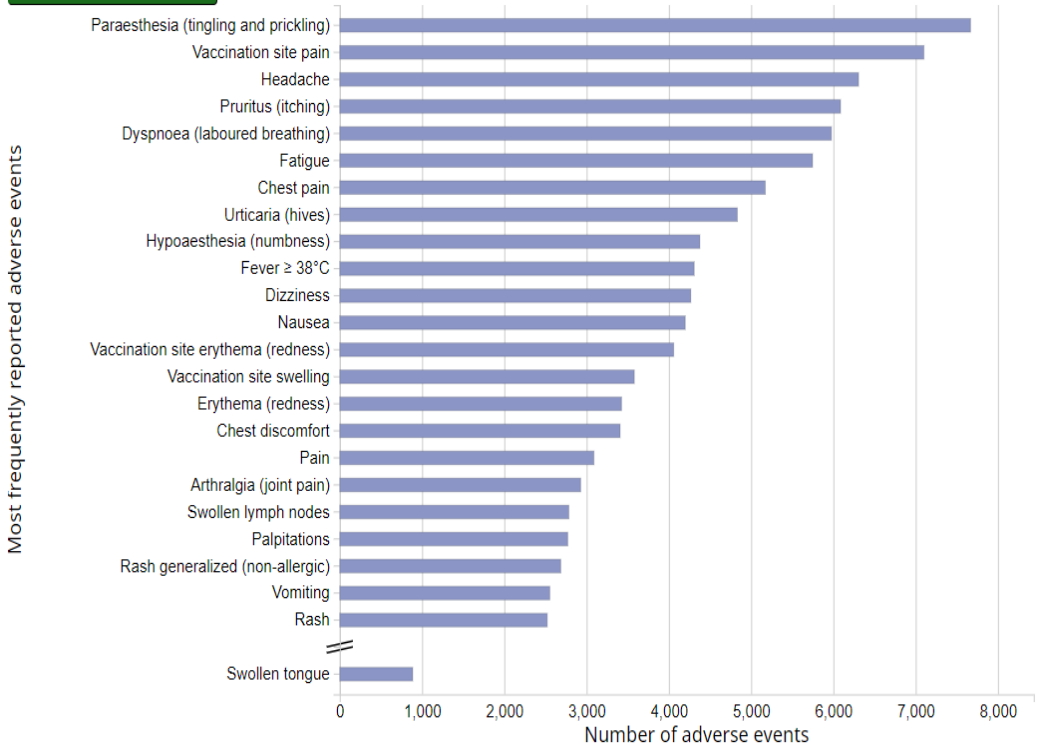


Figure 4. Number of the most frequently reported adverse events by vaccine type (Total) up to and including March 3, 2023 (n=138,141)

Show more adverse events

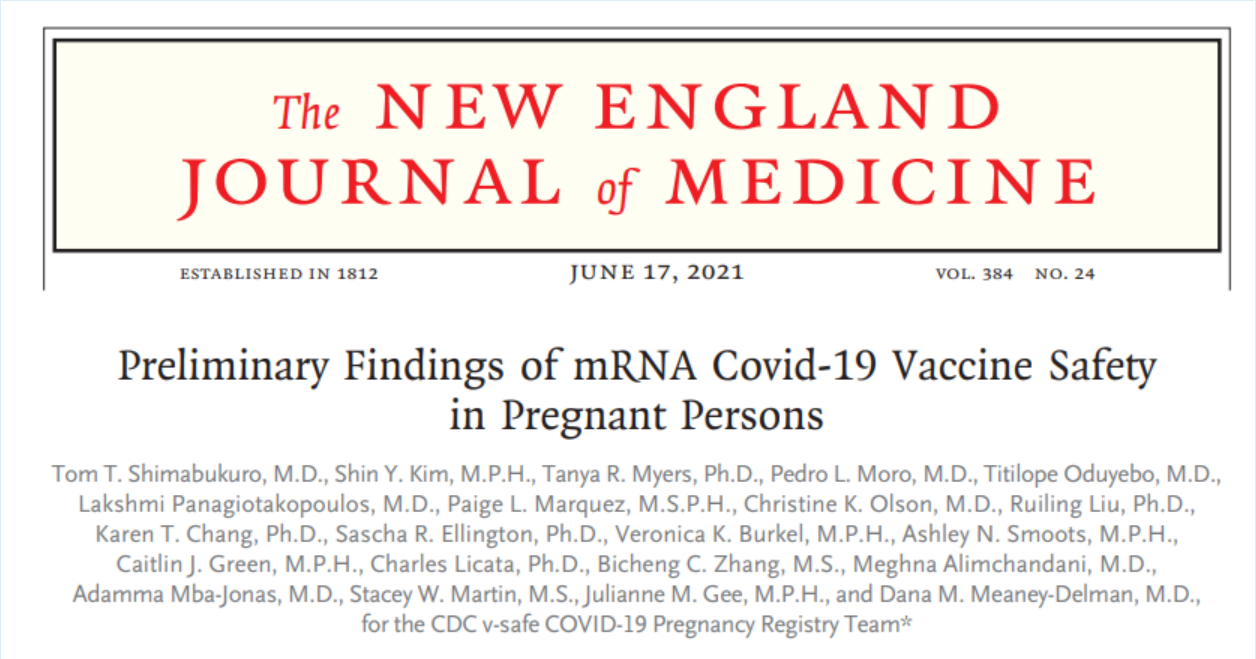


Adverse events during pregnancy

Table 1. Count of reported adverse events of special interest by vaccine type (Total) up to and including March 3, 2023 (n=5,913).

AESI Category	AESI	Total number of events
Pregnancy outcomes[3]	Fetal growth restriction	5
	Spontaneous abortion	87
	Subtotal	92

https://health-infobase.canada.ca/covid-19/vaccine-safety/#a5



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 17, 2021 VOL. 384 NO. 24

Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons

Tom T. Shimabukuro, M.D., Shin Y. Kim, M.P.H., Tanya R. Myers, Ph.D., Pedro L. Moro, M.D., Titilope Oduyebo, M.D., Lakshmi Panagiotakopoulos, M.D., Paige L. Marquez, M.S.P.H., Christine K. Olson, M.D., Ruiling Liu, Ph.D., Karen T. Chang, Ph.D., Sascha R. Ellington, Ph.D., Veronica K. Burkel, M.P.H., Ashley N. Smoots, M.P.H., Caitlin J. Green, M.P.H., Charles Licata, Ph.D., Bicheng C. Zhang, M.S., Meghna Alimchandani, M.D., Adamma Mba-Jonas, M.D., Stacey W. Martin, M.S., Julianne M. Gee, M.P.H., and Dana M. Meaney-Delman, M.D., for the CDC v-safe COVID-19 Pregnancy Registry Team*

https://www.nejm.org/doi/pdf/10.1056/NEJMoa2104983?articleTools=true

ADVERSE-EVENT FINDINGS ON THE VAERS

During the analysis period, the VAERS received and processed 221 reports involving Covid-19 vaccination among pregnant persons; 155 (70.1%) involved nonpregnancy-specific adverse events, and 66 (29.9%) involved pregnancy- or neonatal-specific adverse events (Table S4). The most frequently reported pregnancy-related adverse events were spontaneous abortion (46 cases; 37 in the first trimester, 2 in the second trimester, and 7 in which the trimester was unknown or not reported), followed by stillbirth, premature rupture of membranes, and vaginal bleeding, with 3 reports for each. No congenital anomalies were reported to the VAERS, a requirement under the EUAs.

https://www.nejm.org/doi/full/10.1056/nejmoa2104983

Trimester of pregnancy at time of vaccination in completed weeks[†]	**163**
First (0–13 weeks)	81 (49.7)
Second (14–27 weeks)	53 (32.5)
Third (28+ weeks)	29 (17.8)
Vaccine brand (%)	
Pfizer-BioNTech	130 (58.8)
Moderna	90 (40.7)
Most frequently reported nonpregnancy-specific adverse events (%)[‡]	**155 (70.1)**
Fatigue	44
Headache	43
Chills	30
Pain in extremity	27
Nausea	25
Pain	21
Fever	18
Injection site pain	17
Dizziness	17
Injection site erythema	11
Pregnancy- or neonatal- specific conditions (%)	**66 (29.9)**
Miscarriage[§]	46
Stillbirth	3
Premature rupture of membranes	3
Vaginal bleeding	3
Fetal hydrops	2
Preterm delivery	2
Neonatal death in 22-week preterm birth[‖]	1
Other[¶]	6

https://www.nejm.org/doi/suppl/10.1056/NEJMoa2104983/suppl_file/nejmoa2104983_appendix.pdf

European Journal of Clinical Pharmacology
https://doi.org/10.1007/s00228-023-03482-8

RESEARCH

Safety of COVID-19 vaccines in pregnancy: a VAERS based analysis

Greta Santi Laurini[1] · Nicola Montanaro[2] · Domenico Motola[1]

Received: 27 September 2022 / Accepted: 18 March 2023
© The Author(s) 2023

Abstract

Purpose Since vaccination against COVID-19 is recommended in pregnant people, we aimed to provide further evidence on the safety profile of COVID-19 vaccines in pregnancy.

Methods Data on COVID-19 vaccines adverse events following immunizations (AEFIs) in pregnant people were retrieved from the open-access Vaccine Adverse Event Reporting System (VAERS) from December 2020 to April 2022.

Results From December 2020 to April 1, 2022, a total of 4,869 reports involving pregnant women at COVID-19 vaccination were reported to VAERS. Among vaccines recipients, most belonged to the age group between 30 and 39 years old (3,029; 62.21%) and nearly half experienced an adverse event within 48 h of immunization (2,344; 48.14%). Overall, 21,816 suspected adverse reactions associated with COVID-19 vaccines were reported, and for as many as 80.43% of patients, they were described as non-serious. Most reactions occurred after administration of the mRNA-1273 (53.34%) and the BNT162b2 (40.68%) vaccines, while only a small proportion were related to the Johnson & Johnson's vaccine (5.69%). The most common non-pregnancy specific adverse events were headache (482; 2.21%), fatigue (472; 2.16%), and pyrexia (436; 2.00%), while adverse pregnancy outcomes with the highest reporting rate were abortions spontaneous (762; 3.49%), and vaginal haemorrhage (229; 1.05%).

Conclusion This post-marketing survey on VAERS data have provided updated evidence on the safety of COVID-19 vaccines during pregnancy, thus supporting clinicians in recommending maternal immunization.

Of all **4,869** reports involving pregnant women at COVID-19 vaccination, just 43 stated the stage of pregnancy.

Table 2 Most reported non-pregnancy-specific adverse event in VAERS

Non-pregnancy-specific Adverse Events	Events Reported	%[a]
Headache	482	2.21
Fatigue	472	2.16
Pyrexia	436	2.00
Chills	396	1.82
Pain in extremity	383	1.76
Pain	344	1.58
Nausea	320	1.47
Dizziness	228	1.05
Myalgia	198	0.91
COVID-19	188	0.86
Vomiting	173	0.79
SARS-CoV-2 test positive	172	0.79
Injection site pain	150	0.69
Vaccination site pain	110	0.50
Dyspnoea	110	0.50
Arthralgia	109	0.50
Malaise	105	0.48

European Journal of Clinical Pharmacology
https://doi.org/10.1007/s00228-023-03482-8

Table 3 Most reported pregnancy-specific adverse event in VAERS

Pregnancy-specific Adverse Events	Events Reported	%[a]
Abortion spontaneous	762	3.49
Vaginal haemorrhage	229	1.05
Delivery	197	0.90
Ultrasound antenatal screen abnormal	150	0.69
Caesarean section	127	0.58
Foetal death	106	0.49
Foetal heart rate abnormal	94	0.43
Uterine dilation and curettage	92	0.42
Premature labour	89	0.41
Premature delivery	88	0.40
Ultrasound foetal abnormal	76	0.35
Induced labour	61	0.35
Pre-eclampsia	61	0.28
Stillbirth	56	0.28

[a]The percentages refer to the total number of AEs reported in the VAERS database

European Journal of Clinical Pharmacology
https://doi.org/10.1007/s00228-023-03482-8

the pregnancy. Under-reporting, on the other hand, which is the main limitation VAERS is subject to, is expected to be very low because the data were collected during the most intensive vaccine safety monitoring effort in U.S. history, and especially because reporting of serious adverse events in pregnancy by health professionals is required by the CDC.

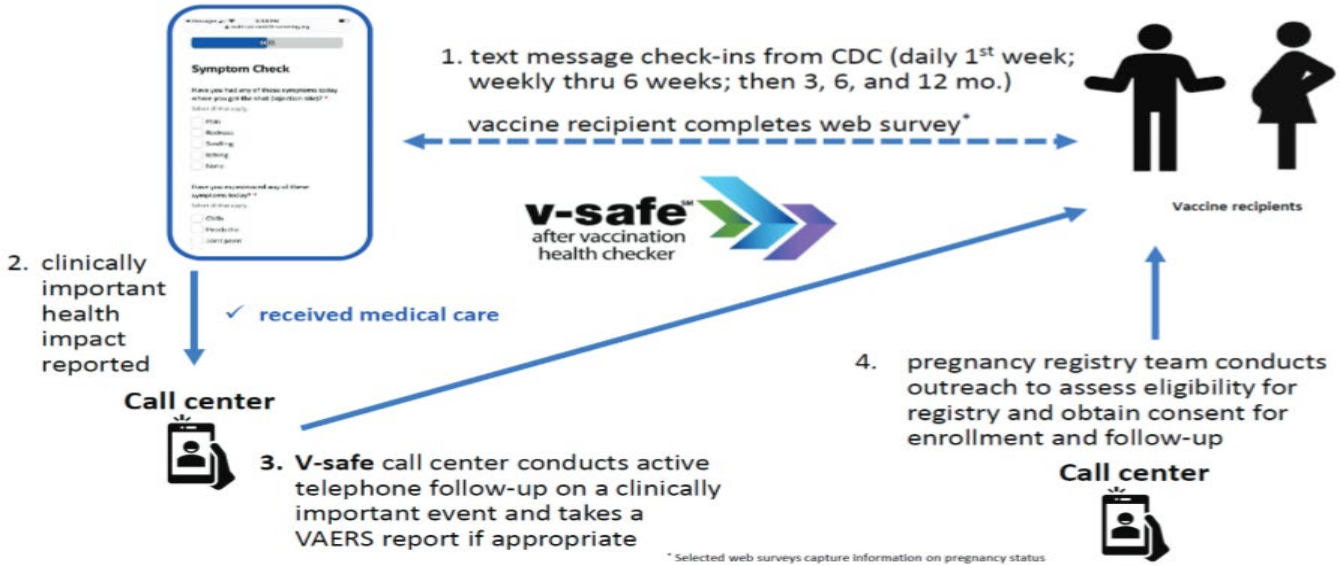
European Journal of Clinical Pharmacology
https://doi.org/10.1007/s00228-023-03482-8

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Receipt of mRNA Covid-19 Vaccines and Risk of Spontaneous Abortion

Zauche LH et al **DOI: 10.1056/NEJMc2113891**



V-safe enrollees are asked to complete daily surveys for the first 7 days after vaccination, then weekly through 6 weeks post-vaccination and then at 3, 6, and 12 months.

Table 1. Risk of Spontaneous Abortion among Participants in the v-safe Covid-19 Vaccine Pregnancy Registry, December 14, 2020, through July 19, 2021.

Gestational Age	Participants at Risk	Participants Who Reported Spontaneous Abortion	Week-Specific Risk	Cumulative Risk
	number of persons		*percent*	*percent (95% CI)*
6 to <7 weeks	904	15	1.7	1.7 (0.8–2.5)
7 to <8 weeks	982	18	1.8	3.5 (2.3–4.6)
8 to <9 weeks	1032	37	3.6	6.9 (5.4–8.5)
9 to <10 weeks	1087	39	3.6	10.3 (8.4–12.0)
10 to <11 weeks	1118	19	1.7	11.8 (9.9–13.7)
11 to <12 weeks	1184	12	1.0	12.7 (10.7–14.6)
12 to <13 weeks	1274	9	0.7	13.3 (11.3–15.2)
13 to <14 weeks	1394	5	0.4	13.6 (11.6–15.6)
14 to <15 weeks	1534	0	0	13.6 (11.6–15.6)
15 to <16 weeks	1632	2	0.1	13.7 (11.7–15.7)
16 to <17 weeks	1742	2	0.1	13.8 (11.8–15.8)
17 to <18 weeks	1848	2	0.1	13.9 (11.9–15.9)
18 to <19 weeks	1941	3	0.2	14.0 (12.0–16.0)
19 to <20 weeks	2052	2	0.1	14.1 (12.1–16.1)

Zauche LH et al **DOI: 10.1056/NEJMc2113891**

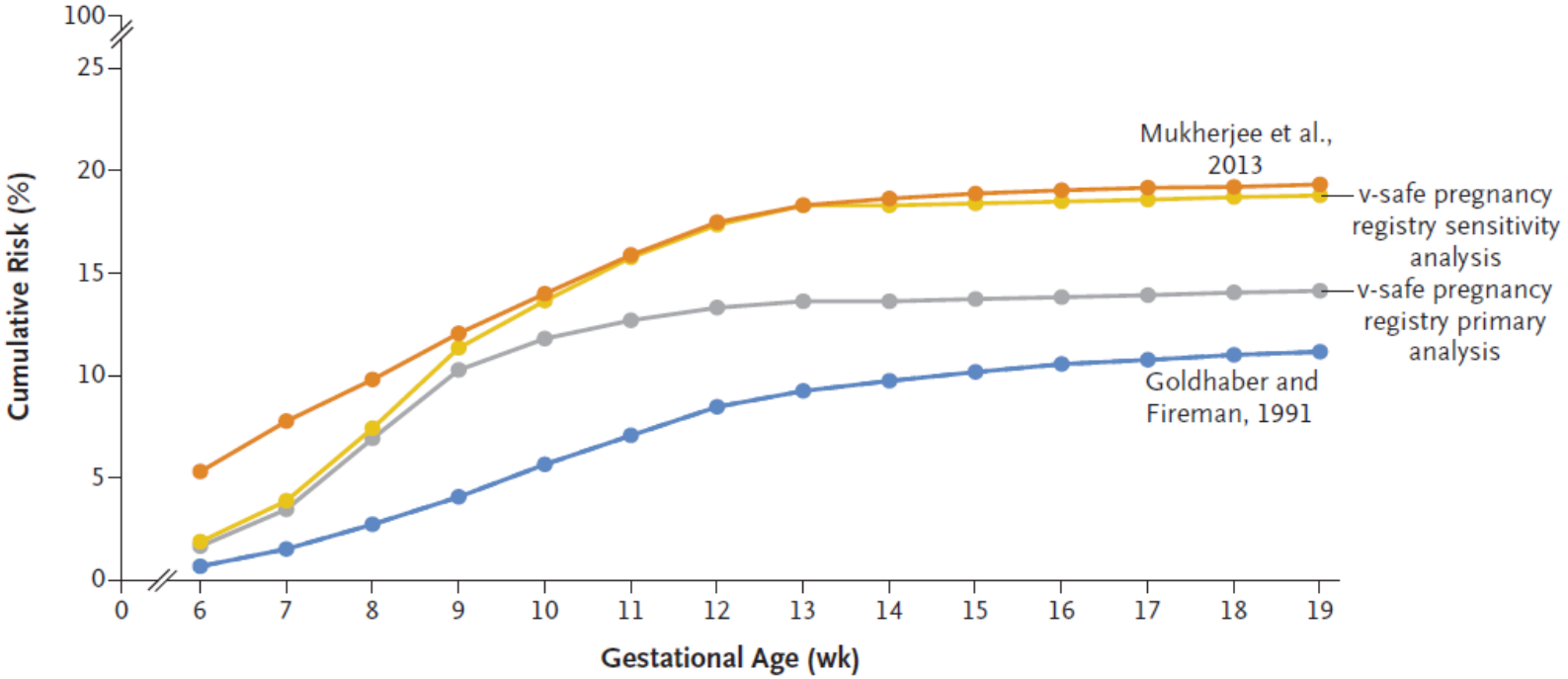


Figure 1. Cumulative Risk of Spontaneous Abortion in the v-safe Covid-19 Vaccine Pregnancy Registry and in Two Historical Cohorts.

Data from Mukherjee[2] were presented as race-specific rates and are provided here for White women to maximize comparability with the v-safe pregnancy registry.

Zauche LH et al DOI: 10.1056/NEJMc2113891

ansm
Agence nationale de sécurité du médicament et des produits de santé

Enquête de Pharmacovigilance sur les effets indésirables des vaccins COVID-19 chez les femmes enceintes et allaitantes - Période du 03/12/2021 au 21/04/2022 (31/05/2022)

Enquête de Pharmacovigilance sur les effets indésirables des vaccins COVID-19 chez les femmes enceintes et allaitantes - Focus n°1 : Analyse des cas de contractions utérines post-vaccination Covid-19 chez les femmes enceintes - période du 08/10/2020 au 06/01/2022 (21/01/2022)

Enquête de Pharmacovigilance sur les effets indésirables des vaccins COVID-19 chez les femmes enceintes et allaitantes - Focus n°2 : Vaccination Covid-19 et Procréation Médicale Assistée (PMA) - période du 08/10/2020 au 19/02/2022 (04/03/2022)

Canadian r l'immunisation

Enquête de Pharmacovigilance sur les effets indésirables des vaccins Covid19 chez les femmes enceintes et allaitantes

Rapport N°10

03/12/2021 au 21/04/2022

CRPV de Lyon - CRPV de Toulouse

2. Vaccin Comirnaty® Pfizer-BioNTech

Pour le vaccin Comirnaty®, **599** notifications d'effets indésirables ont été enregistrées dans la BNPV dont **107 nouveaux cas**. Au total **923** effets indésirables ont été listés.

a. Effets indésirables sur le déroulement de la grossesse (interruptions de grossesse, …) (n=271 EI listés)

Sur les 599 notifications d'effets indésirables avec le vaccin Comirnaty®, 256 soit 42,7 % étaient des interruptions de grossesse (228 fausses couches, 20 morts *in utero* et 8 grossesses extra-utérines). Pour certains cas, plusieurs effets indésirables ont été listés.

Le délai moyen d'apparition était de 23 jours après la vaccination….
Parmi les 228 FCS, 112 soit 49,1 % sont survenues dans les 2 semaines suivant la vaccination.

b. Effets indésirables chez le fœtus/nouveau-né (n=73 EIs listés)

- **Pathologies (n=34 EIs listés) :**

10 nouveaux cas sur la période.

Certains effets indésirables graves d'intérêt soumis à discussion sont décrits ci-dessous.

F 25-30 ans, D2 à 27 SA, ATCD non connus. Rupture de la membrane amniotique à J+2 post D2 et **naissance prématurée** à 35 SA.

F 30-35 ans, sans ATCD, D1 entre 0 et 4 SA. **Rupture prématurée des membranes** à 26 SA ayant nécessité une césarienne en urgence avec naissance prématurée à 27 SA + 2 à plus de 5 mois post-vaccination.

F 35-40 ans, ATCD non connus, R1 à 37 SA. **Rupture des membranes** à 37+4 SA dans un contexte d'état grippal à J+3 post-vaccination. Accouchement par voie basse sans complications à 37+6 SA.

F 25-30 ans, ATCD : sleeve gastrectomie, 2 FCS à 6 et 8 SA. R1 à 22 SA. Survenue de gastralgies h+17 post-vaccination ayant conduit à une hospitalisation. **Naissance prématurée à 23 SA,** après rupture spontanée des membranes accompagnée de métrorragies, d'un enfant de 620 g né vivant puis décédé à 40 minutes.

F 30-35 ans, sans ATCD, D2 à 26 SA. **Naissance prématurée** à J+2 post-vaccination. Dossier succinct.

Tableau 4. Effets indésirables chez la mère

SOC	EI cumulés d'effets indésirables chez la mère		
	EI non graves	EI graves	Total
Troubles généraux et anomalies au site d'administration	109	20	129
Affections du système nerveux	63	25	88
Affections gravidiques, puerpérales et périnatales	13	54	67
Affections gastro-intestinales	43	9	52
Affections des organes de reproduction et du sein	15	19	34
Affections musculosquelettiques et du tissu conjonctif	29	3	32
Affections de la peau et du tissu sous-cutané	18	2	20
Affections respiratoires, thoraciques et médiastinales	11	9	20
Affections vasculaires	9	10	19
Infections et infestations	10	6	16
Affections cardiaques	8	7	15
Affections hématologiques et du système lymphatique	8	3	11
Actes médicaux et chirurgicaux	0	9	9
Affections de l'oreille et du labyrinthe	5	4	9
Affections du système immunitaire	8	1	9
Investigations	7	2	9
Affections psychiatriques	6	2	8
Affections congénitales, familiales et génétiques	0	7	7
Affections oculaires	3	4	7
Affections du rein et des voies urinaires	2	3	5
Affections endocriniennes	1	3	4
Affections hépatobiliaires	1	2	3
Lésions, intoxications et complications d'interventions	1	2	3
Troubles du métabolisme et de la nutrition	2	0	2
Tumeurs bénignes, malignes et non précisées (incl kystes et polypes)	0	1	1
Total	372	207	579

Methodological issues related to passive surveillance in pregnant women

- Reporting bias for events occurring long after vaccination
- Identifying a signal for frequent events

Detection of increased risk for frequent pregnancy outcomes

Although it is generally understood that very large populations are needed to detect an increase in adverse events after immunization that are rare (e.g., Guillain-Barré Syndrome, which has a risk of approximately 1 per 1 million influenza vaccine doses), it is less well recognized that when the outcome of interest is frequent among nonvaccinated individuals, large populations are then also needed to detect vaccine-associated risks that are several thousand times greater than 1 per 1 million doses (e.g., 1 per 200 or 1 per 500 doses).

De Serres & Skowronski *Am J Epidemiol.* 2017;185(9):860–862

Detection of increased risk for frequent pregnancy outcomes

For example, without vaccination, the baseline frequency of low birth weight (<2,500 g) is approximately 7%, that of premature birth is 9%, and that of miscarriage is 15%. An additional risk of 1 child with a low birth weight, 1 preterm birth, or 1 miscarriage for every 200 vaccinated pregnant women is likely to be considered an unacceptable vaccine-associated risk for most mothers or obstetricians. However, this meaningful absolute increase in risk of 0.5% translates into minuscule relative risks that study investigators are required to measure (i.e., for an increase in low birth weight from 7% to 7.5%, relative risk = 1.07; for an increase in preterm birth from 9% to 9.5%, relative risk = 1.06; and for an increase in miscarriage from 15% to 15.5%, relative risk = 1.03), with very important sample size implications.

De Serres & Skowronski *Am J Epidemiol.* 2017;185(9):860–862

dienne sur l'immunisation

Low birth weight

Premature birth

Miscarriages

Table 1. Sample Size Requirements for 80% Statistical Power and α of 0.05 Given Specified Baseline Risk, Vaccine Coverage, and Assumed Absolute Risk Increase

Vaccine Coverage	Baseline Risk					
	5%	7%	9%	11%	13%	15%
	Absolute Risk Increase of 1 per 200 Vaccine Doses					
50%	62,461	84,438	105,410	125,378	144,342	162,300
30%	75,696	101,799	126,707	150,418	172,933	194,252
	Absolute Risk Increase of 1 per 500 Vaccine Doses					
50%	379,870	517,696	649,243	774,511	893,500	1,006,210
30%	455,582	619,512	775,966	924,945	1,066,449	1,200,478

De Serres & Skowronski *Am J Epidemiol.* 2017;185(9):860–862

Birth cohort in Canada ~ 370,000

Conclusion

- Passive surveillance results for pregnant women should be presented separately and according to WHO standards
- Passive surveillance has a role but it is limited
- Studies comparing large number of vaccinated and unvaccinated pregnant women are required to obtain robust results about the safety of maternal immunization for the most significant outcomes

Vaccination des personnes enceintes contre la COVID-19 et l’influenza

Marilou Kiely, Ella Diendere et Geneviève Martel

CIQ 2025-03-13

Sécurité

- Révision des articles publiés dans l'avis du CCNI pour identifier les données sur la vaccination au 1er trimestre (CCNI_2023)
- Mise à jour de la littérature (en cours)
- Projet québécois sur l'évaluation de la sécurité de la vaccination COVID-19 en cours de grossesse

Fardeau

- Revue de littérature pour les recommandations intérimaires sur les mesures de prévention en milieu de travail pour les travailleuses enceintes ou qui allaitent (INSPQ)
  - MAJ données jusqu'à 2022 publiée en 2023 (INSPQ_2023)
  - MAJ données 2022-2024 (publication à venir)
- Révision (sommaire) des articles publiés dans l'avis du CCNI pour identifier les données sur le fardeau de l'influenza 1er trimestre (CCNI_2023)
- Recommandations comités d'experts

Sécurité vaccin influenza

- 1 revue systématique + 37 études décrites dans l'avis du CCNI

Études	Personnes vaccinées au 1er trimestre
12 études avec analyse du risque suivant la vaccination au 1er trimestre	>45 000 personnes vaccinées
11 études avec personnes vaccinées au 1er trimestre, mais sans analyse de risque par trimestre	>20 000 personnes vaccinées
14 études sans personnes vaccinées au 1er trimestre ou sans information	NA

Sécurité vaccin influenza

- Revue systématique Wolfe *et al.*, 2023 Wolfe_2023
  - Méta-analyse réalisée seulement pour prématurité, avortement spontanés et faible poids pour l'âge gestationnel.
  - Pour vaccination 1er trimestre – seulement pour prématurité

Issues évaluées	Nb études incluses	aHR (IC à 95 %) tous trimestres	aHR (IC à 95 %) 1er trimestre
Prématurité	5 études avec contrôle confusion + biais temps immortel (>66 749 vaccinées)	1.08 (0.89; 1.30)	
Prématurité	6 études avec contrôle confusion (>19 135 vaccinées)		1.05 (0.92; 1.20)

Sécurité vaccin influenza

- Revue systématique Wolfe *et al.*, 2023 Wolfe_2023
  - Autres résultats pertinent pour la vaccination au 1er trimestre (étude non incluse dans la méta-analyse)

Issues évaluées	Nb études incluses	aRR (IC à 95 %) 1er trimestre
Mortinaissance (Speake 2020	1 étude de cohorte avec consideration du biais du temps immortel (2391 vaccinées)	1.18 (0.64; 2.18)
Anomalies congénitales (Mohammed 2020, Louik 2016)	2 études avec ajustement pour confusion (856 vaccinées)	0.33 (0.04; 2.73) 1.01 (0.85; 1.21)
SAE (Nordin 2013)	1 études avec ajustement pour confusion (21 553)	Medically attended events 0.97 (0.53;1.78) Thrombocytopenia 0.56 (0.22;1.39) Acute neurologic event 0.92 (0.54;1.6)

Sécurité vaccin influenza

- Revue systématique Wolfe *et al.*, 2023 Wolfe_2023
- Conclusions de l'étude:
  - Vaccination against seasonal influenza during pregnancy is not associated with significant safety issues (evidence of very low certainty)
  - A small but non-significant association with an increased risk of premature birth was found in a meta-analysis of studies that account for immortal time bias
  - There is limited evidence regarding the safety of administration of influenza vaccine in the first trimester, specifically.

Sécurité des vaccins contre la COVID-19 chez les personnes enceintes au Québec: une étude de cohorte rétrospective populationnelle basée sur des données clinico- administratives

Contexte au début de l’étude

- **Personnes enceintes :** population vulnérable avec un risque plus élevé de complications COVID-19
- **Afin de prévenir les formes graves et les complications :** adoption de la vaccination contre la COVID-19 pendant la grossesse dans de nombreux pays dont le Canada
- **Efficacité du vaccin chez les personnes enceintes :** démontrée par des études observationnelles
- **Jusque là:** données rassurantes concernant la sécurité des vaccins COVID-19 au cours de la grossesse
- **Preuves toutefois limitées et inquiétudes encore persistantes :** nécessité d’une surveillance continue des personnes enceintes vaccinées à grande échelle - personnes vaccinées à différents stades de la grossesse

Objectif de l’étude

Évaluer l'association entre la vaccination contre la COVID-19 à différents stades de la grossesse et le risque de complications maternelles et néonatales, chez les personnes enceintes au Québec

Méthologie

Devis	Étude de cohorte rétrospective populationnelle auprès des personnes enceintes ayant accouché dans un Centre hospitalier entre le 1er mai 2021 et le 30 juin 2023
Exposition	Au moins une dose de vaccin à ARNm contre la COVID-19 en cours de grossesse
Comparateur	Aucune dose de vaccin à ARNm contre la COVID-19 en cours de grossesse
Issues	**Issues néonatales :** Mortinaissance, Faible poids de naissance, Faible poids pour l'âge gestationnel, Naissance prématurée/très prématurée, Admission du nouveau-né aux soins intensifs (toute indication) et Issue composite de morbidité néonatale. **Issues maternelles :** Hémorragie primaire du post-partum, Chorioamniotite, Accouchement par césarienne et Admission de la mère aux soins intensifs (toute indication)
Sources de données	1) MED-ECHO, 2) bd labos prélèvements, 3) Registre de vaccination du Québec (RVQ) et 4) SISMACQ
Exclusions	Non appariées au RVQ, grossesses multiples ou plus d'un accouchement pendant la période, âge à l'accouchement < 15 ans ou ≥ 50 ans, âge gestationnel < 20 semaines, début grossesse < 42 semaines+6 jours à la fin de l'étude, vaccin non ARNm reçu.

Méthodologie

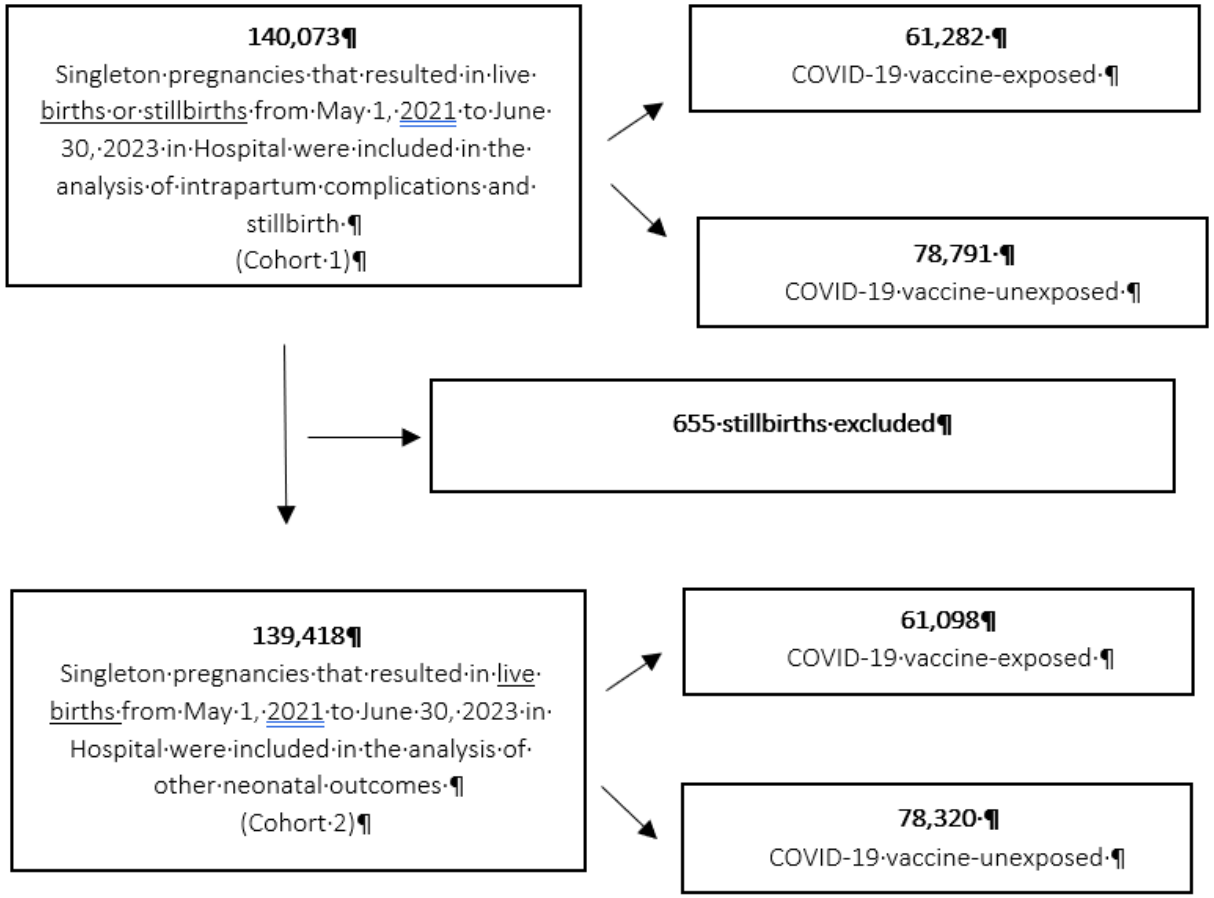
- **Variables de confusion :**

Age de la mère, sexe du bébé, conditions médicales préexistantes, vaccination contre la coqueluche durant la grossesse, infection par le SRAS-CoV-2 durant la grossesse, zone de résidence, mois et année de la conception, indices de défavorisation matérielle et sociale.

- **Analyses statistiques**
  - **Score de propension:** pondération par l'inverse de la probabilité d'être exposé
  - **Modèle de régression:**
    - Régression de Poisson robuste
    - Régression des risques proportionnels de Cox - Tenir compte de la vaccination qui varie dans le temps

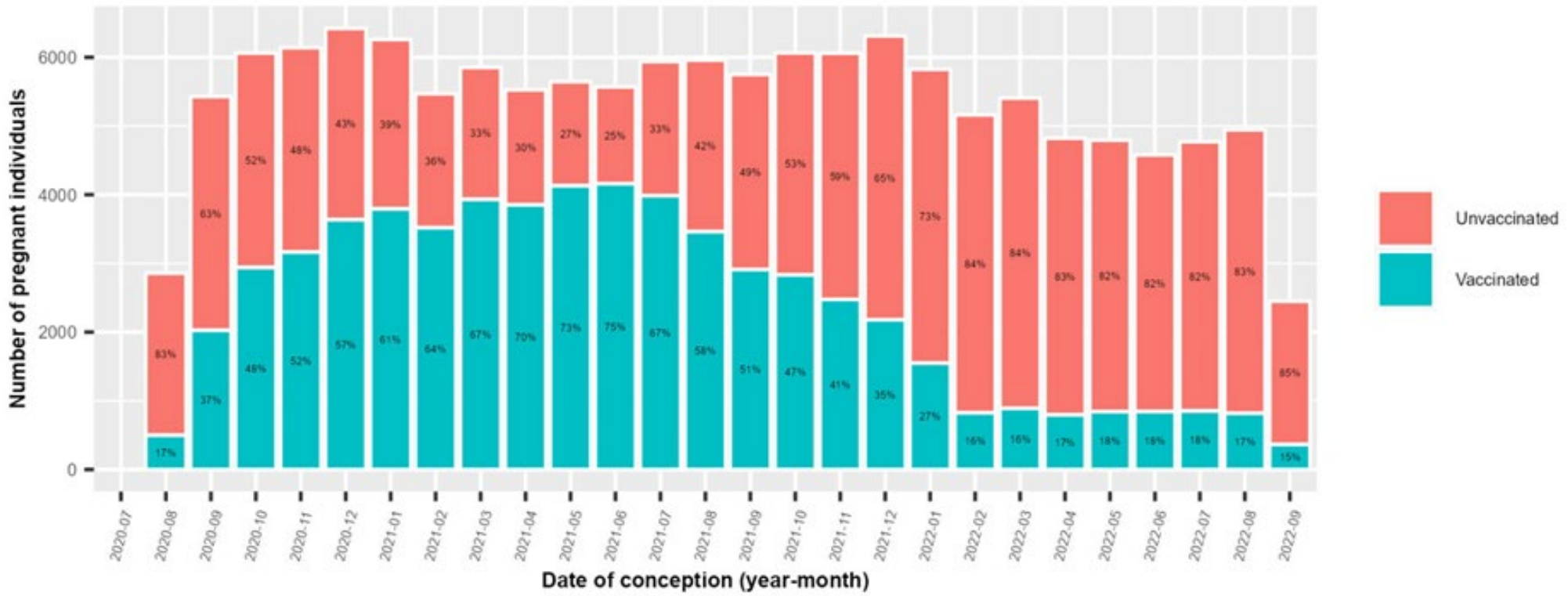
Résultats

Study flowchart (après exclusions)



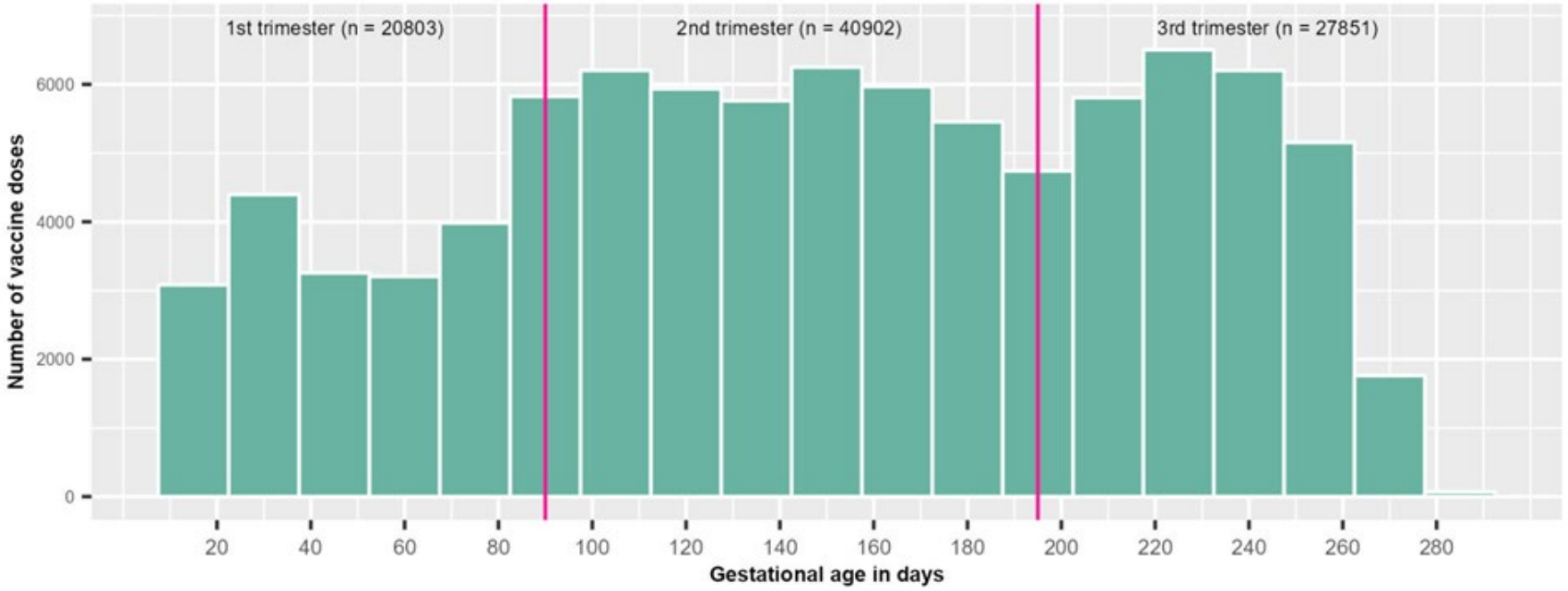
Résultats

Distribution of pregnant individuals by date of conception, stratified by the proportion of vaccinated (at least one dose)/unvaccinated individuals during pregnancy



Résultats

Gestational age at COVID-19 vaccination during pregnancy



Résultats

Association between COVID-19 vaccination during pregnancy and the risk of intrapartum complications

	n (%)		Risk ratio (95% CI)	
Outcomes	≥ 1 dose during pregnancy	No dose during pregnancy	Unadjusted	Adjusted
Pregnancies with a live birth or stillbirth (cohort 1):	N = 61,282	N = 78,791		
Chorioamnionitis	3392 (5.5%)	4472 (5.7%)	0.98 (0.93-1.02)	0.99 (0.95-1.04)
Primary postpartum hemorrhage	6629 (10.8%)	8757 (11.1%)	0.97 (0.94-1.00)	1.03 (0.99-1.06)
Caesarean delivery	15,838 (25.8%)	21,222 (26.9%)	0.96 (0.94-0.98)	0.94 (0.92-0.96)
ICU admission	192 (0.31%)	315 (0.40%)	0.78 (0.63-0.97)	0.80 (0.65-0.98)

Mêmes conclusions pour exposition au 1er trimestre

Résultats

Association between COVID-19 vaccination during pregnancy and the risk of neonatal complications

	n (%)		Risk ratio (95% CI)	
Outcomes	≥ 1 dose during pregnancy	No dose during pregnancy	Unadjusted	Adjusted
Pregnancies with a live birth or stillbirth (cohort 1):	N = 61,282	N = 78,791		
Stillbirth	184 (0.30%)	471 (0.60%)	0.50 (0.42-0.60)	0.84 (0.69-1.02)
Pregnancies with a live birth (cohort 2)	N= 61,098	N=78,320		
Low birth weight	2660 (4.4%)	4100 (5.2%)	0.83 (0.79-0.87)	0.90 (0.85-0.95)
Small for gestational age	5682 (9.3%)	7996 (10.2%)	0.91 (0.88-0.94)	0.94 (0.91-0.98)
NICU admission	190 (0.31%)	303 (0.39%)	0.80 (0.67-0.96)	0.81 (0.65-1.00)
Severe neonatal morbidity indicator	1673 (2.7%)	2526 (3.2%)	0.85 (0.80;0.90)	0.91 (0.85-0.98)

Mêmes conclusions pour exposition au 1er trimestre

Résultats

Association between COVID-19 vaccination during pregnancy and the risk of neonatal complications

	n (%)		Risk ratio (95% CI)	
Outcomes	≥ 1 dose during pregnancy	No dose during pregnancy	Unadjusted	Adjusted
Pregnancies with a live birth (cohort 2)	N= 60,016	N= 79,402		
Preterm birth < 37 w	3079 (5.1%)	4585 (5.8%)	0.89 (0.85-0.93)	0.94 (0.90-0.99)
Pregnancies with a live birth (cohort 2)	N= 53,938	N=85,480		
Very preterm birth < 32 w	319 (0.60%)	613 (0.72%)	0.83 (0.72-0.94)	1.04(0.89-1.21)

Mêmes conclusions pour exposition au 1er trimestre

Limites

- Plusieurs analyses de sensibilité effectuées
- Changement dans la stratégie de dépistage COVID-19 en Janvier 2022
  - Analyses séparées pour les personnes avec accouchement avant Janvier 2022 et date de conception après Janvier 2022.
  - Les conclusions demeurent les mêmes
- Exclure les femmes avec un test SARS-CoV-2 + pendant la grossesse
  - Les conclusions demeurent les mêmes
- Modèle de Cox

Sécurité vaccin COVID-19

- Revue littérature jusqu'à 2023 (nb =45) – maj en cours

Études	Personnes vaccinées au 1er trimestre
9 études avec évaluation de la vaccination au 1er trimestre	>44 000 personnes vaccinées
9 études avec personnes vaccinées au 1er trimestre, mais sans évaluation par trimestre.	>15 000 personnes vaccinées
27 études sans personnes vaccinées au 1er trimestre ou sans information	NA

Sécurité – taille d'échantillon

AVIS DISCUTÉ ET APPROUVÉ À LA RENCONTRE DU CIQ LE :	2015-09-10
RÉDACTEUR(S) :	Gaston De Serres
TITRE :	**Vaccination contre l'influenza des femmes enceintes à tout stade de la grossesse**

Figure 1. Taille d'échantillon
Nombre de femmes vaccinées à surveiller pour détecter une augmentation absolue de 1% (1 par 100 femmes vaccinées) de la fréquence de l'issue défavorable

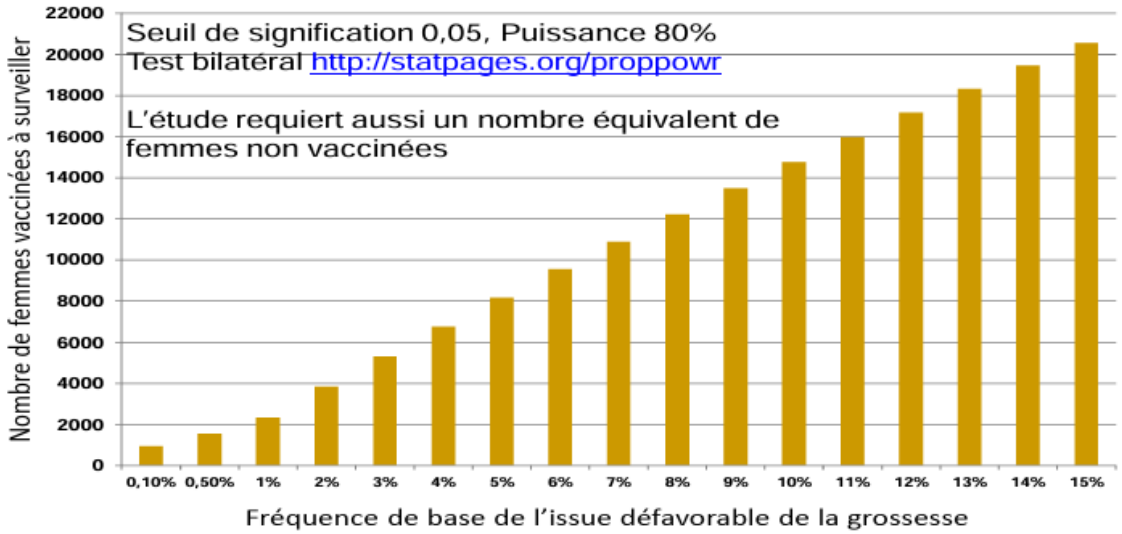
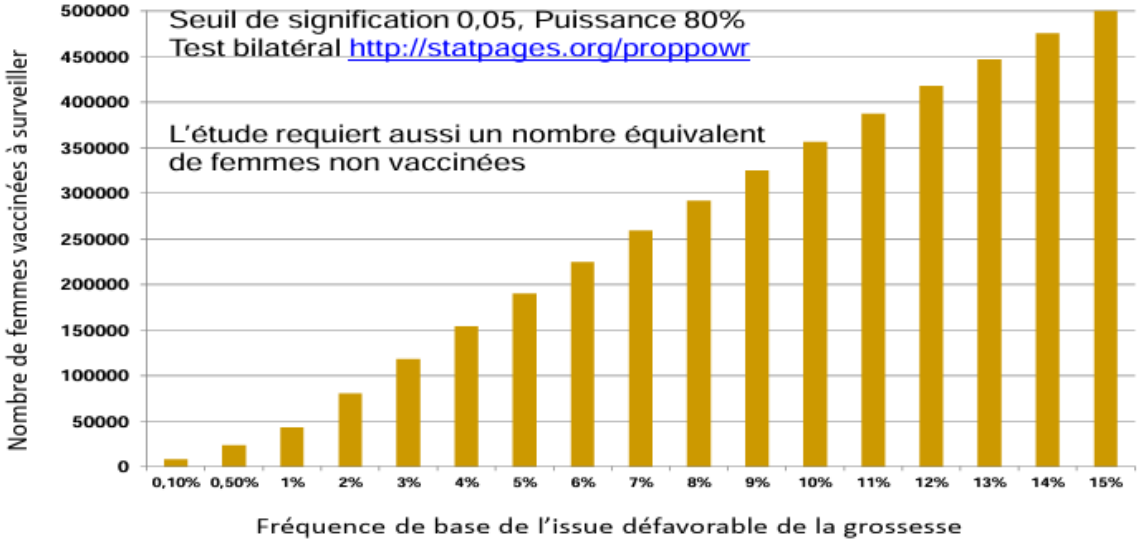


Figure 2. Nombre de femmes vaccinées à surveiller pour détecter une augmentation absolue de 0,2% (1 par 500 femmes vaccinées) de la fréquence de l'issue défavorable



Fardeau influenza

- Les personnes enceintes sont plus susceptibles de contracter une grippe sévère (CCNI, ACIP, JCVI)
  - Particulièrement 2e (ACIP) et 3e trimestre (CCNI, ACIP) ou si comorbidités (Skowronski_2009)
  - Augmentation hospitalisations (CCNI, OMS) et complications (ACIP, JVCI)
  - Les personnes qui contractent l'influenza durant la grossesse ont un risque augmenté de morbidité et mortalité (ATAGI)
- L'infection grippale pendant la grossesse peut augmenter le risque d'issues périnatales graves (CCNI, OMS)
  - Peut augmenter le risque d'avortement spontané en fin de grossesse, de mortinaissance, d'insuffisance pondérale à la naissance et d'accouchement prématuré, mais les données demeurent limitées (CCNI, JCVI, ATAGI)
- Les données probantes suggèrent que la vaccination antigrippale pendant la grossesse est efficace pour réduire le risque d'infection et d'hospitalisation liées à la grippe chez les personnes enceintes et leurs nourrissons jusqu'à 6 mois après l'accouchement (CCNI).

Fardeau COVID-19

- Risque d'hospitalization et/ou mortalité chez les personnes enceintes a réduit significativement dans la période omicron (JCVI).
- Risque de maladie sévère due à une infection par Omicron a été démontré plus faible chez les femmes qui avaient déjà été vaccinées (Australian Immunization Handbook)
- Protection contre hospitalisations dues à la COVID-19 chez les enfants < 6 mois surtout lorsque personnes enceintes vaccinées au > 20 semaines de gestation (Halasa_2022)
- Risque d'accouchement avant terme associé à une infection par Omicron est moins élevé que celui observé pour les infections avec les variants Delta et pré-Delta (INSPQ_2023)
- Association entre infection SARS-CoV-2 et prééclampie rapportée dans la littérature (les données sur une infection, symptomatique ou non, acquise au 1er ou au 2e trimestre de la grossesse sont non concluantes) (INSPQ_2023)

Acceptabilité

Sources de données	Vaccination COVID-19	Vaccination influenza
Étude de CV au Québec 2021 (naissances de 2020-03-02 à 2020-09-31)	ND	31,8 % (naissances de 2020-03-02 à 2020-09-31)
Registre de vaccination /infocentre (saison 2024-2025)	ND	10,8 %
Enquête canadienne 2021	ND	44,2%

Conformité

Pays/Organisme	Recommandation Influenza	Recommandation COVID-19
Canada / NACI **Directives mises à jour sur la vaccination antigrippale pendant la grossesse – décembre 2024** Guidance on the use of COVID-19 vaccines during the fall of 2024	Tous les trimestres	Tous les trimestres
États-Unis / ACIP **Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2024–25 Influenza Season - Août 2024** **https://www.cdc.gov/mmwr/volumes/73/wr/mm7337e2.htm**	Tous les trimestres	Tous les trimestres
UK (JCVI) **Green Book – Influenza et JCVI statement on influenza vaccines for 2025 to 2026 – décembre 2024** Spring 2025, autumn 2025 and spring 2026	Tous les trimestres	Les personnes enceintes ne sont plus ciblées

Conformité

Pays/Organisme	Recommandation Influenza	Recommandation COVID-19
Australie / ATAGI ATAGI statement on the administration of seasonal influenza vaccines in 2024 et Australian immunisation Handbook ATAGI statement on the administration of COVID-19 vaccines in 2024	Tous les trimestres	Vaccination recommandée seulement si la personnes n'a jamais été vaccinée. Aucune mention des trimestres.
OMS OMS_Interim guidance_07-2023 OMS_Interim guidance_08-2023	Tous les trimestres	Tous les trimestres, mais de preference au milieu du 2e trimester pour optimiser la protection de la personne enceinte, le foetus et l'enfant.

Prochaines étapes et discussion

- Finalisation de la revue de littérature pour la sécurité (MAJ > 2023)
- Discussion:
  - Évaluation risques/bénéfices
  - Vaccination au 1er trimestre:
    - Aspects opérationnels ?
    - Cibler toutes les femmes permet augmenter la CV chez personnes à risque?
  - Niveau de preuves disponibles pour vaccination au 1er trimester
    - Nb de personnes vaccinées a augmenté
    - Nécessité de réaliser d'autres études ?

Collaborateurs projet sécurité COVID-19

- Gentiane Perrault-Sullivan
- Nicholas Brousseau
- Isaora Zefania Dialahy
- Shu Qin Wei
- Caroline Quach
- Isabelle Boucoiran
- Amélie Boutin
- Chantal Sauvageau

Supplément

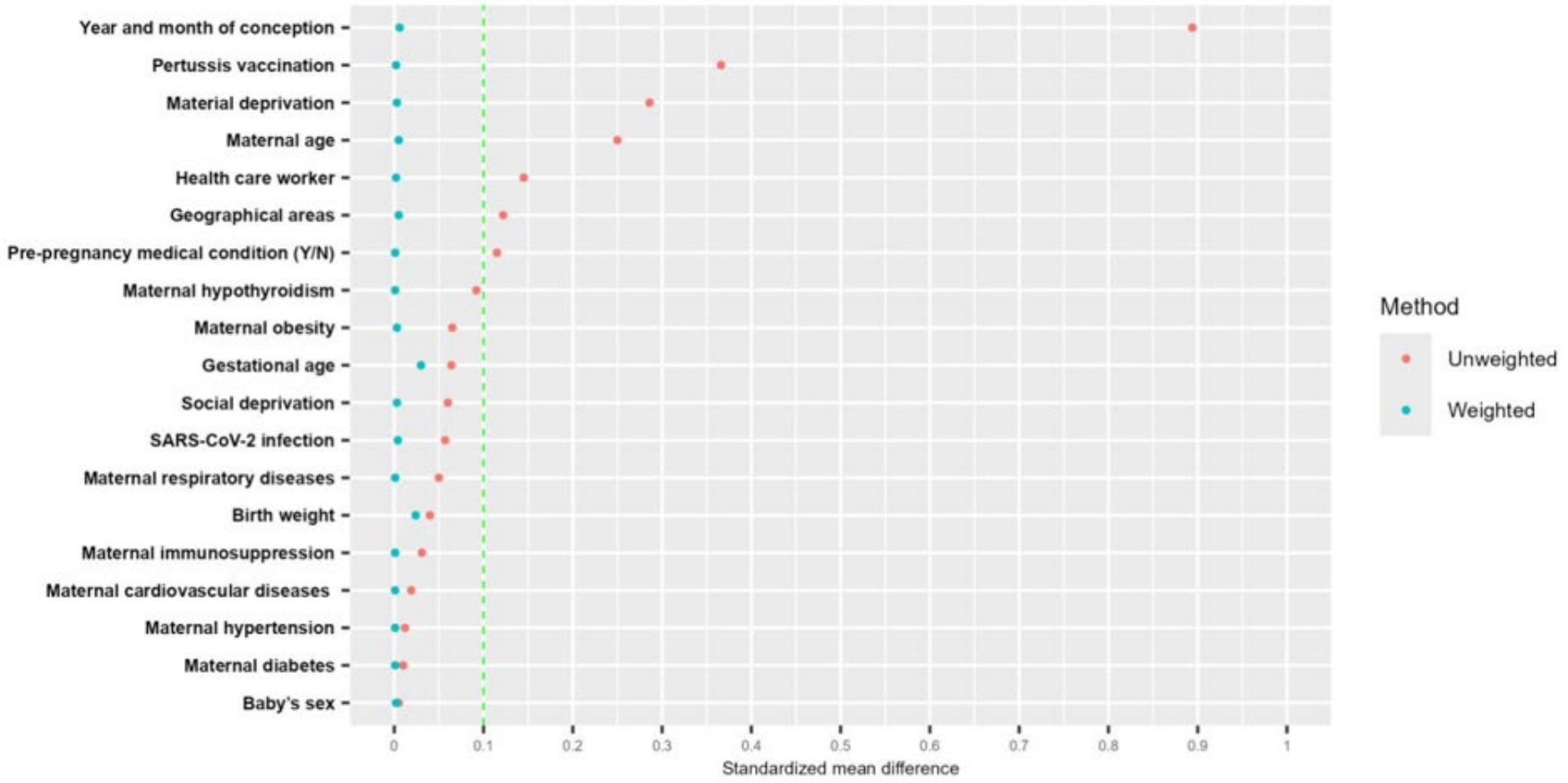
Sécurité vaccin influenza

- Autre étude non incluse dans la revue systématique avec analyse du risque pour le 1er trimestre

Auteurs	Qualité	Période	Méthode	Exposition	Population	Issues	Âge gestationnel à la vaccination (nb vaccinées au 1er trimestre)	Période de suivi	Résultats
Sarna_2022	Bonne	2012-04-01 à 2016-04-12	Cohorte rétrospective	Vaccin inactivé vs non vaccinées	125 666 personnes enceintes 13 696 vaccinées	Anomalies congénitales	1er trimestre: 2817 2e trimestre: 5650 3e trimestre: 5229	1 mois et 6 ans	Ensemble anomalies congénitales: RP 1.02 (IC à 95%: 0.84; 1.24) Anomalies congénitales musculosquelettiques (RP 1.30, IC à 95%: 1.01; 1.67), due principalement à la dysplasie congénitale de la hanche (pas significatif après correction pour tests multiples).

Résultats descriptifs - sécurité

Standardized mean differences before and after weighting using inverse probability of exposure weights



Sécurité vaccin COVID-19

- Études avec évaluation de la vaccination au 1er trimestre

Auteurs	Période	Méthode	Exposition	Population	Issues	Âge gestationnel à la vaccination (nb vaccinées au 1er trimestre)	Période de suivi	Résultats
Bleicher_2021	2020-01-10 à 2020-02-15	Cohorte prospective	Vaccinées ARNm vs non vaccinées	639 personnes enceintes 202 vaccinées	Issues composite de complications de grossesse, MCI	1er trimestre: 36 2e trimestre: 110 3e trimestre: 56	1 mois suivant questionnaire 1	Aucune difference pour le risque d'avortement spontané (<13 semaines de gestation)
Citu_2022	2020-02 à 2022-01	Cohorte rétrospective	Vaccinées ARNm vs non vaccinées	3094 personnes enceintes 927 vaccinées	Avortements spontanés	1er trimestre: 927	Jusqu'au 1er trimestre	Pfizer: RCa 1.04 (0.91; 1.12) Moderna: RCa 1.02 (0.89;1.08)

Sécurité vaccin COVID-19

- Études avec évaluation de la vaccination au 1er trimestre

Auteurs	Période	Méthode	Exposition	Population	Issues	Âge gestationnel à la vaccination (nb vaccinées au 1er trimestre)	Période de suivi	Résultats
Fell_2022	2020-12-14 à 2021-09-30	Cohorte rétrospective	Vaccinées ARNm vs non vaccinées	97 590 personnes enceintes 22 660 vaccinées	Issues obstétriques et néonatales	Dose 1: 1er trimestre: 201 2e trimestre: 8 047 3e trimestre: 13 412	Accouchement	There were no statistically significant increases in study outcomes when those vaccinated during pregnancy were stratified by trimester of vaccination for dose 1.
Fell_2022_2	2021-05-01 à 2021-12-31	Cohorte rétrospective	Vaccinées vs non vaccinées	85 162 personnes enceintes 43 099 vaccinées	Prématurité, SGA, mortinaissance	Dose 1: 1er trimestre: 5213 2e trimestre: 20 715 3e trimestre: 17 171	Accouchement	Prématurité: HRa 0.98 (0.87;1.10) Mortinaissance; no association between vaccination for dose 1 at first trimester and stillbirth.

Sécurité vaccin COVID-19

- Études avec évaluation de la vaccination au 1er trimestre

Auteurs	Période	Méthode	Exposition	Population	Issues	Âge gestationnel à la vaccination (nb vaccinées au 1er trimestre)	Période de suivi	Résultats
Fell_2023	2021-12-20 à 2022-08-31	Cohorte rétrospective	Vaccinées ARNm vs non vaccinées	32 689 personnes enceintes 18 491 vaccinées	Issues obstétriques et néonatales	1er trimester: 5484 2e trimestre: 11 332 3e trimestre: 1675	Accouchement	No increased risks were associated with receiving a third covid-19 vaccine dose during pregnancy for each outcome. Results by trimester of vaccination were consistent with the main findings
Jorgensen_2023	2021-05-01 à 2022-09-01	Cohorte rétrospective	Vaccinées ARNm vs non vaccinées	142 006 enfant, 85 670 de mères vaccinées	Issues néonatales, admission < 6 mois	1er trimestre: 27960 2e trimestre: 45910 3e trimestre: 38410	Jusqu'à 6 mois après l'accouchement	Aucune augmentation du risque. Résultats inchangés pour l'évaluation par trimestre.

Sécurité vaccin COVID-19

- Études avec évaluation de la vaccination au 1er trimestre

Auteurs	Période	Méthode	Exposition	Population	Issues	Âge gestationnel à la vaccination (nb vaccinées au 1er trimestre)	Période de suivi	Résultats
Goldshtein_2022	2021-09 à 2021-10	Cohorte rétrospective	Vaccinées Pfizer vs non vaccinées	24 288 personnes enceintes 16 697 vaccinées	Prématurité, Poids à la naissance, Hospitalisations, anomalies congénitales, jaunice, mortalité toutes causes	1er trimestre: 2134 2e trimestre: 9364 3e trimestre: 5199	1 mois minimum après l'accouchement	Prématurité: RR = 0.87 (0.67-1.12) SGA: RR = 1.14 (0.92-1.40) Malformations congénitales: RR = 0.69 (0.44-1.04) Hospitalisations néonatales: RR = 0.86 (0.67-1.09) Hospitalisations postnéonatales: RR = 0.78 (0.54-1.09) Mortalité: RR = 0.69 (0.14-2.41)
Magnus_2021	2021-02-15 à 2021-08-15	Cas-témoins	Vaccinées vs non vaccinées	13 956 personnes enceintes, 772 vaccinées	Avortement spontané	1er trimestre: 772	Cas= avortement spontané Témoins = identifiés parmi grossesses en cours au 1er trimestre.	RC : 0.91 (0.75 to 1.10) for vaccination in the previous 3 weeks and 0.81 (0.69 to 0.95) for vaccination in the previous 5 weeks.

Sécurité vaccin COVID-19

- Études avec évaluation de la vaccination au 1er trimestre

Auteurs	Période	Méthode	Exposition	Population	Issues	Âge gestationnel à la vaccination (nb vaccinées au 1er trimestre)	Période de suivi	Résultats
Watanabe_2022	Au 2022-04-05	Revue systématique et méta-analyse	Vaccinées vs non vaccinées	Études = 4 233 506 personnes enceintes, 57572 vaccinées	Prématurité SGA	1er trimestre: 3443 2e trimestre: 27 008 3e trimestre: 14220 (incluant étude Goldshtein_2022)	Accouchement	Prématurité: RC 1.81 (0.94; 3.46) SGA : RC 1.09 (0.95; 1.27)

BMJ Open

Safety of COVID-19 vaccines among pregnant individuals in Quebec, Canada: a population-based retrospective cohort study from the Canadian Immunization Research Network

Marilou Kiely ,[1,2] Ella Diendere,[3] Isaora Dialahy,[4] Gentiane Perrault-Sullivan,[3] Nicholas Brousseau ,[2,3] Shu Qin Wei,[5] Denis Talbot ,[1,2] Amélie Boutin,[2,6] Caroline Quach,[7] Sarah Jorgensen,[8] Isabelle Boucoiran [9,10]

To cite: Kiely M, Diendere E, Dialahy I, *et al*. Safety of COVID-19 vaccines among pregnant individuals in Quebec, Canada: a population-based retrospective cohort study from the Canadian Immunization Research Network. *BMJ Open* 2025;**15**:e106494. doi:10.1136/bmjopen-2025-106494

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2025-106494).

Received 12 June 2025
Accepted 26 November 2025

Check for updates

© Author(s) (or their employer(s)) 2025. Re-use permitted under CC BY. Published by BMJ Group.

For numbered affiliations see end of article.

Correspondence to
Dr Marilou Kiely;
marilou.kiely@fmed.qc.ca

ABSTRACT

Objective To estimate the association between maternal COVID-19 vaccination during pregnancy and adverse neonatal and maternal outcomes.

Design Population-based retrospective cohort study using a hospitalisation database linked with other health administrative databases.

Setting Province of Quebec, Canada, from 1 May 2021 to 30 June 2023.

Participants All singleton pregnancies resulting in a live birth or stillbirth at ≥20 weeks of gestation, excluding those with a conception date <42 weeks before the end of the study period.

Primary outcome measures We used robust Poisson regression models to estimate adjusted risk ratios (aRRs) for chorioamnionitis, postpartum haemorrhage, caesarean delivery, preterm birth, very preterm birth, small for gestational age (SGA), maternal and neonatal admission to intensive care unit (ICU, NICU) and severe neonatal morbidity. We used a Cox regression model with a time-varying exposure variable to estimate adjusted HRs (aHRs) for stillbirth. Propensity score weighting was used to adjust for potential confounding.

Results Among 140 073 singleton pregnancies resulting in live birth or stillbirth, 61 282 individuals (43.8%) received at least one dose of messenger RNA COVID-19 vaccine during pregnancy. Vaccination during pregnancy was not associated with an increased risk of chorioamnionitis (aRR 0.99, 95% CI 0.95 to 1.04), postpartum haemorrhage (aRR 1.03, 95% CI 0.99 to 1.06), very preterm birth (aRR 1.04, 95% CI 0.89 to 1.21) and stillbirth (aHR 1.14, 95% CI 0.94 to 1.39). Vaccination during pregnancy was significantly associated with a reduced risk of caesarean delivery (aRR 0.94, 95% CI 0.92 to 0.96), maternal ICU admission (aRR 0.80, 95% CI 0.65 to 0.98), SGA (aRR 0.94, 95% CI 0.91 to 0.98), NICU admission (aRR 0.91, 95% CI 0.85 to 0.96), preterm birth (aRR 0.94, 95% CI 0.90 to 0.99) and severe neonatal morbidity (aRR 0.91, 95% CI 0.85 to 0.98).

Conclusions Our findings suggest that COVID-19 vaccination during pregnancy was not associated with an increased risk of adverse outcomes. Ongoing surveillance of the safety of maternal COVID-19 vaccination is essential as doses continue to be recommended for this group.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study included a large and diverse cohort of individuals vaccinated during pregnancy at different stages of gestation.
⇒ We used propensity score weighting to adjust for potential confounders and employed approaches that accounted for immortal time bias.
⇒ We performed multiple subgroup and sensitivity analyses to assess the robustness of our results.
⇒ Although we adjusted for important known confounders, residual confounding cannot be excluded.

INTRODUCTION

Due to important physiological and immunological changes during pregnancy, pregnant individuals are at higher risk of severe illness from SARS-CoV-2 infection compared with non-pregnant individuals of similar age.[1 2] Indeed, pregnant individuals infected with SARS-CoV-2 are at significantly increased risk of maternal mortality, admission to intensive care unit (ICU), need for mechanical ventilation or any critical care as compared with uninfected pregnant individuals.[3 4] Moreover, there is evidence that COVID-19 infection during pregnancy is associated with an increased risk of adverse pregnancy outcomes, such as preterm birth and stillbirth.[3 5] Hence, preventing COVID-19 in

BMJ Open: first published as 10.1136/bmjopen-2025-106494 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on May 1, 2026 at Institut national de santé publique du Québec . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

pregnant individuals is crucial to mitigate both maternal and neonatal morbidity and mortality.

Other vaccines, such as influenza and pertussis vaccines, are recommended during pregnancy to prevent morbidity and mortality among pregnant individuals and newborns. Many countries, including Canada, have considered pregnant individuals as a priority group for COVID-19 vaccination.[6 7] In Quebec, Canada, the COVID-19 vaccine was offered to all pregnant individuals in late April 2021, although those at higher risk of exposure or severe disease were eligible for vaccination at the start of the COVID-19 vaccination campaign in December 2020. Pregnant individuals were excluded from prelicensure trials for COVID-19 vaccines, but vaccine effectiveness among this population has been well demonstrated in observational studies.[8 9] However, vaccination coverage among pregnant individuals was lower compared with non-pregnant individuals of reproductive age, especially among the youngest and those living in more deprived areas.[10 11] Safety concerns are frequently cited as a reason to decline COVID-19 vaccination during pregnancy.[12–14] Despite reassuring data on the safety of COVID-19 vaccines in pregnant individuals from observational studies, data from large populations, including individuals vaccinated at different trimesters of pregnancy, are still needed to better demonstrate the safety of this strategy. The availability of vaccine safety data has the potential to enhance confidence for both pregnant individuals and healthcare providers.[15–20]

In the context of ongoing SARS-CoV-2 circulation and the waning immunity requiring additional doses of vaccine, vigilant efforts are warranted to support timely decision-making and public health recommendations for pregnant individuals who are particularly vulnerable to more severe presentations of SARS-CoV-2 infection. In addition, as COVID-19 vaccines are still recommended during pregnancy, large-scale vaccine safety studies are needed to ensure that the benefit-risk ratio (RR) remains favourable in this population, accounting for current disease epidemiology. The purpose of this retrospective population-based cohort study was to evaluate the association between COVID-19 vaccination during pregnancy and the risk of adverse neonatal and maternal outcomes in Quebec.

METHODS

We followed the RECORD (REporting of studies Conducted using Observational Routinely-collected health Data) statement and guidelines for observational studies of COVID-19 vaccination during pregnancy.[21 22] The study used health administrative data, and no additional information was collected from participants.

Patients and public involvement

No patients or members of the public were involved in the conduct of this study.

Study design, data sources and participants

We conducted a retrospective population-based cohort study among individuals who gave birth between 1 May 2021 and 30 June 2023, in hospitals in Quebec. The province of Quebec is Canada's second most populous province, where approximately 80 000 births occur annually. The Quebec hospitalisation discharge database (ie, *Maintenance et exploitation des données pour l'étude de la clientèle hospitalière*) was used to identify the study population, using the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada (ICD-10-CA) and the Canadian Classification of Health Interventions (CCI) for diagnostics and procedural codes associated with vaginal or caesarean delivery. It contains data on hospital stays occurring in all public hospitals providing general and specialised care. About 97% of births in Quebec occur in a hospital.[23] Hospital delivery records of mothers were linked with the corresponding newborn records (97% successfully linked). We deterministically linked the cohort with four other databases, using the mothers' unique Quebec health insurance number: (1) The Provincial Laboratory Database, which captures all reverse transcription PCR (RT-PCR) confirmed SARS-CoV-2 infections. The testing strategy changed in Quebec during the study period: in January 2022, RT-PCR testing was restricted to priority groups and COVID-19 rapid antigen tests became widely used. The latter was not available in the provincial database. (2) The Quebec Vaccination Registry, which contains information on vaccine product, number of doses and vaccination dates for all vaccines administered in Quebec. All vaccine providers in Quebec are mandated to enter all administered vaccines in the registry; (3) The presence of pre-existing medical conditions was extracted from the Quebec Integrated Chronic Disease Surveillance System, which links patient-level records from provincial health system administrative databases, including hospitalisation discharge database and the physician claims database[24]; (4) Finally, maternal postal code was used to compute area-level social and material deprivation indices, which use Statistics Canada's 2016 Census data to rank small areas according to deprivation[25] (see online supplemental table S1 in the Supplement for a description of each data source).

All singleton pregnancies that reached at least 20 weeks' gestation and resulted in either a live birth or stillbirth were included.[26] To avoid fixed cohort bias, we excluded individuals who became pregnant less than 42 weeks before the end of the study.[26 27] Pregnant individuals less than 15 years or older than 49 years of age at delivery, those vaccinated with a non-messenger RNA (mRNA) COVID-19 vaccine before delivery, those not linked to the Quebec Vaccination Registry and those with more than one pregnancy during the study period were excluded.[17 28]

BMJ Open: first published as 10.1136/bmjopen-2025-106494 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on May 1, 2026 at Institut national de santé publique du Québec . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Exposure

COVID-19 vaccination campaign started in Quebec in December 2020, targeting certain pregnant individuals, such as healthcare workers or those with medical chronic conditions. Most pregnant individuals were eligible to get vaccinated as of 27 April 2021. A vaccine exposure during pregnancy was defined as the receipt of at least one dose of mRNA COVID-19 vaccine between the estimated date of conception up to 1 day before delivery, except for very preterm and preterm births, for which the exposure period was up to 31 weeks+6 days and 36 weeks+6 days gestation, respectively.[16 29 30] The date of conception was estimated by adding 14 days to the last menstrual period date, which was derived from the gestational age at birth (validated by ultrasound) and the date of birth available in the hospitalisation records.[28 30] Pregnant individuals who received no dose of vaccine during pregnancy (or during the specified exposure window for preterm births) were considered unexposed as well as those who received a first dose of vaccine during the postpartum period (ie, within 6 weeks after delivery). Mothers who received doses in preconception, but none during pregnancy were also considered unexposed. Vaccine exposure during pregnancy was further classified according to first trimester (from 0 to 12 weeks+6 days), second trimester (from 13 weeks to 27 weeks+6 days) and third trimester (≥28 weeks).

Outcomes

We evaluated the following maternal complications among pregnant individuals with a live birth or stillbirth[10 17 19 22 31]: chorioamnionitis, postpartum haemorrhage, caesarean delivery, emergency caesarean delivery and ICU admission (any indication). We assessed the following neonatal

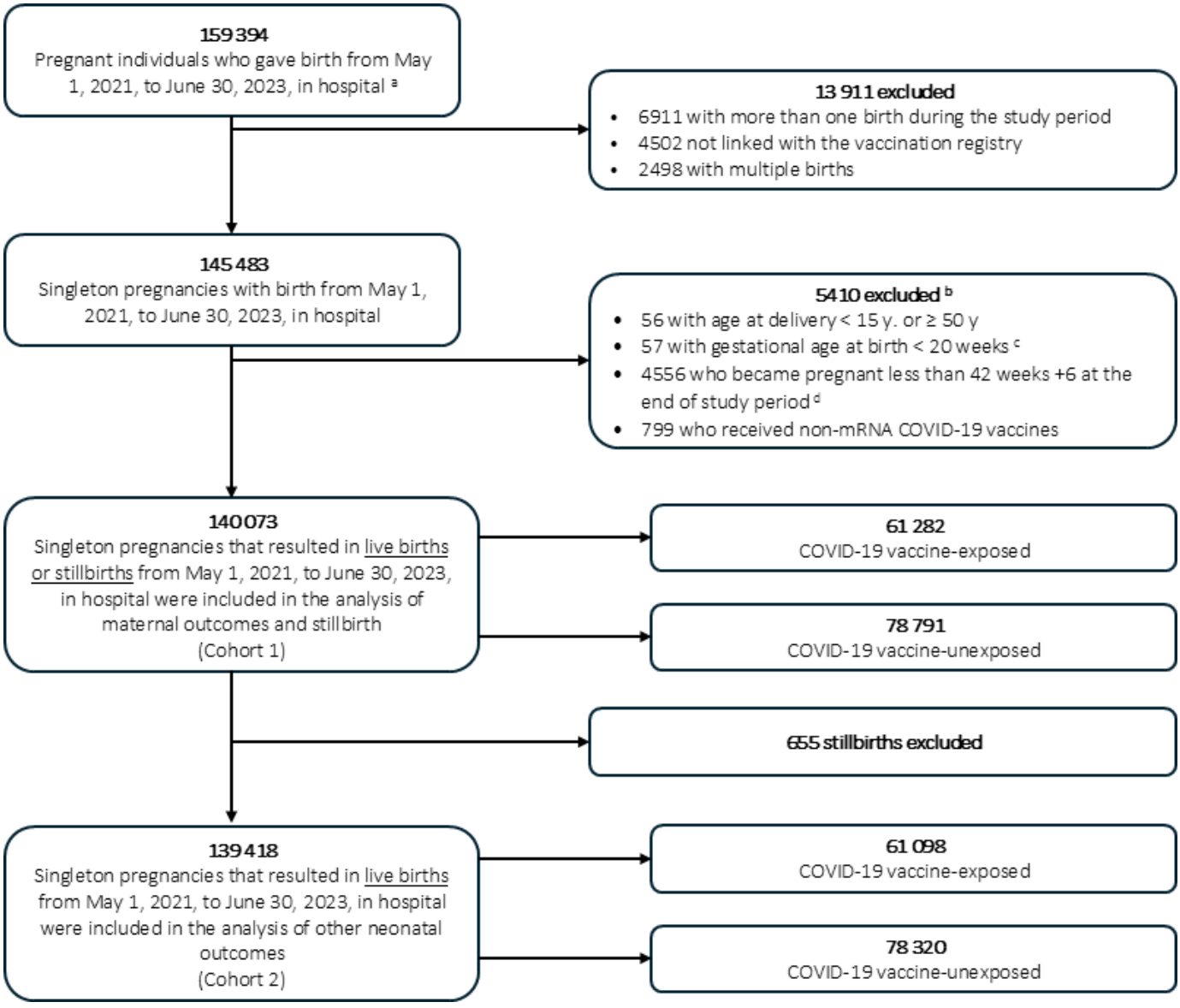


Figure 1 Study flowchart . [a]Date of conception from July 2020 to September 2022. The cohort included only individuals with a unique Quebec health insurance number. [b]Categories are not mutually exclusive. [c]As birth at <20 weeks represents spontaneous abortion for which we do not have all full data. [d]To avoid fixed cohort bias. mRNA, messenger RNA.

BMJ Open: first published as 10.1136/bmjopen-2025-106494 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on May 1, 2026 at Institut national de santé publique du Québec . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 1 Unweighted and weighted baseline characteristics of the total study population and by maternal COVID-19 vaccination during pregnancy

	Unweighted				Inverse probability of treatment weighted		
	Total study population N=140 073	At least 1 dose of COVID-19 vaccine during pregnancy n=61 282	No COVID-19 vaccine during pregnancy n=78 791	Standardised difference*	At least 1 dose of COVID-19 vaccine during pregnancy	No COVID-19 vaccine during pregnancy	Standardised difference*
	n (%)				%		
Maternal age group, year							
15–24	11 517 (8.2)	3243 (5.3)	8274 (10.5)	0.194	7.2	7.1	0.002
25–29	37 430 (26.7)	14 598 (23.8)	22 832 (29.0)	0.117	26.6	26.4	0.004
30–34	53 848 (38.4)	25 712 (42.0)	28 136 (35.7)	0.128	39.2	39.3	0.001
35–39	28 862 (20.6)	13 925 (22.7)	14 937 (19.0)	0.093	20.9	21.1	0.002
40–49	8416 (6.0)	3804 (6.2)	4612 (5.9)	0.015	6.1	6.1	0.002
Mean (SD)	31.5 (5.02)	32.0 (4.71)	31.0 (5.21)	0.207	31.6 (4.9)	31.6 (5.0)	0.014
Infant sex, female	66 393 (47.4)	29 173 (47.6)	37 220 (47.2)	0.007	47.5	47.6	0.002
Unknown/missing	3802 (2.7)	1449 (2.4)	2353 (3.0)				
Birth weight (≥2500 g)	133 313 (95.2)	58 622 (95.7)	74 691 (94.8)	0.040	95.6	95.1	0.024
Prepregnancy medical condition†	32 932 (23.5)	160 099 (26.3)	16 833 (21.4)	0.115	24.4	24.4	<0.001
Cardiovascular diseases	3059 (2.2)	1433 (2.3)	1626 (2.1)	0.019	2.2	2.2	<0.001
Diabetes	1187 (0.8)	550 (0.9)	637 (0.8)	0.010	0.8	0.8	<0.001
Hypertension	1578 (1.1)	735 (1.2)	843 (1.1)	0.012	1.2	1.1	<0.001
Hypothyroidism	12 314 (8.8)	6288 (10.3)	6026 (7.6)	0.092	9.2	9.3	0.001
Immunosuppression	1543 (1.1)	788 (1.3)	755 (1.0)	0.031	1.1	1.2	0.001
Obesity	10 536 (7.5)	5201 (8.5)	5335 (6.8)	0.065	8.0	7.9	0.003
Respiratory diseases	9936 (7.1)	4791 (7.8)	5145 (6.5)	0.050	7.2	7.2	<0.001
Unknown/missing‡	4817 (3.4)	635 (1.0)	4182 (5.3)				
Healthcare worker§	19 830 (14.2)	10 426 (17.0)	9404 (11.9)	0.145	14.6	14.5	0.002
Tdap¶ vaccination during pregnancy	94 828 (67.7)	47 245 (77.1)	47 583 (60.4)	0.366	69.5	69.4	0.002
Geographical areas							
Census metropolitan areas of Montreal	72 678 (51.9)	32 748 (53.4)	39 930 (50.7)	0.055	52.3	52.2	0.005
Others census metropolitan areas	28 844 (20.6)	13 589 (22.2)	15 255 (19.4)	0.069	20.7	20.7	0.001
Cities of 10 000 to 100 000 000 residents	12 769 (9.1)	5121 (8.4)	7648 (9.7)	0.047	8.9	8.8	0.001
Small cities and rural areas: less than 10 000 residents	25 025 (17.9)	9698 (15.8)	15 327 (19.5)	0.095	17.8	17.7	0.004
Unknown/missing	757 (0.5)	126 (0.2)	631 (0.8)				
History of SARS-CoV-2 infection during pregnancy	14 919 (10.7)	5925 (9.7)	8994 (11.4)	0.057	11.2	11.3	0.004
Material deprivation index							

Continued

BMJ Open: first published as 10.1136/bmjopen-2025-106494 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on May 1, 2026 at Institut national de santé publique du Québec . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 1 Continued

	Unweighted				Inverse probability of treatment weighted		
	Total study population N=140 073	At least 1 dose of COVID-19 vaccine during pregnancy n=61 282	No COVID-19 vaccine during pregnancy n=78 791	Standardised difference*	At least 1 dose of COVID-19 vaccine during pregnancy	No COVID-19 vaccine during pregnancy	Standardised difference*
	n (%)				%		
1 (least deprived)	24 213 (17.3)	13 182 (21.5)	11 031 (14.0)	0.197	17.4	17.5	0.002
2	26 301 (18.8)	12 731 (20.8)	13 570 (17.2)	0.091	19.2	19.2	<0.001
3	26 331 (18.8)	11 710 (19.1)	14 621 (18.6)	0.014	19.2	19.2	0.001
4	26 298 (18.8)	10406 (17.0)	15 892 (20.2)	0.082	18.9	18.8	0.001
5 (most deprived)	27 065 (19.3)	9233 (15.1)	17 832 (22.6)	0.194	18.5	18.4	0.001
Unknown/missing	9865 (7.0)	4020 (6.6)	5845 (7.4)				
Social deprivation index							
1 (least deprived)	24 511 (17.5)	11 328 (18.5)	13 183 (16.7)	0.046	17.6	17.5	0.002
2	26 172 (18.7)	11 595 (18.9)	14 577 (18.5)	0.011	18.7	18.7	<0.001
3	26 948 (19.2)	11 993 (19.6)	14 955 (19.0)	0.015	19.5	19.4	0.001
4	26 475 (18.9)	11 484 (18.7)	14 991 (19.0)	0.007	18.9	19.0	0.002
5 (most deprived)	26 102 (18.6)	10 862 (17.7)	15 240 (19.3)	0.042	18.5	18.5	<0.001
Unknown/missing	9865 (7.0)	4020 (6.6)	5845 (7.4)				
Estimated date of conception							
July 2020 to September 2020	8289 (5.9)	2526 (4.1)	5763 (7.3)	0.138	6.2	6.2	<0.001
October 2020 to December 2020	18 623 (13.3)	9741 (15.9)	8882 (11.3)	0.135	17.3	17.3	0.001
January 2021 to March 2021	17 583 (12.6)	11 243 (18.3)	6340 (8.0)	0.308	14.2	14.3	0.002
April 2021 to June 2021	16 741 (12.0)	12 142 (19.8)	4599 (5.8)	0.427	10.9	10.9	<0.001
July 2021 to September 2021	17 647 (12.6)	10 359 (16.9)	7288 (9.2)	0.229	15.5	15.5	<0.001
October 2021 to December 2021	18 435 (13.2)	7489 (12.2)	10 946 (13.9)	0.050	16.5	16.5	0.001
January 2022 to March 2022	16 393 (11.7)	3264 (5.3)	13 129 (16.7)	0.369	8.1	8.1	<0.001
April 2022 to June 2022	14 196 (10.1)	2483 (4.1)	11 713 (14.9)	0.376	6.2	6.1	0.005
July 2022 to September 2022	12 166 (8.7)	2035 (3.3)	10 131 (12.9)	0.355	5.1	5.0	0.003

*A standardised difference of less than 0.1 is considered indicative of balance between groups.
†At least one of prepregnancy medical conditions listed.
‡Individuals not matched between MED-ÉCHO and SISMACQ could be those without health insurance coverage for at least 1 day during the year, or individuals who are not registered (such as newcomers). This could also be due to errors in the health insurance number.
§Employees on the payroll list or members of professional associations.
¶Tdap: tetanus-diphtheria-acellular pertussis vaccine.
MED-ÉCHO, Maintenance et exploitation des données pour l'étude de la clientèle hospitalière; SISMACQ, Le Système intégré de surveillance des maladies chroniques du Québec.

BMJ Open: first published as 10.1136/bmjopen-2025-106494 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on May 1, 2026 at Institut national de santé publique du Québec .
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

outcomes among all pregnancies[10 17 22 29 31 32]: stillbirth (at ≥20 weeks of gestation), and among live births: preterm birth (≥20 weeks+0 days to 36 weeks+6 days) and very preterm birth (≥20 weeks+0 days to 31 weeks+6 days), small for gestational age (SGA) (<10th percentile of gestational age-specific and sex-specific birth weight) and neonatal ICU (NICU) admission (any indication). Preterm and very preterm births were examined overall and separately for spontaneous and provider-initiated preterm birth.[18 33] We assessed neonatal morbidity using a composite indicator based on 15 diagnoses and 7 procedures during the birth admission. All outcomes were identified using ICD-10-CA diagnostic codes, CCI procedure codes or other data available from the maternal delivery or infant birth record, as used in previous studies.[17 34 35] Detailed definitions are presented in online supplemental table S2 in the Supplement.

Covariates

The following variables were considered potential confounders for the association between vaccination and maternal and neonatal outcomes: maternal age at delivery (categorised), infant sex, prepregnancy medical conditions (cardiovascular diseases, diabetes, hypertension, hypothyroidism, immunosuppression, obesity (body mass index ≥30 kg/m^2) and respiratory diseases), healthcare worker status, tetanus-diphtheria-acellular pertussis (Tdap) vaccination during pregnancy (proxy for health behaviours), history of at least one positive SARS-CoV-2 test during pregnancy, geographical areas, month and year of conception and area-level social and material deprivation indices (see online supplemental table S2 in the Supplement for a description of each covariate).

Statistical analysis

We compared baseline characteristics among exposed and unexposed pregnant individuals using standardised differences. An absolute standardised difference less than 0.10 was considered indicative of balance between groups.[36] To control for potential confounding in the association between vaccination and outcomes, we computed inverse probability of treatment weights derived from the propensity score. This score represented the predicted probability, estimated from a logistic regression, of receiving at least one dose of mRNA COVID-19 vaccine during pregnancy conditional on observed baseline characteristics[36] (see online supplemental table S3 in the Supplement). Weights were stabilised and truncated to the 1st and 99th percentiles to address the problem of large weight that can increase variability in the effect being estimated. Unadjusted and inverse probability of treatment weighted RRs and 95% CIs were computed using modified Poisson regression models with a robust, sandwich-type variance estimator to account for weight-induced dependencies.[36 37]

Since the risk of stillbirth is particularly dependent on gestational age and to address immortal time bias, we used methods that handle time-dependent exposures. Adjusted HRs (aHRs) with 95% CI were then computed using a weighted Cox-proportional-hazard regression model with gestational age in days as the time scale and follow-up time beginning at 20 weeks until the end of pregnancy or the occurrence of stillbirth.[16 18 30] Vaccination during pregnancy was considered a time-varying exposure, with pregnant individuals contributing to both exposed and unexposed time during pregnancy. The validation of the proportional hazards assumption was based on the Schoenfeld residuals test.[38] We also used graphical representation of the residuals as a function of time. There were 7.0% (n=9865) of missing data for material and social deprivation indices and less than 5% for infant sex (n=3802, 2.7%), prepregnancy medical condition (n=4817, 3.4%) and geographical areas (n=757, 0.5%). Missing data were not assumed to be missing at random and were handled by assigning individuals with missing data to a separate (missing) category for these variables. Statistical significance was set at 5% and the study was powered at over 80% to detect a 1% absolute increase following vaccination for rare outcomes such as stillbirth. Analyses were conducted in R (V.4.4.2) using a deidentified data set.

Subgroup and sensitivity analyses

We performed the following subgroup and sensitivity analyses to test the robustness of our results. Data were analysed according to the number of COVID-19 vaccine doses received during pregnancy (only 1 dose, 2 doses or ≥3 doses), the trimester of pregnancy (first dose during the first trimester, first dose during the second trimester or first dose during the third trimester) and the vaccine received (BNT162b2 only, mRNA-1273 only or mixed mRNA). Since SARS-CoV-2 infection may be on the causal path between vaccination and pregnancy or neonatal outcomes, we repeated analyses excluding individuals with documented SARS-CoV-2 infection during pregnancy. As individuals who remained unvaccinated during the whole study period could differ more from the exposed group than those who got vaccinated before or after, but not during pregnancy, we limited the unexposed group to those vaccinated during the preconception or during the postpartum period, but not during pregnancy. In addition to censoring the vaccination exposure period for preterm and very preterm births to limit immortal time bias, we used a weighted Cox-proportional-hazard regression model for these outcomes using the same approach used for stillbirth. Pregnancies were followed until 36 weeks+6 days or 31 weeks+6 days. We restricted the analysis of SGA and NICU admission to term birth as these outcomes are associated with preterm birth.[18] For SGA, we considered unexposed those vaccinated during the last 2 weeks of pregnancy as the potential effect of vaccination on fetal growth would likely require more time to have an effect.[18] To account for the changes in COVID-19 testing strategy in Quebec during the study period, we presented results separately for births before January 2022 and for pregnant individuals with a date of

BMJ Open: first published as 10.1136/bmjopen-2025-106494 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on May 1, 2026 at Institut national de santé publique du Québec . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 2 Vaccination characteristics among pregnant individuals who received at least one dose of COVID-19 vaccine during pregnancy

Characteristics	At least one COVID-19 vaccine dose during pregnancy N=61 282, n (%)
COVID vaccinated (at least one dose) according to the trimesters of pregnancy*	
First trimester	19 442 (31.7)
Second trimester	34 854 (56.9)
Third trimester	25 769 (42.0)
Number of doses received during pregnancy	
1	34 371 (56.1)
2	25 563 (41.7)
3	1345 (2.2)
4	3 (0.0)
Dose 1 received during:†	
First trimester	19 442 (31.7)
Second trimester	29 032 (47.4)
Third trimester	12 808 (20.9)
Dose 2 received during:†	
First trimester	1361 (2.2)
Second trimester	11 818 (19.3)
Third trimester	13 732 (22.4)
No dose 2 during pregnancy	34 371 (56.1)
Dose 3 received during:†	
First trimester	0 (0.0)
Second trimester	51 (0.1)
Third trimester	1297 (2.1)
No dose 3 during pregnancy	59 934 (97.8)
Dose 4 received during:†	
First trimester	0 (0.0)
Second trimester	0 (0.0)
Third trimester	3 (0.0)
No dose 4 during pregnancy	61 279 (99.9)
Vaccine types received during pregnancy	
BNT162b2	43 137 (70.4)
mRNA-1273	16 086 (26.2)
Mixed mRNA	2059 (3.4)
Intervals between doses 1 and 2 (days)‡	
0–29	2965 (4.8)
30–55	4934 (8.1)
56+	19 012 (31.0)
Only 1 dose during pregnancy	34 371 (56.1)
Intervals between Doses 2 and 3 (days)‡	
0–119	238 (0.4)
120–179	996 (1.6)
180+	114 (0.2)
No dose 2 and/or 3 during pregnancy	59 934 (97.8)
Intervals between doses 3 and 4 (days)‡	

Continued

BMJ Open: first published as 10.1136/bmjopen-2025-106494 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on May 1, 2026 at Institut national de santé publique du Québec . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 2 Continued

Characteristics	At least one COVID-19 vaccine dose during pregnancy N=61 282, n (%)
0–119	2 (0.0)
120+	1 (0.0)
No dose 3 and/or 4 during pregnancy	61 279 (99.9)

*Categories are not mutually exclusive as individuals could have received a dose in the first, second and third trimesters.
†Vaccination received exclusively during pregnancy. Does not take previous vaccination into account.
‡Only for doses given during pregnancy.
mRNA, messenger RNA.

conception after January 2022. Finally, given the uncertainty in the estimated date of conception, we repeated the analyses with the conception date shifted 2 weeks earlier and 2 weeks later.

RESULTS

There were 159 394 pregnant individuals who gave birth in hospital in Québec from 1 May 2021 to 30 June 2023 (figure 1). After exclusions, there were 140 073 singleton pregnancies that resulted in live births or stillbirths (cohort 1), and 61 282 individuals (43.8%) received at least one dose of a mRNA COVID-19 vaccine during pregnancy. compared with those who were not vaccinated during pregnancy, those vaccinated during pregnancy were more likely to be older than 30 years of age (70.9% vs 60.5%), have a prepregnancy medical condition (26.3% vs 21.4%), be healthcare workers (17.0% vs 11.9%), have received a Tdap vaccine during pregnancy (77.1% vs 60.4%), live in the least materially deprived areas (Quintile 1: 21.5% vs 14.0%) and have conceived between October 2020 and September 2021 (table 1). After propensity score weighting, the distribution of baseline characteristics was similar between vaccinated and unvaccinated individuals, with all standardised differences less than 0.1 (table 1 and online supplemental figure S1 in the Supplement).

Among the 61 282 individuals vaccinated during pregnancy, 34 371 received 1 dose (65.1%) and 26 911 (43.9 %) ≥2 doses. A greater proportion of vaccinated individuals received BNT162b2 from Pfizer-BioNTech (70.4%) compared with mRNA-1273 from Moderna (26.2%), while a small proportion received mixed mRNA vaccines (3.4%) (table 2). Nearly a quarter (23.2%) of all doses administered during pregnancy were received in the first trimester (figure 2). The distribution of SARS-CoV-2 infections during pregnancy is presented in online supplemental figure S2 in the Supplement.

Vaccination during pregnancy was not significantly associated with an increased risk of chorioamnionitis (5.5% vs 5.7%, adjusted RR (aRR) 0.99, 95% CI 0.95 to 1.04). COVID-19 vaccination during pregnancy was not significantly associated with postpartum haemorrhage (10.8% vs 11.1%, aRR 1.03, 95% CI 0.99 to 1.06), compared with individuals not vaccinated during pregnancy. The risk of caesarean delivery was significantly lower among vaccinated individuals compared with unvaccinated individuals (25.8% vs 26.9%, aRR 0.94, 95% CI 0.92 to 0.96), as well as the risk of emergency caesarean delivery (14.9% vs 16.0%, aRR 0.95, 95% CI 0.92 to 0.98). A reduced risk was also observed for maternal ICU admission (0.31% vs 0.40%, aRR 0.80, 95% CI 0.65 to 0.98) (table 3).

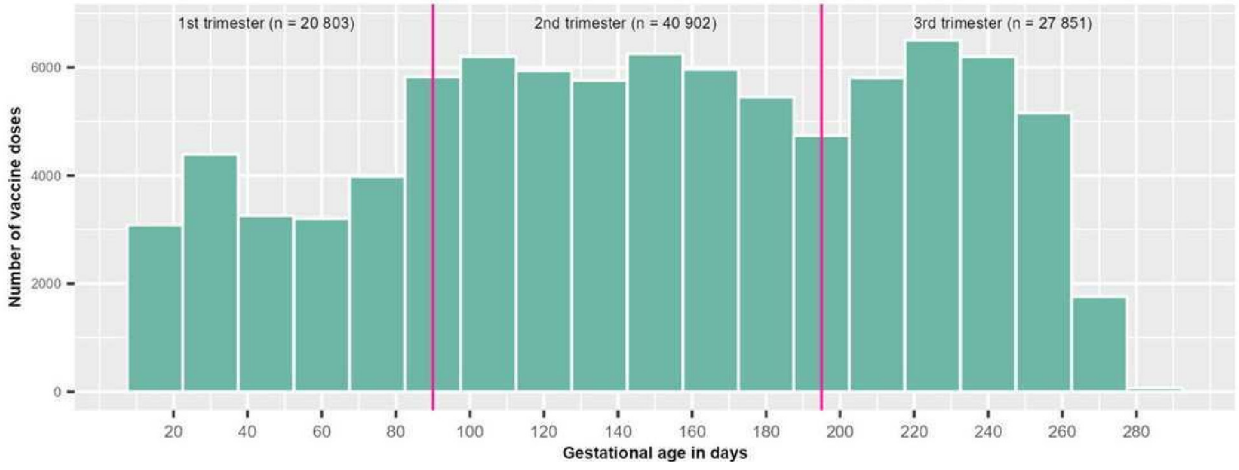


Figure 2 Gestational age at COVID-19 vaccination during pregnancy. Including all doses administered during pregnancy. If an individual received two doses during a trimester, both doses have been counted.

BMJ Open: first published as 10.1136/bmjopen-2025-106494 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on May 1, 2026 at Institut national de santé publique du Québec . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 3 Association between COVID-19 vaccination during pregnancy and the risk of adverse maternal outcomes

Outcomes	N (%)		Risk ratio (95% CI)	
	≥1 dose during pregnancy	No dose during pregnancy	Unadjusted	Adjusted*
Pregnancies with a live birth or stillbirth (cohort 1)	N=61 282	N=78 791		
Chorioamnionitis	3392 (5.5)	4472 (5.7)	0.98 (0.93 to 1.02)	0.99 (0.95 to 1.04)
Postpartum haemorrhage	6629 (10.8)	8757 (11.1)	0.97 (0.94 to 1.00)	1.03 (0.99 to 1.06)
Caesarean delivery	15 838 (25.8)	21 222 (26.9)	0.96 (0.94 to 0.98)	0.94 (0.92 to 0.96)
Emergency caesarean delivery	9138 (14.9)	12 629 (16.0)	0.93 (0.91 to 0.95)	0.95 (0.92 to 0.98)
Maternal ICU admission	192 (0.31)	315 (0.40)	0.78 (0.66 to 0.94)	0.80 (0.65 to 0.98)

*Adjusted for maternal age at delivery, infant sex, maternal pre-existing conditions, healthcare provider status, SARS-CoV positive test during pregnancy, social and material deprivation indexes, month and year of conception, Tdap vaccination during pregnancy and geographical areas using inverse probability of treatment weighting.
ICU, intensive care unit; Tdap, tetanus-diphtheria-acellular pertussis.

We did not find a significant association between vaccination during pregnancy and very preterm birth (0.60% vs 0.72%, aRR 1.04, 95% CI 0.89 to 1.21) or stillbirth (0.3 vs 0.4 per 10 000 pregnancy days at risk, aHR 1.14, 95% CI 0.94 to 1.39). Risks of other neonatal outcomes were lower in vaccinated individuals compared with those who were unvaccinated; these reduced risks remained significant after adjustment for SGA (9.3% vs 10.2%, aRR 0.94, 95% CI 0.91 to 0.98), NICU admission (3.8% vs 4.4%, aRR 0.91, 95% CI 0.85 to 0.96), severe neonatal morbidity (2.7% vs 3.2%, aRR 0.91, 95% CI 0.85 to 0.98) and preterm birth (5.1% vs 5.8%, aRR 0.94, 95% CI 0.90 to 0.99) (tables 4 and 5).

Subgroup and sensitivity analyses

In additional analyses, results remained similar regardless of the trimester of vaccination for the first dose, the vaccine product and the number of doses. The magnitude and the direction of the estimates were also similar after restricting the analysis to those who gave birth during the period of access to SARS-CoV-2 tests, excluding those with a SARS-CoV-2 infection during pregnancy, or varying the date of conception to address uncertainties. Although most subgroup analyses indicated that vaccination was not significantly associated with preterm births, we found a significant increased risk for individuals vaccinated with only one dose during pregnancy. Results did not change after excluding those unvaccinated throughout the entire study period from the unvaccinated group, except for the very preterm outcome, for which the estimate suggested a non-significant reduction in risk associated with vaccination (aRR 0.88, 95% CI 0.74 to 1.04 vs aRR in main analysis 1.04, 95% CI 0.89 to 1.21). Finally, we found a significant increased risk associated with COVID-19 vaccination for very preterm birth, using a Cox regression model and considering vaccination during pregnancy as a time-varying exposure (aHR 1.23, 95% CI 1.05 to 1.43 in the Cox model for very premature birth in online supplemental table S4 vs aRR 1.04, 95% CI 0.89 to 1.21 in table 4). (See all the subgroup and sensitivity analyses in online supplemental table S4 in the Supplement).

DISCUSSION

In this large study examining maternal and neonatal outcomes in more than 140 000 singleton pregnancies and including more than 60 000 individuals vaccinated with a mRNA vaccine during pregnancy, we found no evidence that COVID-19 vaccination during pregnancy was associated with a significant increased risk of chorioamnionitis, postpartum haemorrhage, caesarean delivery, maternal ICU admission, stillbirth, SGA, NICU admission, severe neonatal morbidity or premature births. Results did not differ according to the trimester of vaccination, the number of doses received during pregnancy and the vaccine product.

Our study adds to existing evidence that COVID-19 vaccination during pregnancy does not increase the risk

BMJ Open: first published as 10.1136/bmjopen-2025-106494 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on May 1, 2026 at Institut national de santé publique du Québec . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 4 Association between COVID-19 vaccination during pregnancy and the risk of adverse neonatal outcomes

Outcomes	N (%)		Risk ratio (95% CI)	
	≥1 dose during pregnancy	No dose during pregnancy	Unadjusted	Adjusted*
Pregnancies with a live birth (cohort 2)	N=61 098	N=78 320		
Small for gestational age	5682 (9.3)	7996 (10.2)	0.91 (0.88 to 0.94)	0.94 (0.91 to 0.98)
NICU admission	2272/59 832† (3.8)	3353/76 437† (4.4)	0.86 (0.82 to 0.91)	0.91 (0.85 to 0.96)
Severe neonatal morbidity	1631/59 832† (2.7)	2455/76 437† (3.2)	0.85 (0.80 to 0.90)	0.91 (0.85 to 0.98)
Pregnancies with a live birth (cohort 2)	N=60 016	N=79 402		
Preterm birth <37 weeks	3079 (5.1)	4585 (5.8)	0.89 (0.85 to 0.93)	0.94 (0.90 to 0.99)
Spontaneous	2187 (3.6)	3244 (4.1)	0.89 (0.85 to 0.94)	0.95 (0.89 to 1.01)
Pregnancies with a live birth (cohort 2)	N=53 938	N=85 480		
Very preterm birth <32 weeks	319 (0.60)	613 (0.72)	0.83 (0.72 to 0.94)	1.04 (0.89 to 1.21)
Spontaneous	219 (0.41)	436 (0.51)	0.80 (0.68 to 0.94)	0.99 (0.82 to 1.19)

*Adjusted for maternal age at delivery, infant sex, maternal pre-existing conditions, healthcare provider status, SARS-CoV-2 positive test during pregnancy, social and material deprivation indexes, month and year of conception, Tdap vaccination during pregnancy and geographical areas using inverse probability of treatment weighting.
†For these issues, the information was only available in the newborn record linked with the mother record.
NICU, neonatal intensive care unit; Tdap, tetanus-diphtheria-acellular pertussis.

of adverse maternal and neonatal outcomes. Our findings for maternal outcomes are consistent with conclusions reported in a systematic review and meta-analysis from Watanabe *et al* including 81 349 pregnant individuals who received at least one COVID-19 vaccination during pregnancy and 255 246 pregnant individuals not vaccinated.[39] The pooled adjusted ORs were 0.95 (95% CI 0.83 to 1.07) for postpartum haemorrhage, 1.06 (95% CI 0.86 to 1.31) for chorioamnionitis and 1.05 (95% CI 0.93 to 1.21) for caesarean delivery. A Canadian study of 32 689 live births and stillbirths, including 18 491 individuals who received a third dose during pregnancy, reported aHRs for postpartum haemorrhage (1.01, 95% CI 0.89 to 1.16) and caesarean (0.90, 95% CI 0.87 to 0.94) that were similar to our estimates.[16] Authors observed a significant reduction in the risk of chorioamnionitis (aHR 0.67, 95% CI 0.49 to 0.90) which was not observed in our study. Our findings of a reduced risk for NICU admission and SGA were also consistent with those reported by Wanatabe *et al*, with pooled adjusted ORs of 0.88 (95% CI 0.80 to 0.97) and 0.99 (95% CI: 0.04 to 1.04), respectively. Vaccination was also associated with a reduced risk of SGA (aHR of 0.93, 95% CI: 0.88 to 0.99) in a study from England and Wales, which included 865 654 pregnant individuals, of whom 60 875 received the first dose during pregnancy.[40] Our results were also consistent with those reported in a study from Israel with 24 288 newborns, including 16 697 prenatally exposed to vaccination. They also reported no significant association with preterm birth (aRR 0.95, 95% CI 0.83 to 1.10) and SGA (aRR 0.97, 95% CI 0.87 to 1.08).[41] For stillbirth, studies that accounted for immortal time bias reported results consistent with a reduced risk associated with vaccination. Fell *et al* found a statistically significant reduction of risk, while Magnus *et al* reported an aHR of 0.86 with 95% CI that included the null value.[18 33] Although our estimate for stillbirth differs in direction, all estimates were consistent in showing that vaccination was not associated with an increased risk of stillbirth. A recent matched analysis of 276 confirmed stillbirths and 822 live births in the US Vaccine Safety Datalink found no association between COVID-19 vaccination during pregnancy and stillbirth (adjusted OR 1.02, 95% CI 0.76 to 1.37).[42]

Two studies that accounted for immortal time bias by treating vaccination as a time-varying exposure and using extended Cox regression models found that COVID-19 vaccination during pregnancy was not associated with an increased risk of preterm birth. The first study from Canada, which included 85 162 births and 43 099 individuals vaccinated during pregnancy, reported an aHR of 1.02 (95% CI 0.96 to 1.08) for preterm birth and 0.80 (95% CI 0.67 to 0.95) for very preterm birth.[33] In the second study conducted in Sweden and Norway and involving 157 521 births—including 28 506 individuals vaccinated during pregnancy—the aHR for preterm birth, pooled across both countries, was 0.98 (95% CI 0.91 to 1.05).[18] The positive association with vaccination (at least one dose) observed in our sensitivity analysis for

BMJ Open: first published as 10.1136/bmjopen-2025-106494 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on May 1, 2026 at Institut national de santé publique du Québec . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 5 Association between COVID-19 vaccination during pregnancy and the risk of stillbirth using a Cox regression model with time-varying exposure variable

	Vaccinated		Unvaccinated		HR (95% CI)	
Outcomes	Cases	Person-time at risk (days)	Cases	Person-time at risk (days)	Unadjusted	Adjusted*
Pregnancies with a live birth or stillbirth (cohort 1)						
Stillbirth	184	6 624 602	471	11 897 842	0.76 (0.64 to 0.91)	1.14 (0.94 to 1.39)

*Adjusted for maternal age at delivery, infant sex, maternal pre-existing conditions, healthcare provider status, SARS-CoV-2 positive test during pregnancy, social and material deprivation indexes, month and year of conception, Tdap vaccination during pregnancy and geographical areas using inverse probability of treatment weighting.
Tdap, tetanus-diphtheria-acellular pertussis.

very preterm birth should be interpreted with caution since it may reflect a type 1 error due to multiple testing or residual confounding by unmeasured characteristics and should be reassessed in future studies. There was also uncertainty in the estimate for very preterm birth due to the small number of events. Finally, we found a significant increased risk of preterm births among individuals vaccinated with only one dose during pregnancy, compared with those who were unvaccinated during pregnancy. However, individuals who gave birth prematurely may have been more likely to receive only one dose during pregnancy.

Strengths of this study include the large number of individuals vaccinated during pregnancy, as well as the variability in the timing of vaccination within the included cohort. This study also included periods during which vaccination was not limited to high-risk groups. The use of the provincial hospitalisation discharge database linked with the population-based vaccination registry ensures the cohort is representative of individuals who gave birth during the study period and provides accurate information on COVID-19 vaccine exposure during pregnancy. Nevertheless, this study has several limitations. Despite the availability of important potential confounders of the association between vaccination and outcomes and the adjustment done using propensity score weighting, we could not exclude the possibility of residual confounding. Indeed, we did not have information on some known risk factors for the outcomes of interest, such as parity, education level, ethnicity and smoking, which could be associated with vaccination. Although we did not have information on general attitudes regarding vaccination or health behaviours, Tdap vaccination during pregnancy was used as a proxy measure. Pregnant individuals with a more favourable health profile may be more likely to accept vaccination, a phenomenon called 'healthy vaccine effect', which could bias results downward.[43] Due to the data source used, our cohort included only pregnancies that reached at least 20 weeks of gestation. This could have introduced a selection bias if COVID-19 vaccination in early pregnancy (less than 20 weeks of gestation) led to an increased risk of pregnancy loss before 20 weeks of gestation. Published studies found no evidence of a significant increased risk of miscarriage following vaccination, although the RR or OR was slightly higher than 1 in some studies.[44–46] Non-differential misclassification of exposure and outcomes due to uncertainty for the date of conception was possible, but we observed similar results after varying the date of conception in sensitivity analyses. Non-differential outcomes misclassification is also possible due to errors in the codes assigned for some diagnostics.

Although the risk of hospitalisation and death among pregnant individuals has significantly decreased during the Omicron period, this group remains at higher risk of severe maternal complications, especially among those with severe COVID-19 symptoms and who are unvaccinated.[47 48] Vaccination during pregnancy can effectively reduce this risk.[3] Maternal vaccination could also protect young infants against severe disease during the first months of life through the transplacental passage of antibodies.[47] We observed a reduction in the risk of caesarean delivery, maternal and neonatal ICU admission, SGA, severe morbidity index and preterm birth among individuals vaccinated during pregnancy compared with those who were not vaccinated. This is consistent with existing evidence suggesting that COVID-19 vaccination during pregnancy may reduce the risk of adverse maternal and neonatal outcomes.[48] While severe COVID-19 is known to increase the risk of adverse pregnancy outcomes, our analysis suggests that infection prevention does not fully explain the reduced risk, since we adjusted for documented SARS-CoV-2 infection during pregnancy and results remained consistent in sensitivity analysis after excluding individuals with documented infection during pregnancy. Residual confounding is also possible, as we were not able to adequately account for confirmed SARS-CoV-2 infection during pregnancy due to changes in the screening strategy over the study period. In the sensitivity analysis using time-varying exposure and a Cox regression model, the protective effect of COVID-19 vaccines on preterm birth was annulled (aHR 1.01, 95% CI 0.96 to 1.06). Findings from this study, consistent with those of other studies, provide additional reassurance that COVID-19 vaccination during pregnancy is not associated with an increased

BMJ Open: first published as 10.1136/bmjopen-2025-106494 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on May 1, 2026 at Institut national de santé publique du Québec . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

risk of adverse maternal or neonatal outcomes. These findings would likely contribute to reducing vaccine hesitancy and increasing the acceptability of the COVID-19 vaccination during pregnancy. Future studies should include more pregnant individuals vaccinated during the first trimester to better assess outcomes with an earlier gestational onset or those plausibly associated with early pregnancy exposure. The comparison of different approaches for handling immortal time bias in estimating the effects of vaccination during pregnancy would be of interest.[49] Finally, ongoing surveillance of the safety of maternal COVID-19 vaccination is essential, as additional doses of COVID-19 vaccine are recommended for pregnant individuals in many countries.

CONCLUSIONS

Our findings, consistent with existing evidence, support that COVID-19 vaccination during pregnancy is not associated with an increased risk of adverse maternal and neonatal outcomes. Ongoing surveillance of the safety of maternal COVID-19 vaccination is essential to ensure the benefit-RR remains favourable in this population. Future studies should focus on outcomes plausibly associated with vaccination earlier in pregnancy, such as congenital anomalies.

Author affiliations
[1]Médecine sociale et préventive, Université Laval Faculté de Médecine, Québec City, Quebec, Canada
[2]Centre de recherche du CHU de Québec-Université Laval Site CHUL, Québec City, Quebec, Canada
[3]Institut national de santé publique du Québec, Québec City, Quebec, Canada
[4]Quebec National Institute of Public Health, Quebec City, Quebec, Canada
[5]OriginElle Fertility Clinic and Women's Health Center, Montreal, Quebec, Canada
[6]Pédiatrie, Université Laval, Québec City, Quebec, Canada
[7]Department of Epidemiology, Biostatistics and Occupational Health, University of Montreal, Montreal, Quebec, Canada
[8]Marshfield Clinic Research Institute, Marshfield, Wisconsin, USA
[9]CHU Sainte-Justine, Montreal, Quebec, Canada
[10]Université de Montréal, Montreal, Quebec, Canada

Acknowledgements This study received funding from the Canadian Immunization Research Network (CIRN) through a grant from the Canadian Institutes of Health Research and The Public Health Agency of Canada (450980). CIRN is a national network, supported through a Canadian Institutes of Health Research (CIHR) grant, composed of key vaccine researchers who develop and test methodologies related to the evaluation of vaccines as they pertain to safety, immunogenicity and effectiveness and programme implementation and evaluation. The views here do not necessarily represent the views of the Public Health Agency of Canada. DT, IB and AB are supported by Fonds de recherche du Québec research career awards.

Contributors MK, GP-S and ED conceptualised the design and initial protocol for this study. ID, NB, SQW, DT, AB, CQ, SJ and IB provided feedback on the study protocol. ID and MK performed the analysis. MK wrote the first draft of the manuscript, and all authors critically reviewed the manuscript for intellectual content and approved the final version before submission. The corresponding author, MK, attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. MK is responsible for the overall content as the guarantor.

Funding This study received funding from the Canadian Immunization Research Network (CIRN) through a grant from the Canadian Institutes of Health Research and The Public Health Agency of Canada (450980). CIRN is a national network, support through a Canadian Institutes of Health Research (CIHR) grand, composed of key vaccine researchers who develop, and test methodologies related to the evaluation of vaccines as they pertain to safety, immunogenicity and effectiveness and program implementation and evaluation. The views herein do not necessarily represent the views of the Public Health Agency of Canada. DT, IB and AB are supported by Fonds de recherche du Québec research career awards.

Competing interests IB has received consultant fees from Moderna and Pfizer, and research support from Altona and Moderna outside of the submitted work. Other authors have no competing interests to declare.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by CHU de Québec-Université Laval Research Center (# 2024-7273). Patient consent was not required for this study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. Underlying data cannot be publicly shared by the authors, as it belongs to the Ministère de la Santé et des Services sociaux du Québec, and access to the data was granted to researchers under the legal mandate of the Quebec National Director of Public Health. Data access requests should be directed to the research access centre designated by Quebec government, in accordance with the Act respecting health and social services information (https://statistique.quebec.ca/en/institut/services-for-researchers/data).

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution 4.0 Unported (CC BY 4.0) license, which permits others to copy, redistribute, remix, transform and build upon this work for any purpose, provided the original work is properly cited, a link to the licence is given, and indication of whether changes were made. See: https://creativecommons.org/licenses/by/4.0/.

ORCID iDs
Marilou Kiely https://orcid.org/0000-0002-0235-3630
Nicholas Brousseau https://orcid.org/0000-0001-6042-3177
Denis Talbot https://orcid.org/0000-0003-0431-3314
Isabelle Boucoiran https://orcid.org/0000-0001-9545-6024

REFERENCES

1 Falahi S, Abdoli A, Kenarkoohi A. Maternal COVID-19 infection and the fetus: Immunological and neurological perspectives. *New Microbes New Infect* 2023;53:101135.
2 Alesci A, Pergolizzi S, Fumia A, *et al*. Immune System and Psychological State of Pregnant Women during COVID-19 Pandemic: Are Micronutrients Able to Support Pregnancy? *Nutrients* 2022;14:2534.
3 Allotey J, Stallings E, Bonet M, *et al*. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ* 2020;370:m3320.
4 Smith ER, Oakley E, Grandner GW, *et al*. Adverse maternal, fetal, and newborn outcomes among pregnant women with SARS-CoV-2 infection: an individual participant data meta-analysis. *BMJ Glob Health* 2023;8:e009495.
5 Wei SQ, Bilodeau-Bertrand M, Liu S, *et al*. The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. *CMAJ* 2021;193:E540–8.
6 Sarwal Y, Sarwal T, Sarwal R. Prioritizing pregnant women for COVID-19 vaccination. *Int J Gynaecol Obstet* 2021;155:57–63.
7 Public Health Agency o Canada. Immunization in pregnancy and breastfeeding: Canadian immunization guide. 2007. Available: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-

BMJ Open: first published as 10.1136/bmjopen-2025-106494 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on May 1, 2026 at Institut national de santé publique du Québec . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

specific-populations/page-4-immunization-pregnancy-breastfeeding.html
8 Lapinsky SC, Baxter NN, Sutradhar R, *et al*. A Population-Based Test-Negative Matched Case-Control Analysis of SARS-CoV-2 Vaccine Effectiveness Among Pregnant People in Ontario, Canada. *J Obstet Gynaecol Can* 2024;46:102239.
9 Jorgensen SCJ, Hernandez A, Fell DB, *et al*. Estimated Effectiveness of Postpartum Maternal Messenger RNA COVID-19 Vaccination Against Delta and Omicron SARS-CoV-2 Infection and Hospitalization in Infants Younger Than 6 Months. *JAMA Pediatr* 2023;177:427–30.
10 Blakeway H, Prasad S, Kalafat E, *et al*. COVID-19 vaccination during pregnancy: coverage and safety. *Am J Obstet Gynecol* 2022;226:236.
11 Stock SJ, Carruthers J, Calvert C, *et al*. SARS-CoV-2 infection and COVID-19 vaccination rates in pregnant women in Scotland. *Nat Med* 2022;28:504–12.
12 Battarbee AN, Stockwell MS, Varner M, *et al*. Attitudes Toward COVID-19 Illness and COVID-19 Vaccination among Pregnant Women: A Cross-Sectional Multicenter Study during August-December 2020. *Am J Perinatol* 2022;39:75–83.
13 Carbone L, Mappa I, Sirico A, *et al*. Pregnant women's perspectives on severe acute respiratory syndrome coronavirus 2 vaccine. *American Journal of Obstetrics & Gynecology MFM* 2021;3:100352.
14 Reifferscheid L, Marfo E, Assi A, *et al*. COVID-19 vaccine uptake and intention during pregnancy in Canada. *Can J Public Health* 2022;113:547–58.
15 Dick A, Rosenbloom JI, Gutman-Ido E, *et al*. Safety of SARS-CoV-2 vaccination during pregnancy- obstetric outcomes from a large cohort study. *BMC Pregnancy Childbirth* 2022;22:166.
16 Fell DB, Dimanlig-Cruz S, Török E, *et al*. Pregnancy, fetal, and neonatal outcomes after a first booster dose of covid-19 vaccine during pregnancy in Ontario, Canada: population based, retrospective cohort study. *BMJ Med* 2023;2:e000632.
17 Fell DB, Dhinsa T, Alton GD, *et al*. Association of COVID-19 Vaccination in Pregnancy With Adverse Peripartum Outcomes. *JAMA* 2022;327:1478–87.
18 Magnus MC, Örtqvist AK, Dahlqwist E, *et al*. Association of SARS-CoV-2 Vaccination During Pregnancy With Pregnancy Outcomes. *JAMA* 2022;327:1469–77.
19 Naleway AL, Crane B, Irving SA, *et al*. Vaccine Safety Datalink infrastructure enhancements for evaluating the safety of maternal vaccination. *Ther Adv Drug Saf* 2021;12:20420986211021233.
20 Sadarangani M, Soe P, Shulha HP, *et al*. Safety of COVID-19 vaccines in pregnancy: a Canadian National Vaccine Safety (CANVAS) network cohort study. *Lancet Infect Dis* 2022;22:1553–64.
21 Benchimol EI, Smeeth L, Guttmann A, *et al*. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. *PLoS Med* 2015;12:e1001885.
22 Fell DB, Dimitris MC, Hutcheon JA, *et al*. Guidance for design and analysis of observational studies of fetal and newborn outcomes following COVID-19 vaccination during pregnancy. *Vaccine (Auckl)* 2021;39:1882–6.
23 Institut de la statistique du Québec. Portrait des enfants du québec: de la grossesse aux premiers mois de la vie. 2023. Available: https://statistique.quebec.ca/fr/produit/publication/portrait-enfants-quebec-grossesse-premiers-mois-vie
24 Blais C, Jean S, Sirois C, *et al*. Le Système intégré de surveillance des maladies chroniques du Québec (SISMACQ), une approche novatrice. *Maladies Chroniques et Blessures Au Canada* 2014;34:247–56.
25 Gamache P, Hamel D, Blaser C. Material and social deprivation index: a summary. INSPQ Website. Available: https://www.inspq.qc.ca/en/publications/2639 [Accessed 13 Nov 2023].
26 Neophytou AM, Kioumourtzoglou MA, Goin DE, *et al*. Educational note: addressing special cases of bias that frequently occur in perinatal epidemiology. *Int J Epidemiol* 2021;50:337–45.
27 Strand LB, Barnett AG, Tong S. Methodological challenges when estimating the effects of season and seasonal exposures on birth outcomes. *BMC Med Res Methodol* 2011;11:49.
28 Vazquez-Benitez G, Kharbanda EO, Naleway AL, *et al*. Risk of Preterm or Small-for-Gestational-Age Birth After Influenza Vaccination During Pregnancy: Caveats When Conducting Retrospective Observational Studies. *Am J Epidemiol* 2016;184:176–86.
29 Lindsay L, Calvert C, Shi T, *et al*. Neonatal and maternal outcomes following SARS-CoV-2 infection and COVID-19 vaccination: a population-based matched cohort study. *Nat Commun* 2023;14:5275.
30 Scheller NM, Pasternak B, Mølgaard-Nielsen D, *et al*. Quadrivalent HPV Vaccination and the Risk of Adverse Pregnancy Outcomes. *N Engl J Med* 2017;376:1223–33.
31 World Health Organization (WHO). COVID-19 vaccines: safety surveillance manual. module on safety surveillance of COVID-19 vaccines in pregnant and breastfeeding women. 2021. Available: https://iris.who.int/bitstream/handle/10665/342538/WHO-MHP-RPQ-PVG-2021.1-eng.pdf?isAllowed=y&sequence=1
32 Kramer MS, Zhang X, Platt RW. Analyzing risks of adverse pregnancy outcomes. *Am J Epidemiol* 2014;179:361–7.
33 Fell DB, Dimanlig-Cruz S, Regan AK, *et al*. Risk of preterm birth, small for gestational age at birth, and stillbirth after covid-19 vaccination during pregnancy: population based retrospective cohort study. *BMJ* 2022;378:e071416.
34 Fakhraei R, Crowcroft N, Bolotin S, *et al*. Obstetric and perinatal health outcomes after pertussis vaccination during pregnancy in Ontario, Canada: a retrospective cohort study. *Cmajo* 2021;9:E349.
35 Lain SJ, Algert CS, Nassar N, *et al*. Incidence of Severe Adverse Neonatal Outcomes: Use of a Composite Indicator in a Population Cohort. *Matern Child Health J* 2012;16:600–8.
36 Austin PC, Stuart EA. Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. *Stat Med* 2015;34:3661–79.
37 Talbot D, Mésidor M, Chiu Y, *et al*. An Alternative Perspective on the Robust Poisson Method for Estimating Risk or Prevalence Ratios. *Epidemiology* 2023;34:1–7.
38 Schoenfeld D. Partial residuals for the proportional hazards regression model. *Biometrika* 1982;69:239–41.
39 Watanabe A, Yasuhara J, Iwagami M, *et al*. Peripartum Outcomes Associated With COVID-19 Vaccination During Pregnancy: A Systematic Review and Meta-analysis. *JAMA Pediatr* 2022;176:1098–106.
40 Raffetti E, Bolton T, Nolan J, *et al*. COVID-19 diagnosis, vaccination during pregnancy, and adverse pregnancy outcomes of 865,654 women in England and Wales: a population-based cohort study. *Lancet Reg Health Eur* 2024;45:101037.
41 Goldshtein I, Steinberg DM, Kuint J, *et al*. Association of BNT162b2 COVID-19 Vaccination During Pregnancy With Neonatal and Early Infant Outcomes. *JAMA Pediatr* 2022;176:470–7.
42 Denoble AE, Vazquez-Benitez G, Sheth SS, *et al*. Coronavirus Disease 2019 (COVID-19) Vaccination and Stillbirth in the Vaccine Safety Datalink. *Obstet Gynecol* 2024;144:215–22.
43 Savitz DA, Fell DB, Ortiz JR, *et al*. Does influenza vaccination improve pregnancy outcome? Methodological issues and research needs. *Vaccine (Auckl)* 2015;33:6430–5.
44 Kharbanda EO, Haapala J, DeSilva M, *et al*. Spontaneous Abortion Following COVID-19 Vaccination During Pregnancy. *JAMA* 2021;326:1629–31.
45 Rimmer MP, Teh JJ, Mackenzie SC, *et al*. The risk of miscarriage following COVID-19 vaccination: a systematic review and meta-analysis. *Hum Reprod* 2023;38:840–52.
46 Magnus MC, Gjessing HK, Eide HN, *et al*. Covid-19 Vaccination during Pregnancy and First-Trimester Miscarriage. *N Engl J Med* 2021;385:2008–10.
47 Halasa NB, Olson SM, Staat MA, *et al*. Maternal Vaccination and Risk of Hospitalization for Covid-19 among Infants. *N Engl J Med* 2022;387:109–19.
48 Male V, Jones CE. Vaccination in pregnancy to protect the newborn. *Nat Rev Immunol* 2025;25:649–61.
49 Hernández-Díaz S, Huybrechts KF, Chiu YH, *et al*. Emulating a Target Trial of Interventions Initiated During Pregnancy with Healthcare Databases: The Example of COVID-19 Vaccination. *Epidemiology* 2023;34:238–46.

BMJ Open: first published as 10.1136/bmjopen-2025-106494 on 23 December 2025. Downloaded from http://bmjopen.bmj.com/ on May 1, 2026 at Institut national de santé publique du Québec . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.