Topic	Research priorities
COVID	Continuous monitoring of data on: safety, immunogenicity, efficacy, and effectiveness of both the original, and bivalent mRNA COVID-19 vaccines, through clinical trials and studies in real-world settings for both adult and pediatric populations, including relative VE between COVID-19 vaccine products, degree and duration of protection conferred by each booster dose against circulating variants. **Research should also consider:** - the clinical implications of previous SARS-CoV-2 infection; repeated immunization; and - outcomes after any infection such as Multisystem Inflammatory Syndrome in Children (MIS-C), post-COVID-19 condition (long COVID), or infection-induced myocarditis and/or pericarditis in older and younger adult, adolescent, and pediatric populations. - clinical trials among children considered immunocompromised and children with evidence of previous infection. This should include examining the clinical implications of previous SARS-CoV-2 infection or MIS-C on the safety, efficacy, and effectiveness of COVID-19 vaccines in pediatric populations
	Continuous monitoring of COVID-19 epidemiology and VE in special populations (e.g., those with high-risk medical conditions, or social risk factors placing them at high-risk for severe outcomes) and the long-term consequences of COVID-19 in these populations.
	Further evaluations of the optimal interval between booster dose and primary series, and between any subsequent booster doses as well as further evaluations of the optimal interval between previous SARS-CoV-2 infection and booster dose administration.
	Evaluations of whether bivalent Omicron-containing mRNA COVID-19 vaccines can be used as part of a primary series.
	Vigilant monitoring and reporting of adverse events of special interest, including myocarditis and/or pericarditis, to accurately inform potential risks associated with booster doses, for all COVID-19 vaccines, including bivalent Omicron-containing mRNA vaccines. Global collaboration should be prioritized to enable data sharing so decision makers around the world can weigh benefits and risks of multiple booster doses of COVID-19 vaccines.
	Vigilant vaccine safety reporting internationally and across Canadian jurisdictions for timely assessment of any potentially rare or very rare AEs in children following administration of COVID-19 vaccines (alone or with other vaccines). In addition, efforts should be made to facilitate global collaboration to enable data sharing so decision makers around the world can weigh benefits and risks of COVID-19 vaccination for their own specific pediatric populations. (October 2022 NACI Peds Statement)
	Continuous monitoring of vaccine coverage and acceptance in the Canadian population, specifically following the authorization of new bivalent/ multi-valent Omicron-containing mRNA COVID-19 vaccines.
Influenza	Comparing vaccine types (RIV, egg-based and mammalian cell culture-based) based on efficacy, effectiveness, immunogenicity, and safety between seasons and

	against different influenza subtypes. A more robust, comprehensive, and consistent body of evidence, including further data on comorbidities, pregnant individuals, health status, and other potential confounders is needed to evaluate the relative effectiveness and safety of Supemtek compared to other injectable influenza vaccines.
	Risk/benefit analysis of simultaneous (i.e. same day) and/or sequential administration of influenza vaccines with COVID-19 vaccines, including: • Efficacy/effectiveness, immunogenicity and safety • Potential for increased reactogenicity, particularly with influenza vaccines that might be more likely to cause local or systemic reactions; what is the frequency of reactogenicity with adjuvanted and high-dose inactivated vaccines compared with standard-dose, unadjuvanted inactivated vaccines? • What should be the minimum interval between vaccines if not administered on the same day (e.g., treat as live vaccine)? Differences between the mRNA and viral vector COVID-19 vaccine platforms? • Considerations for special populations
	Concurrent administration with other adjuvanted vaccines. • Data are limited regarding concurrent administration of adjuvanted vaccines with other adjuvanted or nonadjuvanted vaccines.
	Further evaluation of VE stratified by characteristics in addition to influenza strain type and subtype would allow for better identification of when the effects of repeated influenza vaccination should be considered and which specific populations may be affected. • Further evaluation of the effects of long-term repeated influenza vaccination on VE over more than 2 consecutive seasons. • Further evaluation of the effects of repeated influenza vaccination on VE stratified by age group and vaccine type. • Investigation of the effects of repeated influenza vaccination on severe influenza-related outcomes, such as hospitalization and death. • Evaluation of the effects of repeated influenza vaccination that accounts for previous influenza exposure through vaccination and/or natural infection. • Further investigation of the immunological mechanisms underlying the effects of repeated influenza vaccination on VE, including the antigenic distance hypothesis and immunological imprinting.
	Impact of influenza illness during pregnancy on perinatal outcomes • Studies reporting on adverse birth outcomes following maternal influenza illness are limited in quantity and provide inconsistent findings. LAIV vaccine • LAIV is not contraindicated in breastfeeding (lactating) individuals; however, there is limited data and unknown real-risk for the use of LAIV in this population. Currently, NACI references a “theoretical risk to the fetus” from administering LAIV to a pregnant individual. Influenza vaccine safety in pregnant persons • Limited evidence regarding the safety of administration of influenza vaccine in the first trimester of pregnancy. • Limited peer-reviewed evidence regarding the safety and effectiveness of

	administration during pregnancy of more recently licensed influenza vaccines that are based upon new, different technologies, including quadrivalent mammalian cell culture-based vaccines (e.g., IIV4-cc; Flucelvax® Quad) and recombinant influenza vaccines (e.g., RIV4; SupemtekTM). Unknowns regarding patients' knowledge, understanding and beliefs about influenza vaccination during pregnancy, especially given the heterogeneity of Canada's population (i.e., differences in socioeconomic and cultural backgrounds and differences in trust in the medical system).
	• Limited available data directly comparing the performance of IIV3-Adj, IIV-HD, IIV4-SD, IIV4-cc, or RIV4 on efficacy, effectiveness, and/or immunogenicity. • Comparative analysis between influenza vaccines that claim to be superior vs standard quadrivalent inactivated influenza vaccine; we are interested in evidence for traditional egg-based influenza vaccines and new non-egg based technology vaccines on the market, such as cell culture-based vaccines and recombinant influenza vaccines. • Impact of the implementation of HD Influenza vaccine in Long Term Care Facilities (LTCF), and the impact on LTCF outbreaks. • Studies on the use of RIV in pregnant individuals and in other vulnerable populations are available to inform vaccine-associated risks.
	It has been identified that Indigenous populations are at increased risk of severe influenza outcomes. • Limited literature on influenza-associated outcomes (i.e., hospitalizations and deaths) among Indigenous peoples in Canada.
Monkeypox	Study of the protection offered by Imvamune® vaccine against monkeypox infection, disease and transmission (in pre-exposure and post-exposure vaccination scenarios), including: - Understanding which immune responses are protective against infection and disease and defining protective thresholds, including the duration of protection - Understanding how the impact of previous orthopox infection or vaccination impacts the protection of vaccination - Real-world evidence on the vaccine effectiveness against monkeypox when used as a single SC dose, with extended intervals, and/or in combination with fractional intradermal dosing.
	Studies to inform on vaccine safety vaccine including both clinical trials and post-market safety surveillance.
	Studies to assess vaccine efficacy/effectiveness and safety of Imvamune® in priority populations, including people who are pregnant or breastfeeding, children <18 years of age, and people who are immunocompromised.
	Study into the epidemiology of the disease to better understand the modes of transmission, the disease presentation, and to identify the populations at highest risk for severe disease in order to inform and optimize disease prevention strategies.
	Study into the optimal immunization strategies for outbreak control (e.g., ring vaccinations, population groups at medium/low risk of infection).
HPV	Evaluation of long-term immunogenicity kinetics and outcomes for a 2-dose versus 3-dose HPV9 vaccine immunization schedule.

	Direct comparison between alternative 2-dose immunization schedules for HPV9 vaccine; 0,6 months versus 0,12 months.
	Data to support an optimal HPV immunization schedule for persons 15 years and older.
	Understanding the factors that contribute to low uptake of the HPV vaccine in certain areas
Pneumococcal	Direct comparison of vaccine efficacy of PNEU-P-23 and PNEU-C-13 via randomized controlled trial among the general population of adults 65 years of age and older looking at the outcomes of IPD, VT IPD, CAP, and VT CAP (2018 NACI Statement)
	Estimates/assessments of the PNEU-C-15 and PNEU-C-20 vaccine effectiveness in the general population of individuals 65 years of age and older and in additional populations (e.g., indigenous people, people living with chronic medical, social and immunocompromising conditions). (2022 NACI Statement)
	Cost-effectiveness analyses on the use of PNEU-C-15 and PNEU-C-20 in adults 18-49 years of age with risk factors that place them at high risk of IPD.(2022 NACI Statement)
	Assessment of the effects of community immunity and serotype replacement of PNEU-C-15 childhood programs over time on the incidence of IPD, VT IPD, CAP, and VT CAP and on carriage within the Canadian population of individuals 65 years of age and older and in additional populations (e.g., indigenous, people living with chronic medical, social and immunocompromising conditions). (2022 NACI Statement)
	Estimates of efficacy and effectiveness of PNEU-C-15 and PNEU-C-20 boosters in immunocompetent adults over 65 years of age. (2022 NACI Statement)
	Estimates of efficacy and effectiveness of PNEU-C-15 and PNEU-C-20 boosters in immunocompetent adults over 65 years of age. (2022 NACI Statement)
	Assessment of pneumococcal vaccination programs on the reduction of myocardial infarction and stroke. (2022 NACI Statement)
Varicella / Herpes Zoster	Duration of vaccine-induced immunity; correlate of protection; and the need for booster doses
	Long-term epidemiological impact of vaccination on varicella and herpes zoster, especially if low levels of vaccine coverage are achieved. **Comment:** For a long time, active surveillance for Varicella and Zoster have been done within IMPACT, however with the shifting epidemiology, this could be a extended to the Serious Outcomes Surveillance (SOS) network within CIRN.
	Additional data on the safety, immunogenecity and effectiveness (long-term) of varicella vaccine (HZ) in susceptible HIV-infected and other immunocompromised individuals
	Safety and efficacy of HZ vaccine in individuals with prior history of HZ infection
Meningococcal	The potential of serogroup B vaccines to protect against meningococcal serogroup B strains circulating in Canada and against other meningococcal serogroups;
	The safety, immunogenicity and effectiveness of Bivalent Factor H Protein vaccines in specific subpopulations (e.g., pregnant women, immunocompromised).
	Defining the best approach in the control around childhood and adolescence?
	Breakthrough infections: are there differences between the strains in terms of breakthrough cases (why are we seeing disease in vaccinated cases)?

	Look nationally at the potential impact of various schedules on the epidemiology of new cases
	Understanding use of Meningococcal B vaccine for populations other than high risk (contingent on work already being led by the Meningococcal WG of NACI)
Hepatitis A&B	Studies on post-exposure efficacy and vaccine failure or breakthrough disease following the receipt of one vs. two doses of HA vaccine.
	Improved data on HB infection in diabetics to better understand risk.
	Data to support the need or not for a birth dose of HB vaccine.
RSV	Establishing correlates of protection against severe RSV infection in humans and development of a commercially available test for RSV antibody.
	RSV monoclonal antibody efficacy/effectiveness in infants living in remote communities, especially in Inuit infants in the far North.
	Burden of RSV disease in infants with Down syndrome and efficacy/effectiveness of RSV monoclonal antibody to prevent hospitalization in this population.
	Efficacy/effectiveness of RSV monoclonal antibody in otherwise healthy premature infants born at < 29 wGA.
Rabies	Studies for intradermal post-exposure prophlaxis
	How can we add the global understanding of effectiveness of ID vs. IM?
	Issues with utilization of rabies vaccine
Diphtheria, Tetanus, Pertussis, Polio, Hib (DTaP-IPV-Hib)	Optimal timing for Tdap administration, resulting in optimal transplacental antibody transfer and infant protection;
	Further work on determining the long-term impact of maternal vaccination in pregnancy on vaccine effectiveness in children and adults (e.g. long-term effect on disease epidemiology as a result of lower infant antibody levels)
Mumps	Optimal timing of the second dose in a two dose schedule and an additional / outbreak dose
	The impact of an additional outbreak dose of mumps-containing vaccine on the immunologic response and its effectiveness in reducing disease burden
Measles	Determining the optimal time between the first and second dose.
	Better understanding of transmission would be helpful for public health decision making. Measles transmission among health care workers, as well as the cohort who received only one dose to determine if this group is contributing to measles transmission in Canada. Characterization of measles transmission in Canada in certain settings such as planes, airports, malls and attraction parks or zoos. There is data from past outbreaks and clusters that could be further grouped and analyzed.
	Most appropriate public health management of measles case on international flights. Existing national guidance present a variety of options for public health management --- different provinces and territories adopt different approaches. In order to move forward with revisiting the guidance it is important to document what people are doing and their subsequent experience: there's a real need for quantitative numbers (what is effective and what is feasible?)
Ebola	Establishing Immune correlates of protection.
	Studies on post-exposure protection including the degree of protection (e.g., decreasing infectiousness and clinical illness in individuals that had already acquired infection) and the optimal window of vaccination for PEP

	Establishing safety and immunogenicity data for pregnant and breastfeeding women, those under 17 years of age and immunocompromised individuals.
	Studies on transmissibility of the vaccine virus , including whether the vaccine virus is secreted in human breast milk.
	Long term vaccine efficacy and duration of immune response, and the potential need and optimal conditions for a booster.