An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI)

Guidance on the use of COVID-19 vaccines during the fall of 2024

PROTECTING AND EMPOWERING CANADIANS TO IMPROVE THEIR HEALTH

Public Health Agency of Canada
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Preamble

The National Advisory Committee on Immunization (NACI) is an External Advisory Body that provides the Public Health Agency of Canada (PHAC) with independent, ongoing and timely medical, scientific, and public health advice in response to questions from PHAC relating to immunization.

In addition to burden of disease and vaccine characteristics, PHAC has expanded the mandate of NACI to include the systematic consideration of programmatic factors in developing evidence based recommendations to facilitate timely decision-making for publicly funded vaccine programs at provincial and territorial levels.

The additional factors to be systematically considered by NACI include: economics, ethics, equity, feasibility, and acceptability. Not all NACI statements will require in-depth analyses of all programmatic factors. While systematic consideration of programmatic factors will be conducted using evidence-informed tools to identify distinct issues that could impact decision-making for recommendation development, only distinct issues identified as being specific to the vaccine or vaccine-preventable disease will be included.

This statement contains NACI's independent advice and recommendations, which are based upon the best current available scientific knowledge. This document is being disseminated for information purposes. People administering the vaccine should also be aware of the contents of the relevant product monograph. Recommendations for use and other information set out herein may differ from that set out in the product monographs of the Canadian manufacturers of the vaccines. Manufacturer(s) have sought approval of the vaccines and provided evidence as to its safety and efficacy only when it is used in accordance with the product monographs. NACI members and liaison members conduct themselves within the context of PHAC's Policy on Conflict of Interest, including yearly declaration of potential conflict of interest.

Background

Over the past several years, NACI has recommended individuals receive a recently updated COVID-19 vaccine starting in the fall, when increased activity of respiratory viruses is observed. Receiving an updated vaccine is expected to offer additional protection against SARS-CoV-2 infection and severe COVID-19 disease since the strain(s) in the updated vaccines are likely to be more closely related to circulating strains, and the additional dose is expected to increase the immune response that has waned over time.

As COVID-19 activity is expected during the upcoming fall and winter months, and COVID-19 disease can compound the impact on the health system of other fall and winter respiratory viruses, NACI continues to provide early guidance on the use of COVID-19 vaccines to facilitate planning by provinces and territories. An updated vaccine to replace the current XBB.1.5 vaccine may be available starting in the fall of 2024, depending on the epidemiology of SARS-CoV-2 and recommendations of international advisory groups expected in mid-spring 2024.

Methods

On December 5, 2023, and January 19, 2024, the NACI COVID-19 Working Group (COVID-19 WG) reviewed the available information on SARS-CoV-2 epidemiology and seroprevalence, vaccine effectiveness (VE) of XBB.1.5 vaccines, and concurrent administration with COVID-19 vaccines. Preliminary cost-effectiveness estimates for a fall 2024 campaign were also reviewed.

On February 7, NACI reviewed the evidence presented to the COVID-19 WG, including evidence for children, with additional evidence on the epidemiology in adults assessed prior to reaching consensus on the proposed recommendations. The statement was approved on April 9, 2024.

Further information on NACI's process and procedures is available elsewhere [1, 2].

Overview of evidence

Information available as of February 7, 2024 (except where otherwise noted) is summarized below.

Epidemiology

- The evolutionary trajectory of SARS-CoV-2 remains uncertain and seasonality of SARS-CoV-2 has not been established. However, based on previous years and consistent with other respiratory viruses, a surge in COVID-19 activity is expected during the fall and winter months.
- Omicron sublineages of SARS-CoV-2 continue to circulate in Canada and globally. From sequencing data up to the week of March 10, 2024, JN.1 sublineages, are the most prevalent among all positive cases sampled across Canada at present [3].
- There is high infection-acquired seroprevalence in the Canadian population [4]. Among adults, infection-acquired seroprevalence decreases with increased age, with older individuals having higher levels of immunity derived from vaccination alone compared to younger age groups.

Vaccine protection and hybrid immunity

- VE trends across earlier COVID-19 vaccine products (including the first original strain mRNA and protein subunit vaccines, and the subsequent bivalent mRNA vaccines) have demonstrated short-term protection against infection, with duration of protection typically lasting longer against severe outcomes compared to infection [5, 6]. These trends are also expected with the XBB.1.5 vaccines.
- There are limited follow-up studies evaluating VE following vaccination with updated COVID-19 vaccines during the fall/winter 2023-2024 vaccination campaigns; however, emerging evidence suggests that waning VE against symptomatic infection may occur in the first 4 months, similar to previous COVID-19 vaccines [7].
    - Available study results showed that the short-term relative vaccine effectiveness of XBB.1.5 mRNA COVID-19 vaccines in adults has been estimated to be approximately 50% to 60% against symptomatic disease and 60 to 70% against hospitalization.
    - For symptomatic disease based on a US study, vaccine effectiveness was somewhat lower for strains that were likely BA.2.86/JN.1 (49%, 95% CI: 19 to 68%, with a median of 80 days from vaccination to testing positive) than for strains that were likely XBB* sub-lineages (60%, 95% CI: 36 to 74%, with a median of 73 days from vaccination to testing positive), although confidence intervals (CI) overlapped [7-10].
- There are currently no VE estimates of the XBB.1.5 monovalent vaccine in newly vaccinated or previously vaccinated pediatric populations, but trends are expected to be similar to those observed in adults, as with previous formulations.
- In clinical trials and observational studies, XBB.1.5 vaccines have been shown to induce cross-reactive immune responses against earlier SARS-CoV-2 variants and XBB* sublineages, as well as more antigenically distant Omicron subvariants that became more prevalent in the fall/winter 2023-2024 season, including BA.2.86 and its sublineage JN.1, however titres to JN.1 were lower than against XBB* sublineages [11-16].
- Hybrid immunity offers greater protection against infection and severe disease than prior infection or vaccination alone, particularly when hybrid immunity is in the context of a recent infection; however, this protection wanes over time [17-25].
- Several systematic review and meta-analysis studies have demonstrated that a primary series was associated with lower risk of developing multisystem inflammatory syndrome in children (MIS-C) among children and adolescents under 18 years of age compared to the unvaccinated, with VE estimates against MIS-C ranging from 78 to 95% in observational studies [26-28].
- To the extent that vaccination prevents infection, it also prevents post-COVID-19 condition (PCC). People who are vaccinated and become infected have additional protection against PCC compared to those who are not vaccinated. There appears to be a positive relationship between the number of doses received and level of protection against PCC [29-31].

* Includes all descendant lineages, unless otherwise specified.

Vaccine safety

- Evidence on vaccine safety is available from COVID-19 clinical trials and ongoing national and international COVID-19 vaccine safety monitoring. In clinical trials, booster doses of updated COVID-19 vaccines (bivalent or monovalent XBB.1.5) have been shown to have similar reactogenicity as booster doses of original COVID-19 vaccines. [11, 32, 33] No new adverse events have been identified to date with the use of the XBB.1.5 COVID-19 vaccines.

For more information, please see the section on safety and adverse events in the COVID-19 vaccines chapter of the Canadian Immunization Guide (CIG).

Concurrent administration with other vaccines

- The effects of concurrent administration of COVID-19 vaccines and other vaccines on VE, safety outcomes and immunogenicity outcomes have been assessed in randomized-controlled trials and observational studies [34-68]. The majority of studies assessed concurrent administration of COVID-19 vaccines with influenza vaccines. One study assessed concurrent administration with a pneumococcal vaccine and another with herpes zoster vaccine. All studies were conducted with original or bivalent (original + BA.1 or BA.4/5) COVID-19 vaccines. No data are currently available for concurrent administration of XBB.1.5 monovalent vaccines and other vaccines.
- Most studies reported no safety issues after concurrent administration of vaccines compared to separate administration. In some studies, reactogenicity after concurrent administration of COVID-19 vaccines and influenza vaccines was increased compared to influenza vaccination alone, but comparable to COVID-19 vaccination alone [43, 48, 53, 56].
- A statistical signal for ischemic stroke among adults 65 years of age and older was detected in the US Vaccine Safety Datalink (VSD) in October 2022 following administration of Pfizer-BioNTech Comirnaty BA.4/5 bivalent. This signal has weakened over time since October 2022 and as of April 2023, it was no longer being detected [69]. The signal was not detected with Moderna Spikevax BA.4/5 vaccines. While subsequent analyses in the US showed variable and inconsistent results on the association of ischemic stroke and bivalent mRNA vaccines concurrently administered with influenza vaccines, most analyses, from several countries, did not show an association between bivalent mRNA vaccines and ischemic stroke, given alone or concurrently administered with influenza vaccines [45, 50, 59, 62, 70, 71]. The totality of data available at this time does not support an association between ischemic stroke and bivalent mRNA vaccines given alone or concurrently with influenza vaccines. Future analyses should account for potential confounding factors including variation in stroke incidence by calendar period.
- Some studies have reported reduced immune responses against SARS-CoV-2 with concurrent administration of COVID-19 vaccines and influenza vaccines [36, 43, 46, 48],

however the majority of studies (including those that analyzed concurrent administration with pneumococcal vaccine and herpes zoster vaccine) report non-inferior immune responses with concurrent administration compared to administration of COVID-19 vaccines alone [47, 54, 55, 58, 64, 65, 67]. In the studies that did report lower immune responses after concurrent administration with influenza vaccine, the clinical significance of these decreases and impact on VE is not known.

- One study conducted in the US showed similar VE against COVID-19 and influenza-related outpatient visits, emergency department visits and hospitalizations after concurrent administration of Pfizer-BioNTech Comirnaty BA.4/5 bivalent and seasonal influenza vaccines compared to either vaccine alone [68]. A study from Italy reported no difference in the rate of breakthrough SARS-CoV-2 infections between groups that received Pfizer-BioNTech Comirnaty original concurrently with standard dose quadrivalent influenza vaccine and groups that received Pfizer-BioNTech Comirnaty original alone [53].

Economics

- Canadian provinces and territories continue to access supply of COVID-19 vaccines that were procured under federal pandemic investments, and therefore the vaccine product cost has been assumed by the Government of Canada. This supply is expected to be available at no cost to provinces and territories in the fall of 2024. However, provinces and territories continue to bear the costs associated with administering the vaccination program.
- Modelling and cost-effectiveness analyses are underway to inform future COVID-19 vaccine program decisions. These analyses are expected to become more important for jurisdictional decision-making as programs transition to traditional procurement pathways, which consider program requirements and budget assessments, and are led by provinces and territories.
    - A preliminary model-based cost-utility analysis of various age eligibilities for a fall COVID-19 vaccination program suggests that a program for all ages prevents the most COVID-attributable infections and severe outcomes, while a program offered to the population aged 65 and older has the smallest number needed to vaccinate to prevent a severe outcome.
    - From a health system perspective, vaccination programs for the following population groups in the fall were identified as likely cost-effective options at a cost-effectiveness threshold of $50,000 per quality-adjusted life year (QALY) gained: adults aged 65 and older (incremental cost-effectiveness ratio [ICER] of $8,099 per QALY); adults 50 years and older (ICER of $12,518 per QALY); or the entire vaccine-eligible population (ICER of $16,104 per QALY). From the societal perspective, a program offered to the entire vaccine-eligible population was less costly and more effective than all other program options considered.
    - These findings were found to be robust in probabilistic and one-way sensitivity analyses, including an analysis that considered alternate assumptions about vaccine prices.
    - Key assumptions for this analysis include different levels of vaccine coverage by age group (increasing uptake with increasing age), increased transmission of

SARS-CoV-2 in the fall and less transmission in the spring, and higher protection from infection and disease for people with prior protection from infection and/or vaccination compared to people with no prior protection.

- A publication providing more details pertaining to the economic analysis is anticipated in the coming months.

Ethics, equity, feasibility, and acceptability

- NACI continues to simplify COVID-19 recommendations where possible, balancing available scientific evidence, expert advice and programmatic considerations. While broad recommendations support access to those who want to be vaccinated, risk-based recommendations highlight those for whom vaccination is particularly important and can facilitate more tailored communication of guidance to individuals at high-risk.
- Overall COVID-19 vaccine uptake is declining with each additional campaign, but continues to be highest in older adults (particularly those 80 years of age and older, where there was a 53% uptake of the XBB.1.5 COVID-19 vaccine as of February 25, 2024) [72].
- Establishing a clear minimum interval of 3 months from the last dose for previously vaccinated individuals will allow flexibility for programs and ensure that vaccination opportunities are not missed. This would be particularly important for high-risk individuals receiving both a spring and fall 2024 COVID-19 dose.

Timing of vaccination

- The selection of the strain to be included in the COVID-19 vaccine available in the fall of 2024 is expected to occur in spring 2024.
- There is not yet sufficient data to determine the best time to start the COVID-19 vaccination program in the fall, although preliminary observations from previous seasons suggest that COVID-19 activity began to increase before fall vaccination campaigns were rolled out. In 2023, the national percent positivity of COVID-19 testing began to increase in mid-August.

For further information on NACI's recommendations on the use of COVID-19 vaccines, please refer to NACI: Statements and publications and the COVID-19 vaccines chapter of the CIG.

Recommendations

Please see Table 3 for an explanation of strong versus discretionary NACI recommendations.

Beginning in the fall of 2024, NACI recommends the following for the use of the most recently updated COVID-19 vaccines*:

1. **COVID-19 vaccination is recommended for previously vaccinated and unvaccinated individuals at increased risk of SARS-CoV-2 infection or severe COVID-19 disease as follows:**
    - **All adults 65 years of age or older**
    - **Those 6 months of age and older who are:**
        - **Residents of long-term care homes and other congregate living settings**
        - **Individuals with underlying medical conditions that place them at higher risk of severe COVID-19, including children** with complex health needs**
        - **Individuals who are pregnant**
        - **Individuals in or from First Nations, Métis and Inuit communities*****
        - **Members of racialized and other equity-deserving communities**
        - **People who provide essential community services**

    * Only vaccines containing the latest selected strain should be used in fall 2024.

    ** There is limited evidence on clinical risk factors for severe COVID-19 disease in pediatric populations. Children at increased risk for severe outcomes may include children who are medically fragile/have medical complexities, children with more than one comorbidity, children with neurological disorders, children with chronic lung disease, and children with Down syndrome (Trisomy 21), and other immunocompromising conditions.

    *** Autonomous decisions should be made by Indigenous Peoples with the support of healthcare and public health partners in accordance with the *United Nations Declaration on the Rights of Indigenous Peoples Act*.

    (*Strong NACI recommendation*)

2. **All other previously vaccinated and unvaccinated individuals (6 months of age and older) who are not at increased risk for SARS-CoV-2 infection or severe COVID-19 disease (i.e., not on the list above) may receive the most recently updated vaccine in the fall of 2024.**

    (*Discretionary NACI recommendation*)

3. **For unvaccinated individuals 5 years of age and older who are moderately to severely immunocompromised*, NACI recommends that 2 doses should be given *(Strong NACI recommendation)* and an additional dose (for a total of 3 doses) may be given, regardless of vaccine platform.**

(***Discretionary NACI recommendation***)

- This is an updated recommendation for unvaccinated individuals 5 years of age and older who are moderately to severely immunocompromised to provide additional protection for this population, if needed, due to their unique considerations regarding immunization. This recommendation can be implemented at any time prior to fall 2024.
- Additional doses above the authorized schedule are intended to improve the immune response. For individuals 5 years of age and older, although two doses can provide good protection, not all individuals with immunocompromising conditions will respond to vaccination in the same way and not all will have a previous SARS-CoV-2 infection in order to benefit from the immunological advantage of hybrid immunity. In some cases, an additional dose (i.e., a total of 3 doses for those 5 years of age and older may be needed to develop adequate protection, while some others will not be able to mount a sufficient response even with additional doses. Healthcare providers can use clinical discretion to determine the potential benefit of a third dose.
- New recipients of haematopoietic stem cell transplantation (HSCT) or chimeric antigen receptor (CAR) T-cell therapy are considered immunologically naïve and should be vaccinated with 3 doses beginning at 3 to 6 months post-HSCT/CAR T-cell therapy, regardless of vaccination or infection history prior to transplant/therapy, with 4 to 8 weeks between doses. This is consistent with the premise that 3 antigen exposures are helpful to establish a foundation of robust immunity.
- The recommended interval between doses for unvaccinated individuals who are moderately to severely immunocompromised is 4 to 8 weeks.

For additional information on COVID-19 vaccination for these individuals, please see the COVID-19 vaccines chapter and Immunization of immunocompromised persons chapter in the CIG.

*It should be noted that there is no change to the recommendations published in October 2023 for unvaccinated individuals 6 months to under 5 years of age who are moderately to severely immunocompromised. For these individuals, NACI reiterates the recommendation to receive one additional dose beyond the authorized 2-dose or 3-dose schedule for unvaccinated individuals 6 months to under 5 years of age (i.e., for moderately to severely immunocompromised children 6 months to under 5 years of age, 3 doses of Moderna Spikevax [preferred due to fewer doses required] or 4 doses of Pfizer-BioNTech Comirnaty), with a 4- to 8-week interval between doses. The additional doses are needed in this very young population as they are less likely to have been infected, and therefore less likely to have developed hybrid immunity, compared to individuals 5 years of age and older.

Additional considerations:

- Either an mRNA or protein subunit COVID-19 vaccine can be used in unvaccinated or previously vaccinated individuals who do not have contraindications to the vaccine. The authorized ages for COVID-19 vaccines for XBB.1.5 vaccines (i.e., 6 months of age and older for mRNA COVID-19 vaccines and 12 years of age and older for the protein subunit vaccine) may be the same for the products available in fall 2024.

- For previously vaccinated individuals, the recommended interval is 6 months from the last dose, and the minimum interval is 3 months from the last dose. This minimum interval of 3 months will ensure that those who receive a spring 2024 dose (which includes those who are most at risk for severe disease) will be eligible again for an updated fall 2024 dose when it becomes available. Individuals/immunizers may consider delaying COVID-19 vaccination by 3 to 6 months in circumstances where recent test-confirmed SARS-CoV-2 infection is known for previously vaccinated individuals.
- Consistent with previous guidance, COVID-19 vaccines may be given concurrently (i.e., same day), or at any time before or after non-COVID-19 vaccines (including live and non-live vaccines).
- Regulatory bodies may recommend an update to the antigenic target of COVID-19 vaccines that will be available for the fall of 2024. Using the updated vaccines for fall 2024 vaccination programs are expected to provide better immune responses against circulating SARS-CoV-2 strains compared to earlier vaccines. As demonstrated in previous fall/winter seasons, strains may continue to mutate, with different sublineages emerging that are not an exact antigenic match to available vaccines. However, a certain degree of cross-reactive immune response and associated cross-protection from recent vaccination can be expected based on evidence with COVID-19 vaccines to date, some of which has been described above.

Choice of COVID-19 vaccine

- The decision to include specific vaccines as part of provincial and territorial programs depends on several factors, including vaccine characteristics, cost-effectiveness evaluation, and other programmatic and operational factors, such as implementation strategies.
- Unique to the COVID-19 vaccine context is that acceptability and access to COVID-19 vaccines have been influenced by earlier preferential recommendations for mRNA vaccines. The previous preferential recommendation is no longer in place as the most recently updated mRNA and protein subunit COVID-19 vaccines target the same sublineage, and evidence continues to support the effectiveness and safety profile of the protein subunit vaccine platform (see NACI Updated guidance on the use of protein subunit COVID19 vaccine [Novavax Nuvaxovid]). Product preferences may continue to exist within the population because of the past products they received, and considerable public awareness that developed during the pandemic around specific COVID-19 vaccine products. Public health programs should consider the impact of limiting access to only one COVID-19 vaccine platform on vaccine acceptance and uptake.
- Table 1 provides age group-specific recommendations for age-appropriate COVID-19 vaccines authorized and available for use in Canada based on current XBB.1.5 age authorizations. Table 2 provides a comparison between mRNA and protein subunit COVID-19 vaccines based on previous vaccines and currently available XBB.1.5 vaccines.

Table 1. Available COVID-19 vaccines authorized and recommended by age group (based on authorized ages for currently available XBB.1.5 vaccines[a])

Recipient by age group	Vaccine types authorized and available for use	Recommendations on choice of latest updated COVID-19 vaccine[a]
6 months to under 12 years of age	• mRNA	For children 6 months to under 5 years of age who are moderately to severely immunocompromised: Moderna Spikevax is preferred [b] For all other children 6 months to under 12 years of age: Moderna Spikevax or Pfizer-BioNTech Comirnaty
12 years of age and older	• mRNA • Protein subunit	Moderna Spikevax, Pfizer-BioNTech Comirnaty or Novavax Nuvaxovid

[a] Only vaccines containing the latest selected strain should be used in fall 2024. Product choices may be more limited if not all vaccines are available with the latest strain. The specific indicated ages for updated vaccines in fall 2024 may remain the same as the currently authorized products; however, information is not yet available.

[b] Moderna Spikevax is preferred due to fewer doses required compared to Pfizer-BioNTech Comirnaty.

Table 2. Comparison on the mRNA and protein sub-unit vaccines (based on previous vaccines and currently available XBB.1.5 vaccines [a])

Factor	mRNA COVID-19 vaccines	Protein sub-unit COVID-19 vaccine
Authorized age group[b]	6 months of age and older	12 years of age and older
Immunogenicity[c]	XBB.1.5 products induce a good immune booster response in humans against XBB-related strains, with a lower but still boosted response against JN.1 [(11-14, 16)].	The XBB.1.5 vaccine induces a good immune booster response in humans against XBB-related strains, with a lower but still boosted response against JN.1 [(15)].
Efficacy/effectiveness[c]	Vaccine effectiveness studies with XBB.1.5 and bivalent mRNA vaccines show increased protection against SARS-CoV-2 infection and severe COVID-19 disease compared to waned protection from previous vaccination and/or infection [(73)].	Good vaccine efficacy for the original product. No efficacy or effectiveness data yet available for the XBB.1.5 product.

Safety[c]	mRNA COVID-19 vaccines have been shown to have a good safety profile, with over 100 million doses administered to date in Canada alone [74]. mRNA COVID-19 vaccines have been associated with rare cases of myocarditis and/or pericarditis, particularly in adolescents and young adult males, especially after the second dose in the primary series using the original vaccine and less so after a booster using the original vaccine or bivalent vaccine. No data are currently available regarding the XBB.1.5 products.	Novavax Nuvaxovid original has been shown to have a good safety profile, with over 3 million doses administered to date, globally [75-77]. Novavax Nuvaxovid original has been associated with rare cases of myocarditis and/or pericarditis based on the original vaccine. No data are currently available regarding the XBB.1.5 product.
Use in specific populations (e.g., immunocompromised, pregnant people)	More data available regarding use in these populations than with protein subunit vaccines.	Less data available regarding use in these populations than with mRNA vaccines.
Storage requirements and shelf-life	Depending on the product, stored ultra-frozen or frozen, with refrigerator storage of thawed product from 4 to 10 weeks [78-80]	Refrigerator storage

[a] Some of the information in this table relates to available XBB.1.5 vaccines. The information may be relevant to the fall 2024 vaccines, however the strain(s) and other specific information regarding the fall 2024 vaccines are not yet known.
[b] The specific indicated ages for updated vaccines in fall 2024 may remain the same as current recommendations, although specific information is not yet available.
[c] Prospective head-to-head comparisons between Novavax Nuvaxovid and mRNA COVID-19 vaccines are limited. Interpreting differences in clinical data should be performed with caution.

Research priorities

- Continuous monitoring of data on the safety, immunogenicity, efficacy, and effectiveness of COVID-19 vaccines, including with new formulations, through clinical trials and studies in real-world settings, including the degree and duration of protection conferred against circulating variants/sublineages. The research should also consider the clinical implications of previous SARS-CoV-2 infection; repeated immunization; and outcomes after infection such as post-COVID-19 condition.
- Continuous monitoring VE in special populations at high risk of severe outcomes and on the long-term consequences of infection with SARS-CoV-2.

- Continuous monitoring of the epidemiology of COVID-19, including SARS-CoV-2 variants/sublineages and seasonal trends, to inform future programs.
- The impact on short-term and long-term immunity when the first immunological exposure is infection compared to vaccination, and vice-versa.
- Further evaluations on the optimal vaccine schedule and vaccine dosage for individuals who are moderately to severely immunocompromised to provide optimal vaccine effectiveness and duration of protection.
- Further evaluations on the safety, immunogenicity, and effectiveness on the concurrent administration of COVID-19 vaccines with other vaccines across different age groups, including concurrent administration with high-dose or adjuvanted influenza vaccines. The monitoring of the risk of ischemic stroke should account for potential confounding factors, including variation in stroke incidence by calendar period.

  Continuous monitoring of vaccine acceptance and coverage in Canada, for COVID-19 vaccines and other routine vaccines, including consideration of measures that may reduce the risk of disparities in vaccine confidence and uptake across different sub-populations (including individuals in racialized and other communities experiencing inequities who may be disproportionately affected due to intersecting equity factors).

Table 3. Strength of NACI recommendations

Strength of NACI Recommendation *based on factors not isolated to strength of evidence* (e.g., public health need)	**STRONG**	**DISCRETIONARY**
Wording	"*should/should not be* offered"	"*may/may not be* offered"
Rationale	Known/anticipated advantages outweigh known/anticipated disadvantages ("should"), OR Known/Anticipated disadvantages outweigh known/anticipated advantages ("should not")	Known/anticipated advantages are closely balanced with known/anticipated disadvantages, OR uncertainty in the evidence of advantages and disadvantages exists
Implication	A strong recommendation applies to most populations/individuals and should be followed unless a clear and compelling rationale for an alternative approach is present.	A discretionary recommendation may be considered for some populations/individuals in some circumstances. Alternative approaches may be reasonable.

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