





Seminar Series | Research Results & Implications

The importance of pediatric vaccination



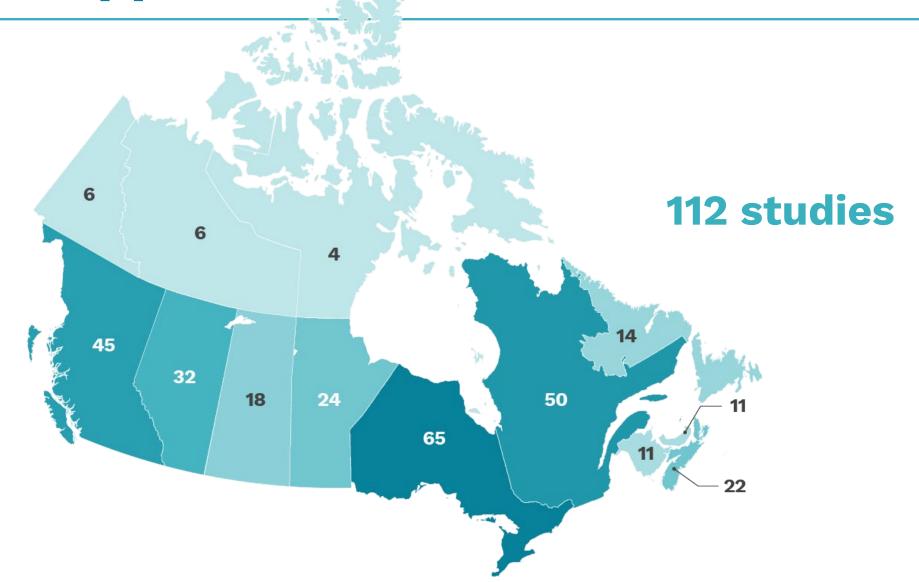
March 23, 2022 | 11:00 a.m. to 12:30 p.m. EDT

Moderator

Tim Evans, MD, PhD

Executive Director, COVID-19 Immunity Task Force

CITF supports studies active across Canada



CITF: Priority areas of research



SEROPREVALENCE STUDIES

Assess the extent of SARS-CoV-2 infection across Canada



IMMUNE SCIENCE

Understand the nature of immunity arising from infection



IMMUNE TESTING

Develop improved antibody testing methods



VACCINE SURVEILLANCE

Help monitor the effectiveness and safety of vaccines



BOOSTERS

Understand if and when different populations need booster shots



PEDIATRIC VACCINATION

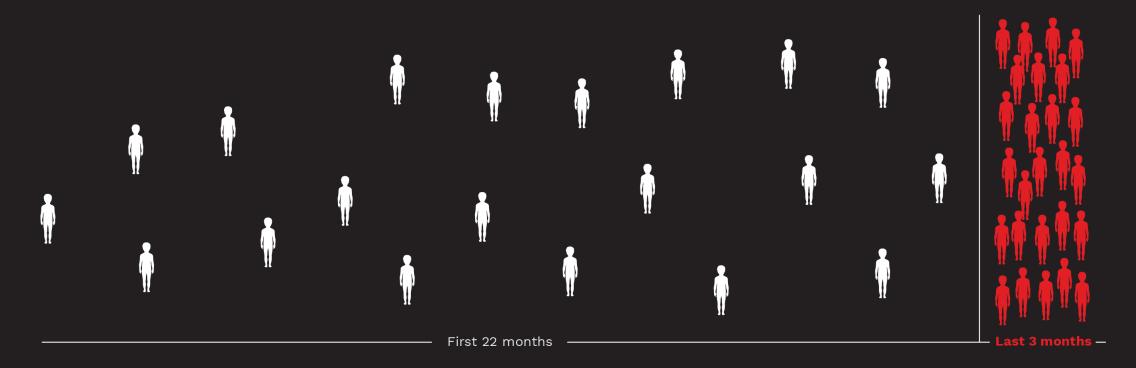
Research safety,
effectiveness and
immunogenicity of vaccines
in children under 21



IMMUNITY MODELLING

Model trends in overall immunity across Canada

Omicron wave has resulted in a surge in pediatric hospitalizations





of COVID-related **pediatric hospitalizations** have occurred in the past **three months**, during the peak of the Omicron wave.

Despite the risks, pediatric vaccinations, which remain the best way of protecting children from COVID-19, remain low across Canada.

Only 57%

of children between the ages of 5 and 11 have received at least one dose of the vaccine to date. In contrast, 88% of 12-to 17-year olds have received at least one dose.



Speakers

Manish Sadarangani, BM, BCh, DPhil, Director, Vaccine Evaluation Center, BC Children's Hospital Research Institute; Associate Professor, Division of Infectious Diseases, Department of Pediatrics, UBC; Physician Lead, Family Immunization Clinic, BC Children's Hospital; PI, CITF-funded SPRING Study

Jonathon Maguire, MD, Professor, Department of Pediatrics, University of Toronto; Scientist, MAP Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute; St. Michael's Hospital, Pediatrician, Department of Pediatrics, St. Michael's Hospital; Unity Health Toronto; PI, CITF-funded TARGetKids! Study

Kate Zinszer, PhD, Assistant Professor, l'École de santé publique, Université de Montréal; Researcher, Centre for Public Health Research (CReSP); PI, CITF-funded EnCORE Study

Jim Kellner, MD, Pediatric Infectious Diseases Specialist, Professor, Pediatrics, University of Calgary; Member, CITF Leadership Group, Leader, CITF Pediatric Network

MANISH SADARANGANI

Disclosures

Salary awards

BC Children's Hospital Foundation

Michael Smith Foundation for Health Research

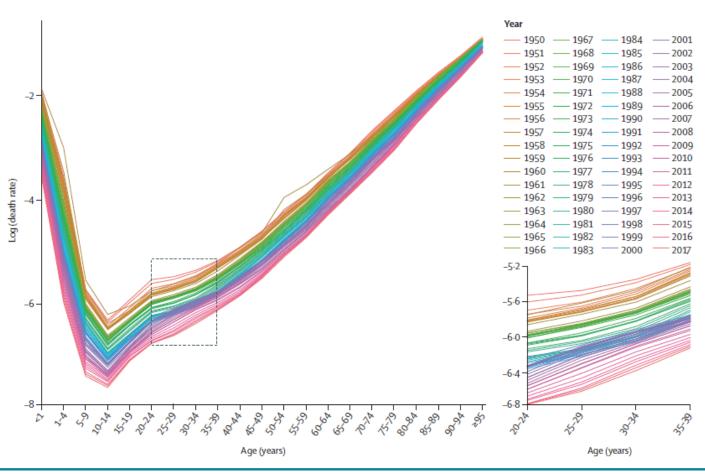
Canadian Child Health Clinician Scientist Program

Research/Project Funding

Merck, Moderna, VBI Vaccines, GlaxoSmithKline, Pfizer, Sanofi-Pasteur, Seqirus, Symvivo

All funds have been paid to my institute, no personal payments have been received.

Why are children important?



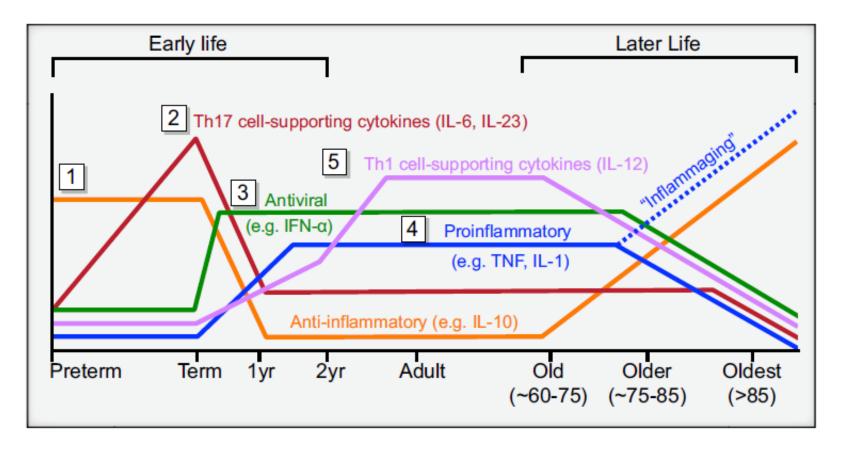
GBD Collaborators. *Lancet* 2018







Different immunity -> different interventions



Kollmann et al. *Immunity* 2012







Different immunity -> different vaccines

But it's complicated... same vs. lower vs. higher doses may be required

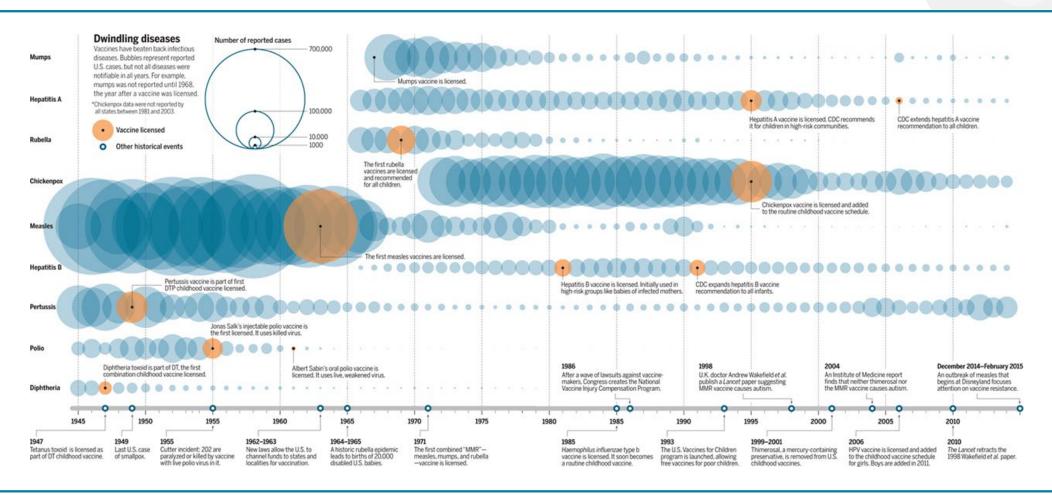
Vaccine	<12 months	1-11 years	12-17 years	≥18 years
COVID-19	Not available	2 lower doses (5-11y)	2 doses	3 doses
Varicella (Chickenpox)	Not used	2 doses	2 doses	2 doses
Hepatitis B	3 doses	3 doses (2 high doses in 11-15y)		3 high doses (≥20y)
Human papillomavirus	Not used	2 doses (9-14y)		3 doses (≥15y)
Inactivated influenza	2 doses (≥6m)	2 doses (1-8y)	1 dose (≥9y)	1 dose
Tetanus/Diphtheria/Pertussis	DTaP	DTaP (1-6y)	Tdap (7-17y)	Tdap







The most effective health intervention?



Wadman. *Science* 2017







COVID-19 in children: The SPRING Study

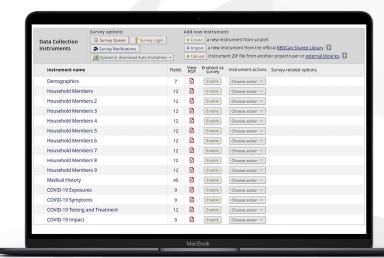
Severe acute resPiratory syndrome-Related coronavirus 2 prevalence In children and youNG adults in British Columbia: an observational study

- Cross-sectional snapshots of children/young adults in BC
- ▶ Longitudinal follow-up of COVID-19 positive cases
- Mostly healthy children
- ▶ Aim to be representative across BC in terms of geographic distribution, sex and ethnicity
- ▶ Inclusion: Age <25 years; Resident in BC
- Electronic COVID-19 Survey
- Samples: dried blood spots; MSD V-Plex pan-CoV panel















COVID-19 infection in children

Nov 2020 - May 2021

Age group	Total sample	% seropositive (95% CI)
0-4	347	3.17 (1.78, 5.59)
5-9	416	4.09 (2.57, 6.45)
10-14	463	3.24 (1.97, 5.28)
15-19	469	3.84 (2.44, 5.98)
20-24	471	7.22 (5.21, 9.92)

Jun 2021 – Mar 2022

Age group	Total sample	% seropositive (95% CI)
0-4	399	7.65 (4.52, 12.64)
5-9	537	5.72 (3.84, 8.44)
10-14	416	
15-19	308	Vaccinated
20-24	380	







JONATHON MAGUIRE

Disclaimer

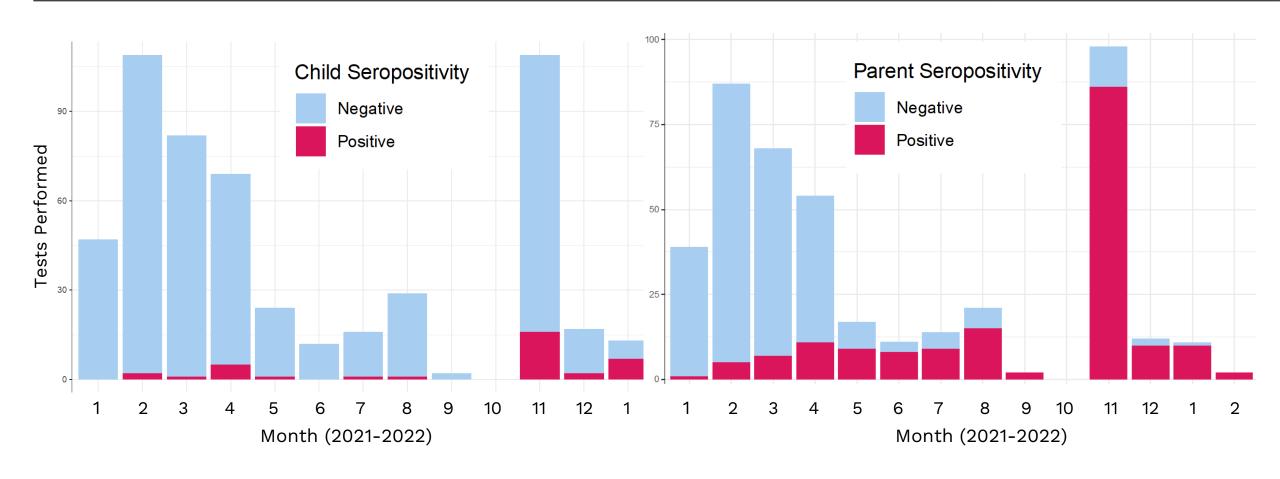
I have no COIs to declare related to this study.



- ▶ The largest primary care research network in Canada
- Ongoing longitudinal data collection at well-child visits
- Over 11,500 children and their parents enrolled since 2008
- ▶ 14 large practices across GTA, Montreal and Kingston

Visit us at www.targetkids.ca

Seropositivity (due to infection and/or vaccination)











KATE ZINSZER

Disclaimer

I have no COIs to declare related to this study.

Seroprevalence due to infection, by study population characteristics

		Baseline (n=1,632) % (95% CI)	F/u 1 (n=933) % (95% CI)	F/u 2 (n=716) % (95% CI)	
Seropositive		5.8 (4.8 - 7.1)	10.1 (8.3 - 12.2)	10.8 (8.7 - 13.3)	
Sex Female Male		6.9 (5.3 - 8.8)	11.7 (9.0 - 15.0)	12.7 (9.6 - 16.7)	
		4.8 (3.5 - 6.5)	8.6 (6.4 - 11.5)	9.1 (6.5 - 12.5)	
Chronic disease Present Absent		4.9 (1.8 - 11.1)	12.0 (7.1 - 19.2)	11.0 (5.7 - 19.8)	
		5.9 (4.8 - 7.2)	9.8 (7.9 - 12.0)	10.9 (8.6 - 13.6)	
Ethnic minority Yes No		10.9 (7.3 - 16.1)	17.7 (11.7 - 25.8)	11.7 (6.1 - 21.0)	
		5.2 (4.1 - 6.5)	9.2 (7.3 - 11.4)	10.7 (8.5 - 13.3)	
Neighbourhood	West Island	3.4 (2.1 - 5.4)	6.5 (4.1 - 10.1)	3.2 (1.3 - 7.1)	
	HOMA	7.8 (5.4 - 11.1)	11.5 (7.9 - 16.5)	11.7 (7.6 - 17.4)	
	Montreal North	9.3 (6.2 - 13.7)	16.2 (10.9 - 23.3)	16.9 (11.2 - 24.8)	
	Plateau	5.2 (3.6 - 7.5)	9.6 (6.8 - 13.5)	13.0 (9.3 - 17.9)	

Caution:

Unpublished results

Baseline (October 2020 to March 2021) (n=1,632)

F/u 1 (May 2021 to August 2021) (n=933)

F/u 2 (November 2021 to February 2022) (n=716)

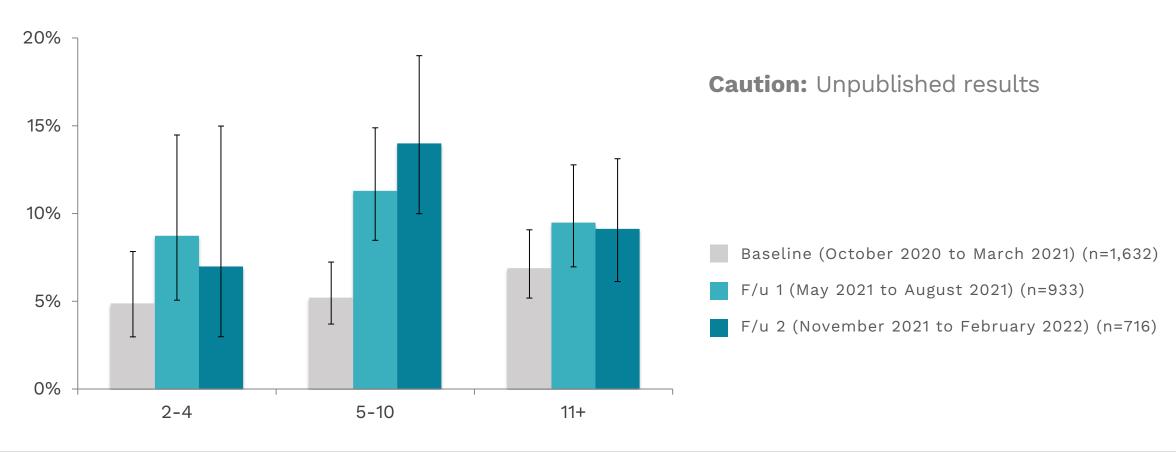








Seroprevalence due to infection, by age group and round of data collection











Seropositivity due to infection

		Adjusted prevalence	Adjusted prevalence ratio	95% CI
	2-4 years	5.89	0.70	0.47-1.03
Age group	5-10 years	9.30	1.10	0.86-1.42
	11-17 years	8.43	REF	
Sex	Female	9.70	1.42	1.12-1.80
Sex	Male	6.84	REF	
Ethnic minority group	Yes	11.03	1.43	1.05-1.96
Ethine minority group	No	7.70	REF	
	Less than Bachelor's	6.71	REF	
Parental education level	Bachelor's	8.23	1.23	0.88-1.71
	Master's degree or higher	9.44	1.41	1.00-1.97
	less than 1 pp bedroom	7.08	REF	
HH density (HH members per bedroom)	1 to less than 2 pp bedroom	8.39	1.19	0.90-1.57
(2+ pp bedroom	11.43	1.61	1.05-2.49

Caution:

Unpublished results









Seroconversion



On average, following 100 children over 1 year, **more than 12** will go from testing negative for SARS-CoV-2 infection to testing positive.

Overall rate of seroconversion for SARS-CoV-2 infection

Total f/u time (years)	# of seroconverted children	Rate per 100 children per year (95% CI)		
1,562	194	12.42 (10.73 - 14.30)		

Caution: Unpublished results







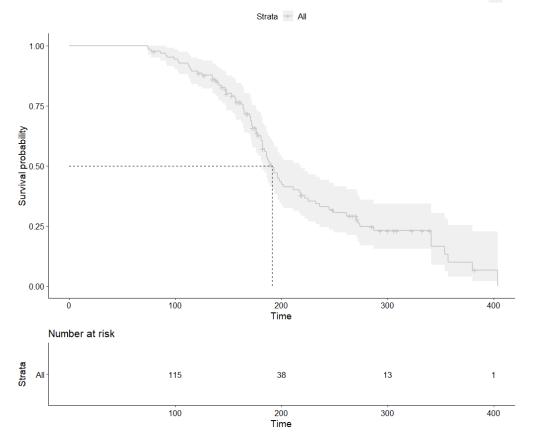


Seroreversion and time to seroreversion among children who were ever seropositive for a SARS-CoV-2 infection

		# ever positive	# who seroreverted	Median time to seroreversion (days)
Seropositive		123	81	191 (182 - 218)
Age	2 - 4 5 - 10 11+	17 53 53	12 28 41	196 (164 - unknown*) 191 (173 - 261) 193 (182 - 222)

^{*}Could not be estimated due to limited sample.

Seroreversion from SARS-CoV-2 infection over time (days)



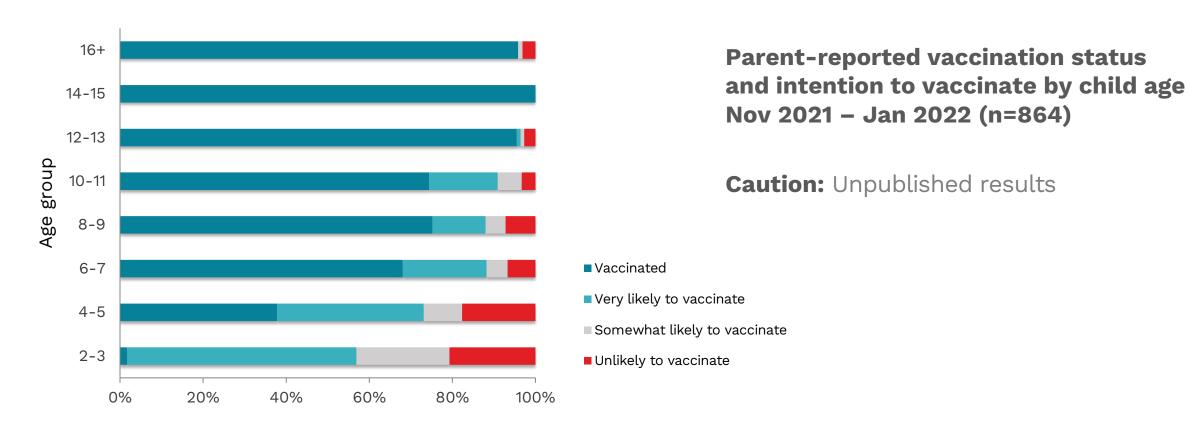
Caution: Unpublished results



















Prevalence	of	vaccine	hesitancy
(reluctance	to	vaccina	ite)

(reluctance to vaccinate)		Adjusted prevalence	Adjusted ratio (95% CI)	Adjusted prevalence	Adjusted ratio (95% CI)
Parental education level	Master's degree or higher	6.8	1 (ref)	5.4	1 (ref)
	Bachelor's	10.4	1.5 (0.7 - 2.3)	8.1	1.5 (0.7 - 2.3)
	Less than a bachelor's	18.5	2.7 (1.7 - 4.3)	10.8	2.0 (0.7 - 3.3)
Neighbourhood	West Island	7.0	1 (ref)	6.4	1 (ref)
	HOMA	8.9	1.3 (0.4 - 2.1)	5.6	0.9 (0.3 - 1.6)
	Montreal North	13.4	1.9 (0.6 - 3.2)	7.5	1.2 (0.2 - 2.1)
	Plateau Mont-Royal	12.9	1.8 (0.7 - 3.0)	9.5	1.5 (0.5 - 2.5)
Ethnic minority group	White	8.4	1 (ref)	5.9	1 (ref)
	Ethnic minority group	27.4	3.3 (1.8 - 4.7)	20.7	3.5 (1.7 - 5.3)

Caution: Unpublished results







F/u 1 (May to Aug 2021)

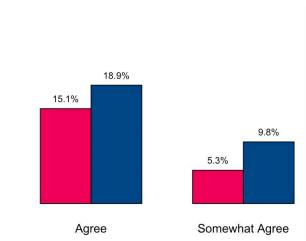


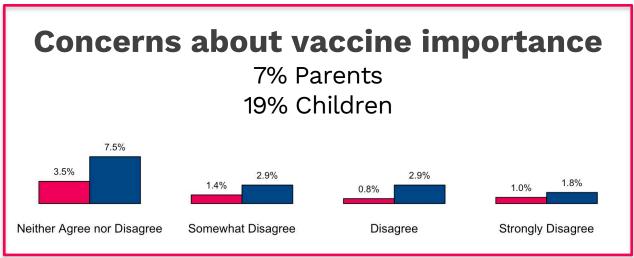
F/u 2 (Nov 2021 to Feb 2022)













Strongly Agree

72.9%

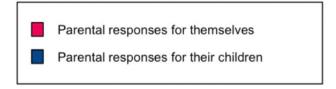
56.2%

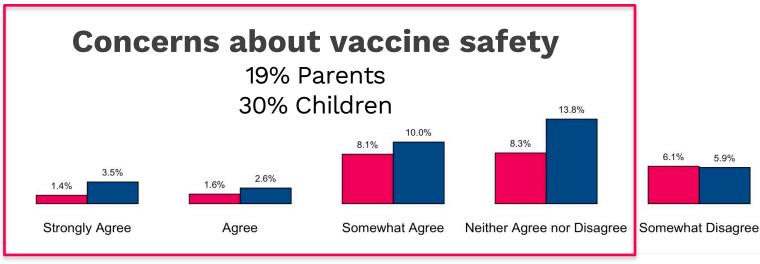


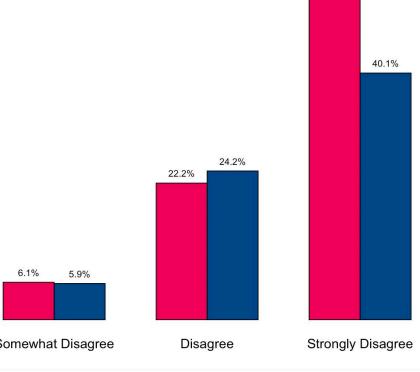




"I worry that COVID-19 vaccines will do more harm than good"







52.5%









- Beliefs about COVID-19 vaccine importance and safety for parents were associated with similar beliefs about COVID-19 vaccine importance and safety for children ~70% of the time (p<0.001).
- Lower family income was associated with:
 - ▶ 3-fold higher odds that parents believed that COVID-19 vaccines are not safe for themselves and their children (p <0.001)</p>
 - ▶ 4-fold higher odds that parents believed COVID-19 vaccines are important and safe for themselves but not their children (p <0.001)</p>

- Non-university education associated with:
 - ▶ 3-4 fold higher odds that parents believed that COVID-19 vaccines are not important (p = 0.002) and not safe (p < 0.001) for both themselves and their children.

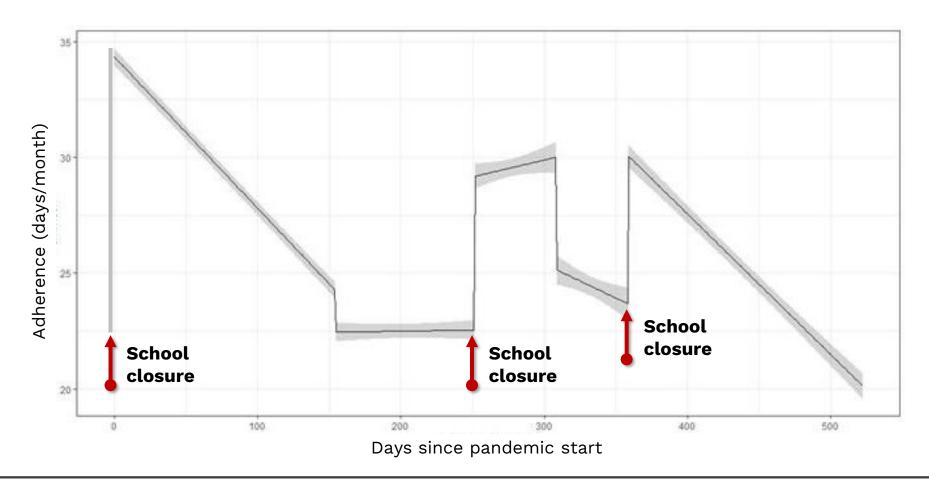








Adherence to public health measures











Summary

- Seropositivity in children is lagging behind seropositivity for parents due to lower vaccination rates and/or fewer infections
- School closures were associated with higher adherence to public health measures which diminished over time.
- 19% of parents had concerns about vaccine importance and 30% had concerns about vaccine safety for children.











JAMES D. KELLNER

Disclaimer

Research grants and clinical trial contracts

All funding managed by and paid to University of Calgary to support research operations; no personal funding to investigator.

Granting agencies: CIHR, Genome Alberta, Alberta Children's Hospital Foundation

Pharmaceutical companies: Moderna (COVID-19 vaccine clinical trial),
Pfizer (pneumococcal surveillance grant), Merck (pneumococcal vaccine clinical trial),
GSK (rotavirus & meningococcous vaccine clinical trials)

Other influential affiliations

Leadership Group COVID-19 Immunity Task Force (CITF)

Alberta Advisory Committee on Immunizations

Data Safety Monitoring Board VIDO-InterVac COVID-19 vaccine trials

Principal Investigator Alberta Childhood COVID-19 Cohort (AB3C) Study

COVID-19 vaccine safety in children

- Vaccine safety will be the primary focus of next month's webinar with review of Canadian and international data (see <u>covid19immunitytaskforce.ca/events</u>)
- In general, adverse events after vaccination in children are uncommon and similar to adults:
 - ▶ More frequent after 2nd dose, but less frequent overall
 - ▶ Most often temporary local symptoms at injection site redness, swelling, pain
 - ▶ Generalized symptoms flu-like symptoms, headache, fever, nausea, vomiting, diarrhea
 - ▶ Severe reactions like anaphylaxis very rare ~5 cases/million doses, all ages
- Review myocarditis/pericarditis today

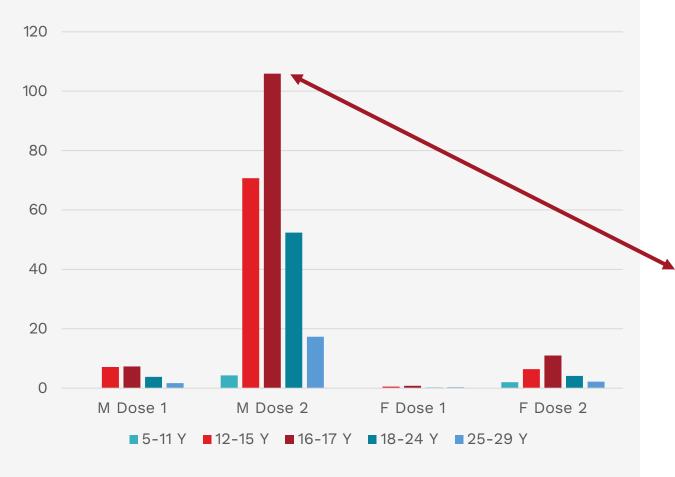
Myocarditis/pericarditis after COVID-19 vaccines

- Post-vaccine cases generally mild (compared with cases after COVID-19 or other infections)
 - ► Acute chest pain, shortness of breath, palpitations, typically 1-3 days after vaccine
- To date, fundamentally associated with mRNA vaccines
 - Moderna (100 μg), Pfizer (30 μg)
- More common:
 - ► Adolescents & young adults
 - ▶ Males vs females ~5 X
 - ▶ After 2nd dose ~6-12 X
 - ▶ After COVID-19 infection rather than vaccination ~6 X



<u>CANVAS-COVID.ca</u>, <u>Canada.ca Vaccine Safety</u>, *JAMA 2022;327(4):331-340*. doi:10.1001/jama.2021.24110

Myocarditis/pericarditis incidence per million doses, USA (Pfizer only)

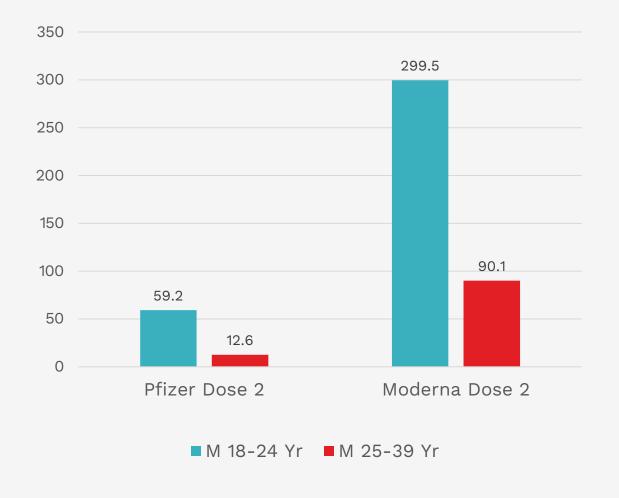


Incidence of myocarditis/pericarditis peaks in late adolescence

- USA, adjudicated VAERS (Vaccine Adverse Event Reporting System) data
- Recent data for 5-11-year-old children
- Peak in late adolescence, dose #2, lower in younger & older persons
 - Mirrors age & gender distribution for myocarditis after viral infections

JAMA 2022;327(4):331-340. doi:10.1001/jama.2021.24110, CDC presentation to ACIP Meeting Jan 5, 2022 (slide 13)

Myocarditis/pericarditis incidence per million doses, Ontario



Myocarditis risk highest after higher dose Moderna vaccine

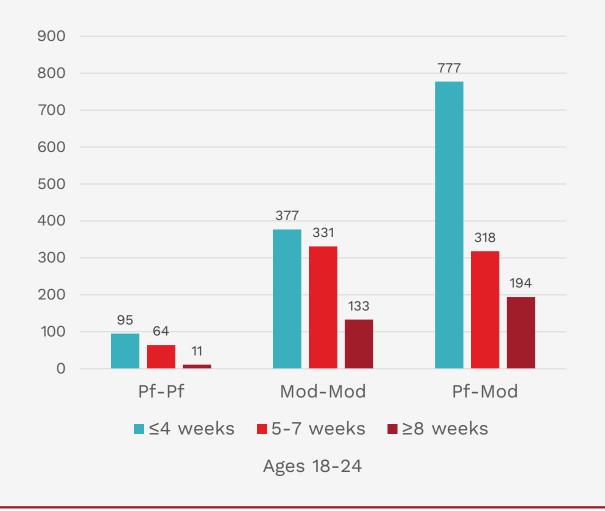
- Ontario males, 2nd dose only
 - ► Moderna not given <18 yr
 - Limitations of small sample sizes and so large confidence intervals
- Rate difference after Moderna vs Pfizer

▶ 18-24 Yr: **5.1** X

▶ 25-39 Yr: **7.2** X

Buchan et al. Preprint medRxiv Dec 2021 doi.org/10.1101/2021.12.02.21267156

Myocarditis/pericarditis incidence per million doses, Ontario



Myocarditis risk lower after longer dose interval

- ▶ Regardless of vaccine used, the risk of myocarditis/pericarditis was 65% -88% lower when 2nd dose given 8 weeks after the 1st dose vs giving it after 3-4 weeks
- Risk of myocarditis highest after
 Moderna vs Pfizer

Buchan et al. Preprint medRxiv Dec 2021 doi.org/10.1101/2021.12.02.21267156

Ways to reduce risk of myocarditis

- Ongoing surveillance and follow-up of myocarditis/pericarditis cases
- ► Pfizer vaccine preferred for those under 30, including lower dose formulation for those under 12
 - ▶ 30 µg adult dose for 12-29 yrs
 - ▶ 10 µg pediatric dose for 5-11 yrs
- ▶ Increased (over 8 weeks) dosing interval is preferred between the first 2 doses (vs 21 days) at all ages
- ▶ Future possibility for use of different vaccines



COVID-19 in children: The SPRING Study

Name	Institute
Manish Sadarangani (PI)	Vaccine Evaluation Center (VEC), BC Children's Hospital (BCCH) Department of Pediatrics, University of British Columbia (UBC)
Bahaa Abu-Raya	
Julie Bettinger	
Adriana Cabrera	
Vivek Gill	
Laura Sauve	
Sarah Silverberg	
David Goldfarb	Department of Pathology and Laboratory Medicine, BCCH; UBC
Sofia Bartlett	Public Health Laboratory, BC Centre for Disease Control (BCCDC)
Agatha Jassem	
Mel Krajden	
Muhammad Morshed	
Inna Sekirov	
Danuta Skowronski	Influenza & Emerging Respiratory Pathogens Lead, BCCDC
Daniel Coombs	Department of Mathematics, UBC
Soren Gantt	VEC, BCCH; Centre de recherche du CHU Sainte-Justine, Montréal







Thank you











TARGet Kids! Leads

Dr. Catherine Birken

Dr. Jonathon Maguire

Site Investigators:

Dr. Nada Abdel-Malek

Dr. Jillian Baker

Dr. Tony Barozzino

Dr. Nicholas Blanchette

Dr. Joey Bonifacio

Dr. Caroline Calpin

Dr. Douglas Campbell

Dr. Sohail Cheema

Dr. Brian Chisamore

Dr. Evelvn Constantin

Dr. Karoon Danayan

Dr. Paul Das

Dr. Marv Beth Derocher

Dr. Anh Do

Dr. Michael Dorev

Dr. Sloane Freeman

Dr. Keewai Fung

Dr. Donna Goldenberg

Dr. Charlie Guiang

Dr. Curtis Handford

Dr. Leah Harrington

Dr. Hailey Hatch

Dr. Sheila Jacobson

Dr. Lukasz Jagiello

Dr. Paul Kadar

Dr. Tara Kiran

Dr. Holly Knowles

Dr. Bruce Kwok

Dr. Sheila Lakhoo

Dr. Margarita Lam-Antoniades

Dr. Eddy Lau

Dr. Patricia Li

Dr. Fok-Han Leung

Dr. Jennifer Loo

Dr. Sarah Mahmoud

Dr. Aleks Meret

Dr. Rosemary Moodie

Dr. Julia Morinis

Dr. Sharon Navmark

Dr. Patricia Neelands

Dr. James Owen

Dr. Michael Peer

Dr. Marty Perlmutar

Dr. Nav Persaud

Dr. Andrew Pinto Dr. Michelle Porepa

Dr. Nasreen Ramii

Dr. Noor Ramji

Dr. Alana Rosenthal

Dr. Janet Saunderson Dr. Rahul Saxena

Dr. Michael Sgro

Dr. Hafiz Shuja

Dr. Susan Shepherd

Dr. Barbara Smiltnieks

Dr. Carolyn Taylor

Dr. Fatima Uddin

Dr. Joanne Vaughan

Dr. Thea Weisdors

Dr. Sheila Wijayasinghe

Dr. Peter Wong Dr. Ethel Ying

Dr. Elizabeth Young

Dr. Michael Zajdman

Research Managers:

Christine Kowal Dalah Mason

Research Coordinator:

Frank Ong

Research Assistants:

Marivic Bustos Dharma Dalwadi

Mateenah Jaleel

Tarandeep Malhi

Ataat Malick

Reiina Reiandran

Sharon Thadani

Julia Thompson

Laurie Thompson

Applied Health Research Centre:

Dr. Peter Juni

Dr. Gerald Lebovic

Karen Pope

Kevin Thorpe

Biostatistician:

Dr. Charlie Keown-Stoneman

Mount Sinai Services Lab:

Dr. Rita Kandel Michelle Rodrigues **Advisory Committee:**

Dr. Ronald Cohn

Dr. Eddy Lau

Dr. Andreas Laupacis

Dr. Patricia Parkin

Dr. Michael Salter

Dr. Peter Szatmari Shannon Weir

Science Review Committee:

Dr. Laura Anderson

Dr. Cornelia Borkhoff

Dr. Patricia Li

Dr. Patricia Parkin

Dr. Nav Persaud

Dr. Peter Wong

Project Team:

Mary Aglipay

Dr. Sarah Carsley

Dr. Katherine Cost

Dr. Laura Kinlin

Dr. Jessica Omand

Dr. Meta van den Heuvel

Dr. Leigh Vanderloo

Thank you to all participating families for their time and involvement in TARGet Kids!



EnCORE children and parents, daycares, schools and school boards



Laura Pierce
Katia Charland
Adrien Saucier
Islem Cheriet
Margot Barbosa Da Torre
Carla Benea

Co-investigators

Britt McKinnon
Caroline Quach (co-PI)
Jesse Papenburg
Guy Boivin
Gaston De Serres
Marie-Ève Hamlin
Patricia Conrod
Monica Zahreddine
Nancy Haley

Collaborators

Cat Tuong Nguyen Nathalie Ratté Isabelle Laurin

Bottom line messages from experts about vaccines

• Infection-acquired seroprevalence has **gone up** over time

- Hard to interpret due to seroreversion
- Association with lower-income neighbourhoods and households with more people per bedroom
- Vaccine hesitancy
 - Correlation between a parent's vaccination status and the likelihood they would vaccinate their children
 - Studies also found that higher vaccine hesitancy was associated with:
 - Lower parental education
 - Lower family income
 - Ethnic minority groups



Bottom line messages from experts about vaccines (cont.)

 Vaccines overall are protecting children and teens against hospitalization and severe disease

- Vaccines are safe: no vaccine-related deaths and few cases of severe adverse events
- Myocarditis/pericarditis:
 - Risk is 5 x lower in vaccinated vs. unvaccinated*
 - Lower dose mRNA vaccine has reduced risk
 - Longer dosing intervals have reduced risk

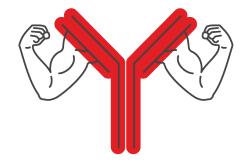


Bottom line messages from experts about vaccines (cont.)

Vaccines also provide other benefits:



Protecting against severe outcomes



Strengthening immunity in children with previous SARS-CoV-2 infection



Allowing for **normalcy** that supports healthy child development

Discussion: While pediatric vaccination is recommended, questions remain

- 1. What measures of vaccine effectiveness/protection should we be focussing on?
 - Breakthrough infections or degree of illness (mild to severe)?
 - ▶ Risks to household contacts, i.e. parents, grandparents
- 2. For those under 5 years old, are vaccines needed?
- 3. Given the number of unvaccinated and partially vaccinated children under 12, can we protect them against SARS-CoV-2 infection?
 - ▶ 5-11 years:
 - Fully vaccinated kids: 36%
 - Partially vaccinated: 21%
 - Unvaccinated kids: 43%
- 4. For the 12 to 17 year age group: high vaccine coverage, should they be boosted and when?
 - Fully vaccinated: 84%, with 11% of those boosted
 - Partially vaccinated: 4%



Questions?



Discover us!

- @COVIDimmunityTF
- @COVIDimmunityTF
- @COVIDimmunitytaskforce
- in COVID-19 Immunity Task Force | Groupe de travail sur l'immunité face à la COVID-19

- @CanCOVID
- in CanCOVID
- CanCOVID