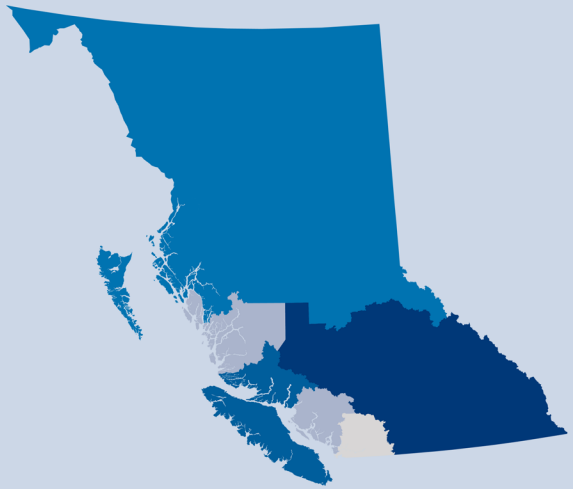


BC Immunization Forum 2023

COVID/Influenza Vaccine Effectiveness

Dr. Danuta Skowronski

Accredited by UBC CPD
THE UNIVERSITY OF BRITISH COLUMBIA
Continuing Professional Development
Faculty of Medicine

BC Centre for Disease Control

Provincial Health Services Authority

BRITISH COLUMBIA | ImmunizeBC

Influenza and COVID-19: Vaccine effectiveness (VE) update

Presentation to: BC Immunization Forum 2023

March 1, 2023

Danuta M Skowronski MD
BC Centre for Disease Control

BC Immunization Forum 2023 Presenter Disclosure

- **Speaker:** Danuta M Skowronski

- **Relationships with financial sponsors:** None

- **This program has received financial support from:** BCCDC Foundation for Public Health, Michael Smith Foundation for Health Research, Public Health Agency of Canada **in the form of** grant paid to institution (BCCDC)
  - The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada

- **<u>Potential for conflict(s) of interest</u>:**
  - Danuta M Skowronski has received funding from BCCDC Foundation for Public Health, Michael Smith Foundation for Health Research, Public Health Agency of Canada **in the form of** grant paid to institution (BCCDC)
  - Potential bias will be mitigated by: using generic names, highlighting where evidence may be limited or inconsistent

Outline of influenza and COVID-19 update

- **Influenza**
  - Enhanced influenza vaccines for elderly adults
  - 2021-22 and 2022-23 influenza VE and WHO recommendations

- **COVID-19**
  - Autumn 2022 seroprevalence findings in BC
  - Hybrid immunity and implications for booster dose recommendations

- **Future directions**
  - Panel discussion and Q&A

Influenza vaccines authorized/available in Canada, 2022-23

Influenza vaccine (IV)	No. Strains	Dose	Type	Abbrev	Example products	Canada	BC
Inactivated (IIV)	Trivalent (IIV3)	Standard (SD) 15 ug HA per strain per 0.5 mL	Egg-based, unadjuvanted	IIV3	Agriflu (6+ m) Influvac (3+ y)	—	—
			Egg-based **adjuvanted**	IIV3-Adj	FluAd (65+ y)	7%	33%
					FluAd Pediatric (6-23 m)	—	—
	Quadrivalent (IIV4)	Standard (SD) 15 ug HA per strain per 0.5 mL	Egg-based, unadjuvanted	IIV4	Afluria Tetra (5+ y)	5%	—
					FluLaval Tetra (6+ m)	31%	—
					Fluzone Quad (6+ m)	39%	59%
					Influvac Tetra (3+ y)	—	—
		High-dose (HD) **60 ug HA** per strain per **0.7 mL**		IIV4-HD	Fluzone High-Dose Quadrivalent (65+ y)	17%	3%
		Standard (SD) 15 ug HA per strain per 0.5 mL	**Cell-culture,** unadjuvanted	IIV4-CC	Flucelvax Quad (2+ y)	—	—
Recombinant (RIV)		**45 ug HA** per strain per 0.5 mL	**Recombinant,** unadjuvanted	RIV4	Supemtek (18+ y)	—	—
Live attenuated (LAIV)	Quadrivalent (LAIV4)	$10^{6.5\text{-}7.5}$ fluorescent focus units per 0.2mL	Egg-based, unadjuvanted	LAIV4	FluMist Quadrivalent (2-59 y)	<1%	4%

Interpreting relative VE (rVE) of enhanced influenza vaccines

$$VE_{Enhanced} = VE_{Standard} + rVE \times (1 - VE_{Standard})$$

What this means:

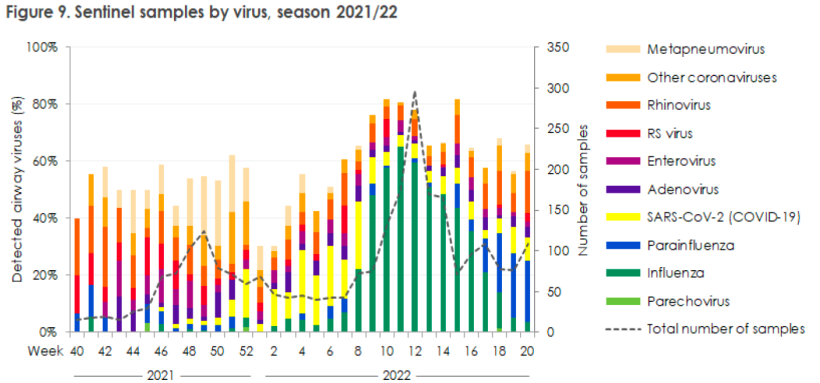
- If the $VE_{Standard} = 0$, then the $VE_{Enhanced} = rVE$
- For the same rVE (e.g. 20%)
  - The higher the $VE_{Standard}$, the lower the absolute gain with enhanced vaccine
    - If $VE_{Standard} = 20\%$; $VE_{Enhanced} = 0.2 + 0.20 \times 0.8 = 36\%$; marginal gain of 16%
    - If $VE_{Standard} = 80\%$; $VE_{Enhanced} = 0.8 + 0.20 \times 0.2 = 84\%$; marginal gain of 4%

rVE: High-dose vs. standard dose IIV, RCT evidence, adults ≥65 years

	Saade et al Vaccine 2022	Johansen et al NEJM Evid 2023
Design	Post hoc analysis of pragmatic cluster RCT	Pragmatic open-label, randomized ***feasibility*** study [not intended to assess clinical outcomes]
Funder	**Sanofi**	**Sanofi**
Study population	US nursing home residents ≥65 years	Danish adults 65-79 years
Vaccines	IIV3-HD vs IIV3-SD	IIV4-HD vs IIV4-SD [all Influvac]
Season	2013-14 (H1 dominant)	2021-22 (H3 dominant)
Outcome data source	Centers for Medicare/Medicaid Services (CMS) data claims	ICD-10 clinical coding
rVE vs Hospitalization % (95%CI) [clinically coded]		
Pneumonia or influenza	18 (4, 31)	64 (24, 85)
Respiratory	11 (0, 20)	40 (-2, 66)
Cardiovascular or MACE	8 (-6, 9)	-1 (-39, 27)
Above two, combined	9 (0, 17)	12 (-16, 33)
All-cause	—	7 (-5, 18)
rVE vs Death % (95%CI)		
All-cause	—	**49 (12, 71)**

How valid are the findings from Johansen et al likely to be?

- *Feasibility* study – not primarily designed/powered to assess actual outcomes
- rVE = 49% means risk of death due to any cause reduced by about half among those given high-dose versus standard dose IIV
  - Study spanned 7 months:
    - Oct 1, 2021 – May 31, 2022 (epi-weeks 39, 2021 to 22, 2022)
    - Denmark experienced a late 2021-22 influenza A(H3N2) epidemic (peak mid-March, 2022)
    - Lots of other respiratory viruses: notably COVID-19 during that period
    - Denmark reported 2021-22 influenza IIV4-SD VE against laboratory-confirmed influenza A illness, both hospitalized and non-hospitalized, was zero



- IF $VE_{Standard}$ = 0, the $VE_{Enhanced}$ = rVE [for severe outcomes]

- IF $VE_{Enhanced}$ = rVE = 49% against all cause mortality
  - Suggests high-dose IIV alone prevented half of all deaths due to any cause in adults 65-79 years in Denmark during the 7 month follow-up period (e.g. deaths due to trauma, cancer, cardiovascular disease, renal disease, influenza, other respiratory ailments, including COVID-19 etc)
  - Do *you think this is possible*?

https://en.ssi.dk/surveillance-and-preparedness/surveillance-in-denmark/annual-reports-on-disease-incidence/influenza-season-2021-2022 and
https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.15.2200278

rVE: High-dose vs. standard dose IIV, Observational evidence

- Lee et al, Vaccine 2021 [**meta-analysis**]: Adults ≥65 years, studies span 2009-10 to 2018-19
  - Funded by Sanofi

Outcome	rVE % (95% CI)
Probable/laboratory-confirmed ILI[a]	**16 (4, 26)**
Hospitalization (clinically coded)	
Influenza coded[b]	**12 (6, 18)**
Pneumonia coded[a,c,d]	**27 (15, 38)**
Pneumonia or influenza coded	13 (7, 19)
Cardiorespiratory coded	18 (15, 21)
All-cause	8 (6, 11)
Mortality (clinically coded)	
Influenza coded[f]	**22 (-18, 49)**
Pneumonia or influenza coded[f]	**40 (19, 56)**
Cardiorespiratory coded	**28 (13, 32)**
All-cause	3 (-5, 10)

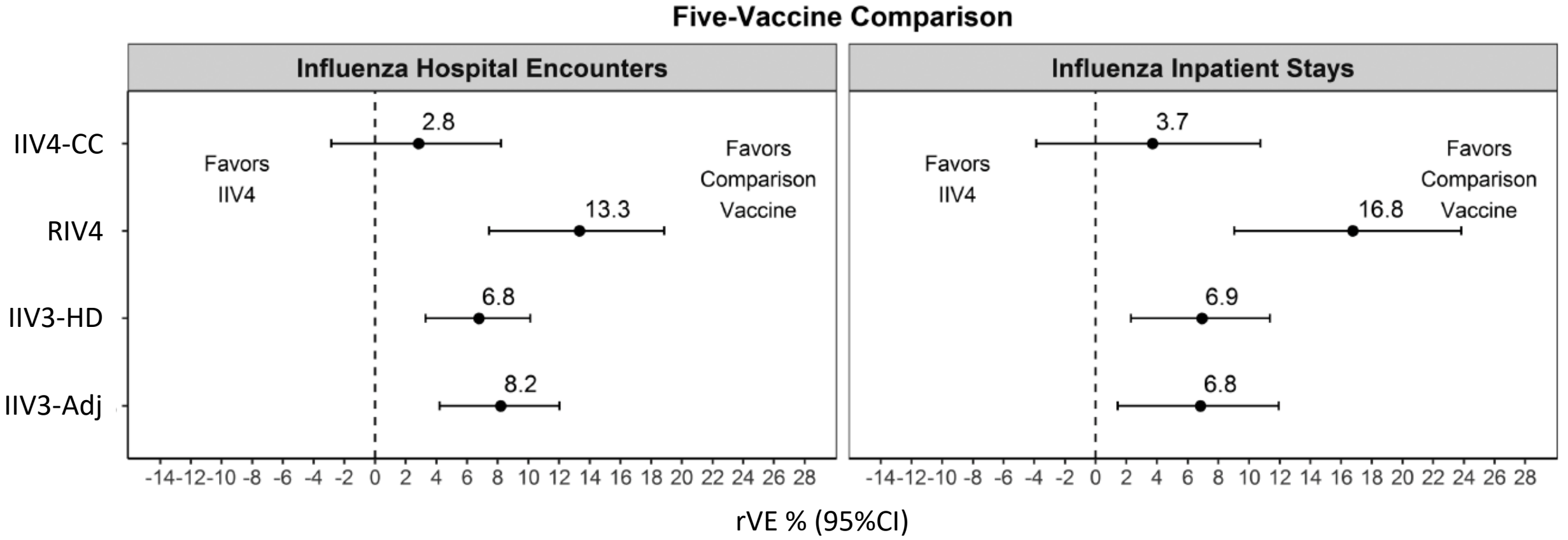
a. Includes DiazGranados RCTs (2009-10, 2011-12, 2012-13)
b. ICD-9-CM 487 coded hospitalizations)
c. Includes Gravenstein cluster RCT in nursing home residents (2013-14)
d. ICD-9-CM 480-486 coded hospitalizations
e. ICD-9-CM 480-488 coded hospitalizations
f. A single study

rVE: Adjuvanted vaccine vs standard or high-dose IIV, observational evidence

- **Adjuvanted vs. standard IIV, adults ≥65 years**
  - **Coleman et al, IORV 2021 [meta-analysis]** **Funded by Sequiris**
    - Studies span 2006-07 to 2018-19
    - Against influenza-coded hospitalization, emergency department or outpatient care: **14% (95%CI: 4, 24)**
  - **McConeghy et al. Clin Infect Dis 2021 [pragmatic, cluster RCT]** **Funded by Sequiris**
    - Nursing home residents, 2016-2017
    - Against pneumonia or influenza hospitalization: **21% (95%CI: 4, 35)**
    - Against respiratory illness hospitalization: **9% (95%CI: -2, 19)**
    - Against all cause hospitalization: **6% (95%CI: 0, 11)**
- **Adjuvanted vs. high-dose IIV, adults ≥65 years**
  - **Domnich et al, Int J Infect Dis 2022 [meta-analysis]** **Funded by Sequiris**
    - Studies span 2016-17 to 2019-20; used non-specific (clinically-coded) outcomes
    - Small and inconsistent differences against inpatient/outpatient outcomes ranging **-14% to +10%**
      - Industry-sponsored studies use less specific outcomes and tend to report larger VEs (in direction of sponsor)

Observational comparison of multiple vaccines simultaneously

- **Izurieta et al, Clin Infect Dis 2021 [Retro cohort]: Adults ≥65 years (half ≥75 years), 2019-2020 season**
  - Medicare fee-for-service (FFS) database
  - Outcome: administrative coding for Influenza emergency room visits and hospitalizations
  - Season dominated by influenza B(Victoria) [included in vaccine], followed by A(H1N1)pdm09, paucity of H3N2
  - Funded by FDA



Summary

- No additional RCTs to assess enhanced vaccines against laboratory-confirmed influenza
- No head-to-head RCTs comparing enhanced vaccine efficacies directly

- **Observational studies: Compared to standard products, enhanced vaccines give some relative improvement**
  - 10-25% against influenza illness
  - 10-25% against hospitalization (as much as 60%); 5-49% against mortality
  - Signals that caution require in the interpretation:
    - Reported reductions in severe outcomes sometimes *very surprisingly* high
    - Higher against non-specific versus specific outcomes also unexpected

- **Observational studies: Compared to each other, small and inconsistent differences b/w enhanced products**
  - Important determinant of differences: use of non-specific outcome and who sponsored the study

- **Conclusion:**
  - Socioeconomic decision whether the marginal gains warrant the increased cost of enhanced vaccines
  - Insufficient evidence to prefer one enhanced vaccine over the other
  - Need better products that get at the root cause of recurrently suboptimal influenza vaccine performance

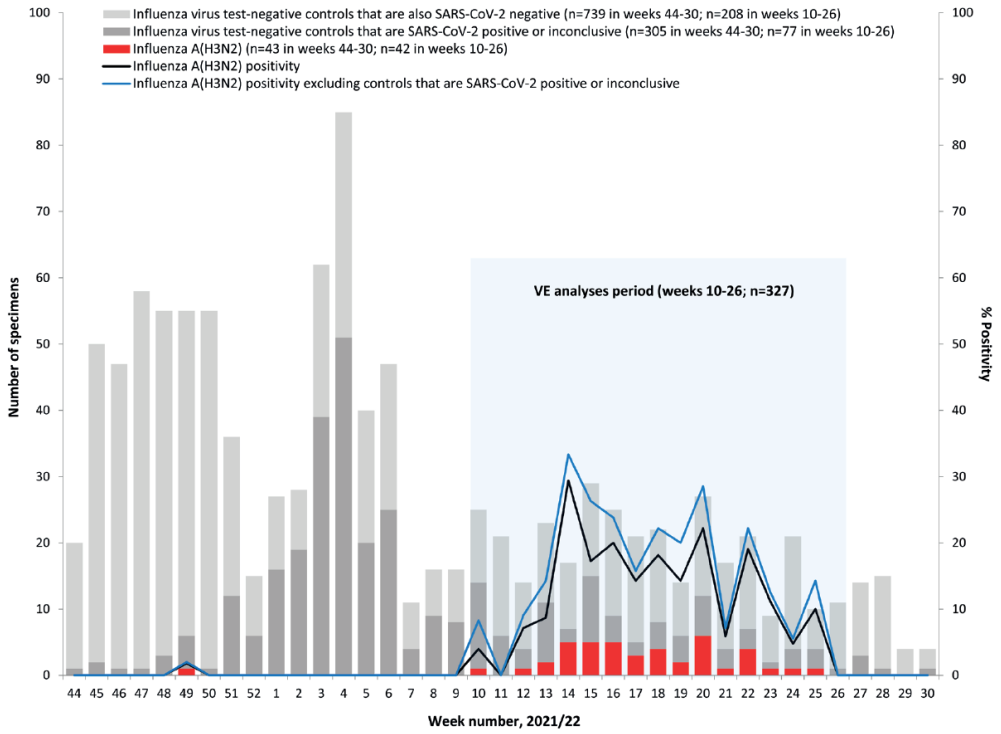
Update on 2021-22 and 2022-23 influenza VE

Eurosurveillance

RAPID COMMUNICATION

Influenza vaccine effectiveness against A(H3N2) during the delayed 2021/22 epidemic in Canada

Shinhye Kim[1] , Erica SY Chuang[1] , Suzana Sabaiduc[1] , Romy Olsha[2] , Samantha E Kaweski[1] , Nathan Zelyas[3] , Jonathan B Gubbay[2,4] , Agatha N Jassem[1,5] , Hugues Charest[6] , Gaston De Serres[6,7,8] , James A Dickinson[9] , Danuta M Skowronski[1,5]



Vaccine strain = A/Cambodia/e0826360/2020
Vaccine clade = 3C.2a1b.2a.1
Circulating clade = 3C.2a1b.2a.2 (antigenic mismatch)

A(H3N2) estimate	N Total	A(H3N2) Cases Vaccinated/Total (% vaccinated)	Controls Vaccinated/Total (% vaccinated)	Adjusted A(H3N2) VE (95% CI)
Overall	327	15/42 (36)	155/285 (54)	**36 (-38, 71)**

Article submitted on 10 Sept 2022 / accepted on 21 Sept 2022 / published on 22 Sept 2022

2021-22 VE estimates against A(H3N2) similar in Europe (29%) & US (36%)

Influenza vaccine effectiveness against influenza A subtypes in Europe: Results from the 2021–2022 I-MOVE primary care multicentre study et al

Esther Kissling[1] | Francisco Pozo[2,3] | Iván Martínez-Baz[3,4] |

Influenza Other Respi Viruses. 2023;17:e13069.
https://doi.org/10.1111/irv.13069

Received: 20 October 2022 | Revised: 26 October 2022 | Accepted: 29 October 2022

A(H3N2) estimate	N Total	A(H3N2) Cases Vaccinated/Total (% vaccinated)	Controls Vaccinated/Total (% vaccinated)	Adjusted A(H3N2) VE (95% CI)
Overall	11, 201	227/1595 (14)	1724/9606 (18)	**29 (12, 42)**

Influenza Vaccine Effectiveness Against Influenza A(H3N2)-Related Illness in the United States During the 2021–2022 Influenza Season

Ashley M. Price,[1,©] Brendan Flannery,[1] H. Keipp Talbot,[2] Carlos G. Grijalva,[2] Karen J. Wernli,[3] C. Hallie Phillips,[3] Arnold S. Monto,[4] Emily T. Martin,[4] Edward A. Belongia,[5] Huong Q. McLean,[5] Manjusha Gaglani,[6,7] Manohar Mutnal,[6,7] Krissy Moehling Geffel,[8] Mary Patricia Nowalk,[8] Sara Y. Tartof,[9] Ana Florea,[9] Callie McLean,[1] Sara S. Kim,[1] Manish M. Patel,[1] and Jessie R. Chung[1]

Clinical Infectious Diseases® https://doi.org/10.1093/cid/ciac941

Received 05 October 2022; editorial decision 30 November 2022; published online 12 December 2022

A(H3N2) estimate	N Total	A(H3N2) Cases Vaccinated/Total (% vaccinated)	Controls Vaccinated/Total (% vaccinated)	Adjusted A(H3N2) VE (95% CI)
Overall	4,284	182/440 (41)	2265/3844 (59)	**36 (20, 49)**

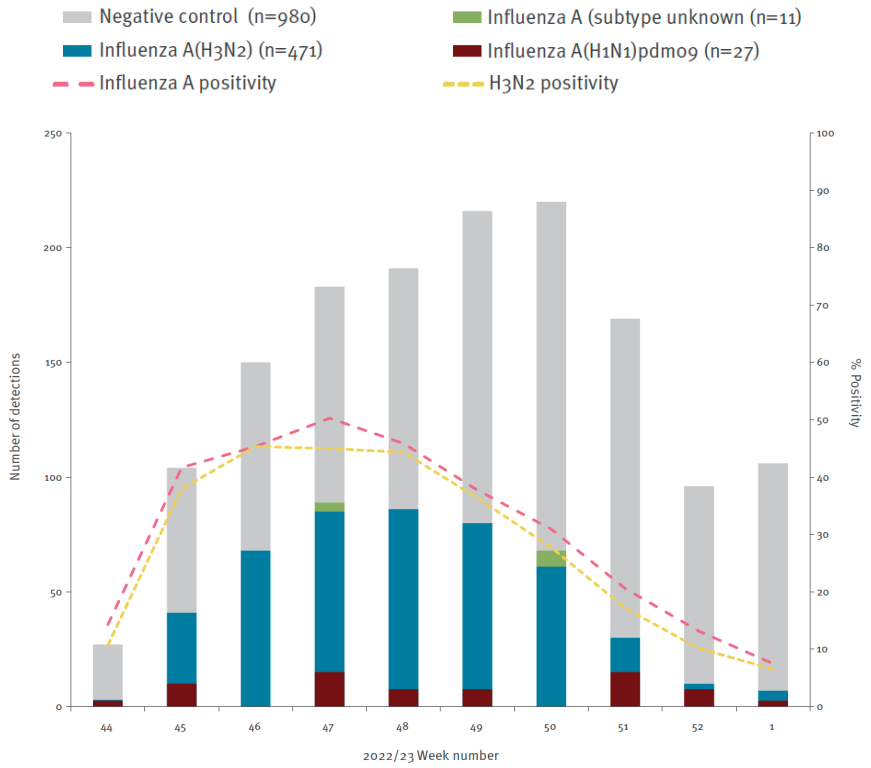
Eurosurveillance

SPSN
Canadian Sentinel Practitioner Surveillance Network for Influenza Vaccine Effectiveness Monitoring
Réseau sentinelle canadien de surveillance de l'efficacité du vaccin antigrippal

RAPID COMMUNICATION

Vaccine effectiveness estimates from an early-season influenza A(H3N2) epidemic, including unique genetic diversity with reassortment, Canada, 2022/23

Danuta M Skowronski[1,2], Erica SY Chuang[1], Suzana Sabaiduc[1], Samantha E Kaweski[1], Shinhye Kim[1], James A Dickinson[3], Romy Olsha[4], Jonathan B Gubbay[4,5], Nathan Zelyas[6], Hugues Charest[7], Nathalie Bastien[8], Agatha N Jassem[1,2], Gaston De Serres[7,9,10]



Vaccine strain = A/Darwin/9/2021
Vaccine clade = 3C.2a1b.2a.2
Circulating clade = 3C.2a1b.2a.2 (antigenic match)

A(H3N2) estimate	N Total	A(H3N2) Cases Vaccinated/Total (% vaccinated)	Controls Vaccinated/Total (% vaccinated)	Adjusted A(H3N2) VE (95% CI)
Overall	1,451	75/471 (16)	361/980 (37)	**54 (38, 66)**
1-19 years	528	25/216 (12)	81/312 (26)	**47 (11, 69)**
20-64 years	704	29/212 (14)	155/492 (32)	**58 (33, 73)**
65+ years	219	21/43 (49)	125/176 (71)	**59 (15, 80)**

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 72 / No. 8
February 24, 2023

Interim Estimates of 2022–23 Seasonal Influenza Vaccine Effectiveness — Wisconsin, October 2022–February 2023

Huong Q. McLean, PhD[1]; Joshua G. Petrie, PhD[1]; Kayla E. Hanson, MPH[1]; Jennifer K. Meece, PhD[1]; Melissa A. Rolfes, PhD[2]; Gregg C. Sylvester, MD[3]; Gabriele Neumann, PhD[4]; Yoshihiro Kawaoka, DVM, PhD[4]; Edward A. Belongia, MD[1]

TABLE 2. Estimated 2022–23 influenza vaccine effectiveness* — Wisconsin, October 2022–February 2023

	Test-negative case-control study, persons aged 6 mos–64 yrs					Community cohort study, persons aged 1–17 yrs				
	Positive influenza test result		Negative influenza and SARS-CoV-2 test results			Vaccinated		Not vaccinated		
Influenza type	Total	No. of persons vaccinated (%)	Total	No. of persons vaccinated (%)	Adjusted VE,* % (95% CI)	No. of person-days	No. of positive influenza test results	No. of person-days	No. of positive influenza test results	Adjusted VE,† % (95% CI)
A	**116**	26 (22)	**429**	160 (37)	54 (23–73)	7,292	6	15,678	28	71 (31–90)
A(H3N2)	**86**	16 (19)	**429**	160 (37)	60 (25–79)	NE	NE	NE	NE	NE

Eurosurveillance

RAPID COMMUNICATION

Vaccine effectiveness estimates from an early-season influenza A(H3N2) epidemic, including unique genetic diversity with reassortment, Canada, 2022/23

Danuta M Skowronski[1,2], Erica SY Chuang[1], Suzana Sabaiduc[1], Samantha E Kaweski[1], Shinhye Kim[1], James A Dickinson[3], Romy Olsha[4], Jonathan B Gubbay[4,5], Nathan Zelyas[6], Hugues Charest[7], Nathalie Bastien[8], Agatha N Jassem[1,2], Gaston De Serres[7,9,10]

SPSN
Canadian Sentinel Practitioner Surveillance Network for Influenza Vaccine Effectiveness Monitoring
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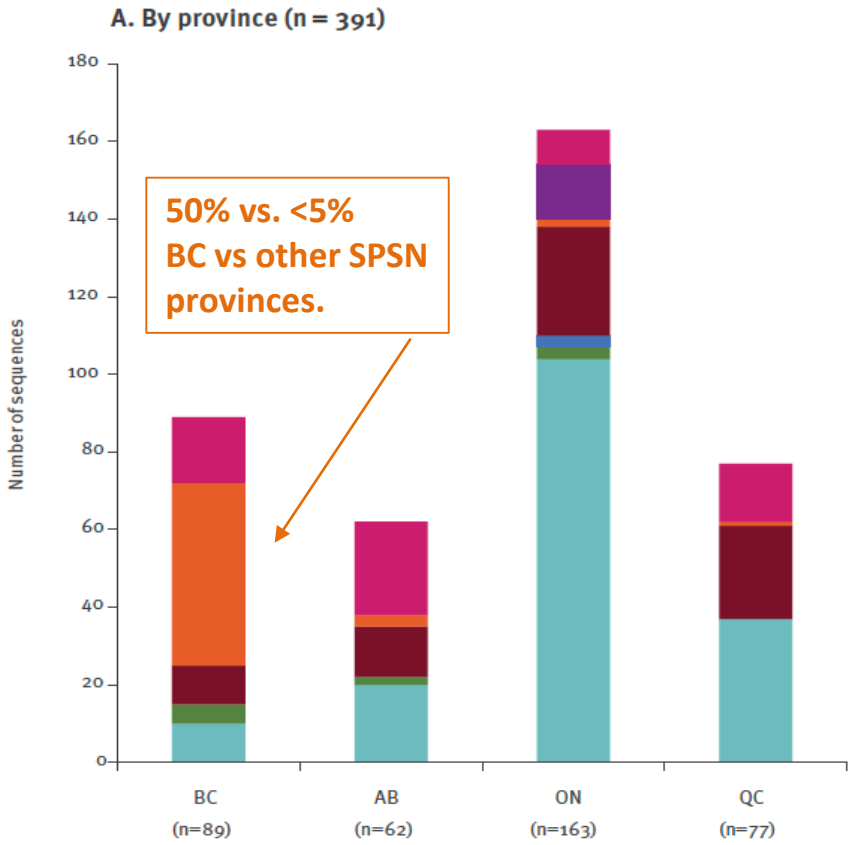


H156
- 3C.2a1b.2a.2 + E50K[C] + I140K[A] + I242M[D] {i, 2b}
- 3C.2a1b.2a.2 + E50K[C] + I140K[A] + **T135A[A][RBS][-CHO]** + S262N[E] {i, 2b}
- 3C.2a1b.2a.2 + E50K[C] + I140K[A] + **T135K[A][RBS][-CHO]** + G275D[C] {i, 2b}
- 3C.2a1b.2a.2 + E50K[C] + I140K[A] + F79V {i, 2b}

S156 (like vaccine)
- 3C.2a1b.2a.2 + H156S[B] + D53N[C] + N96S[D][+CHO] + I192F[B] + E50K[C] + I140K[A] + I223V {ii, 2a.3a.1}
- 3C.2a1b.2a.2 + H156S[B] + D53G[C] + D104G + K276R[C] {iii, 2a.1}
- 3C.2a1b.2a.2 + H156S[B] + D53G[C] + D104G + K276R[C] + I140K[A] + R299K[C] {iv, 2a.1b}

More than 85% of this variant (compared to 50-60% of other variants) were found in people <25 years.

World Health Organization 2023-24 influenza vaccine components

World Health Organization

https://www.who.int/news/item/24-02-2023-recommendations-announced-for-influenza-vaccine-composition-for-the-2023-2024-northern-hemisphere-influenza-season

	A(H1N1)pdm09	A(H3N2)	B/Victoria	B/Yamagata
Recommended Strain, 2022-23	A/Victoria/2570/2019*	A/Darwin/9/2021	B/Austria/1359417/2021	B/Phuket/3073/2013
Clade, 2022-23	6B.1A.5a.2 “5a.2”	3C.2a1b.2a.2 “2a”	V1A.3a.2 “3a.2”	Y3
Recommended Strain, 2023-24	A/Victoria/4897/2022**	—	—	—
Clade, 2023-24	6B.1A.5a.2a.1 “5a.2a.1”***	—	—	—

* Recommended cell culture version, 2022-23: A/Wisconsin/588/2019
**Recommended cell culture version, 2023-24: A/Wisconsin/67/2022 (H1N1)pdm09
***Different from Southern Hemisphere upcoming 2023 vaccine: A/Sydney/5/2021 (clade 6B.1A.5a.2a or “5a.2a”) [all other components same as 2023 SH vaccine]

National influenza mid-season report, 2022–2023: A rapid and early epidemic onset

SURVEILLANCE

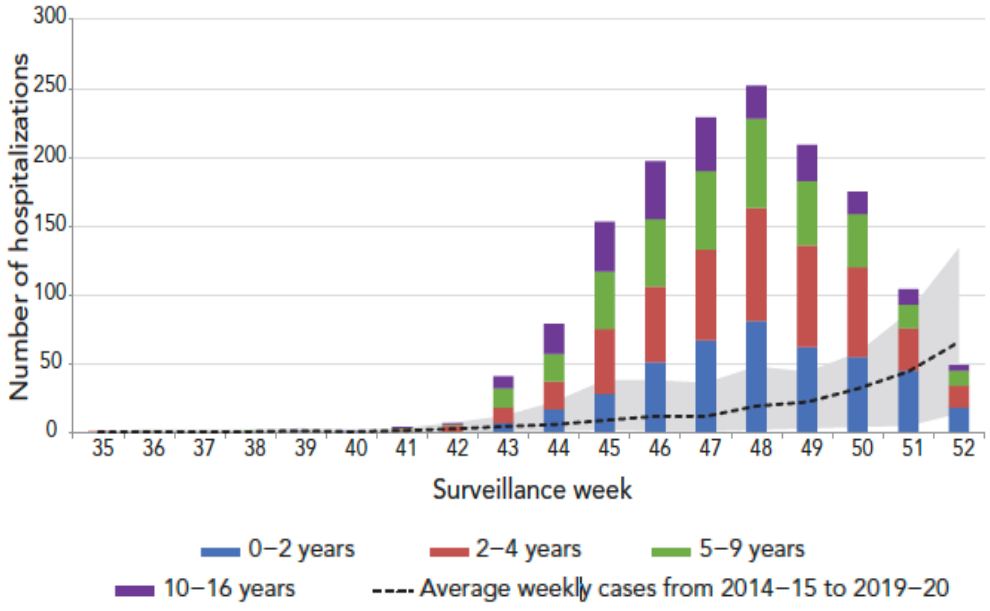
CCDR • January 2023 • Vol. 49 No. 1

Myriam Ben Moussa[1]*, Steven Buckrell[1], Abbas Rahal[1], Kara Schmidt[1], Liza Lee[1], Nathalie Bastien[2], Christina Bancej[1]

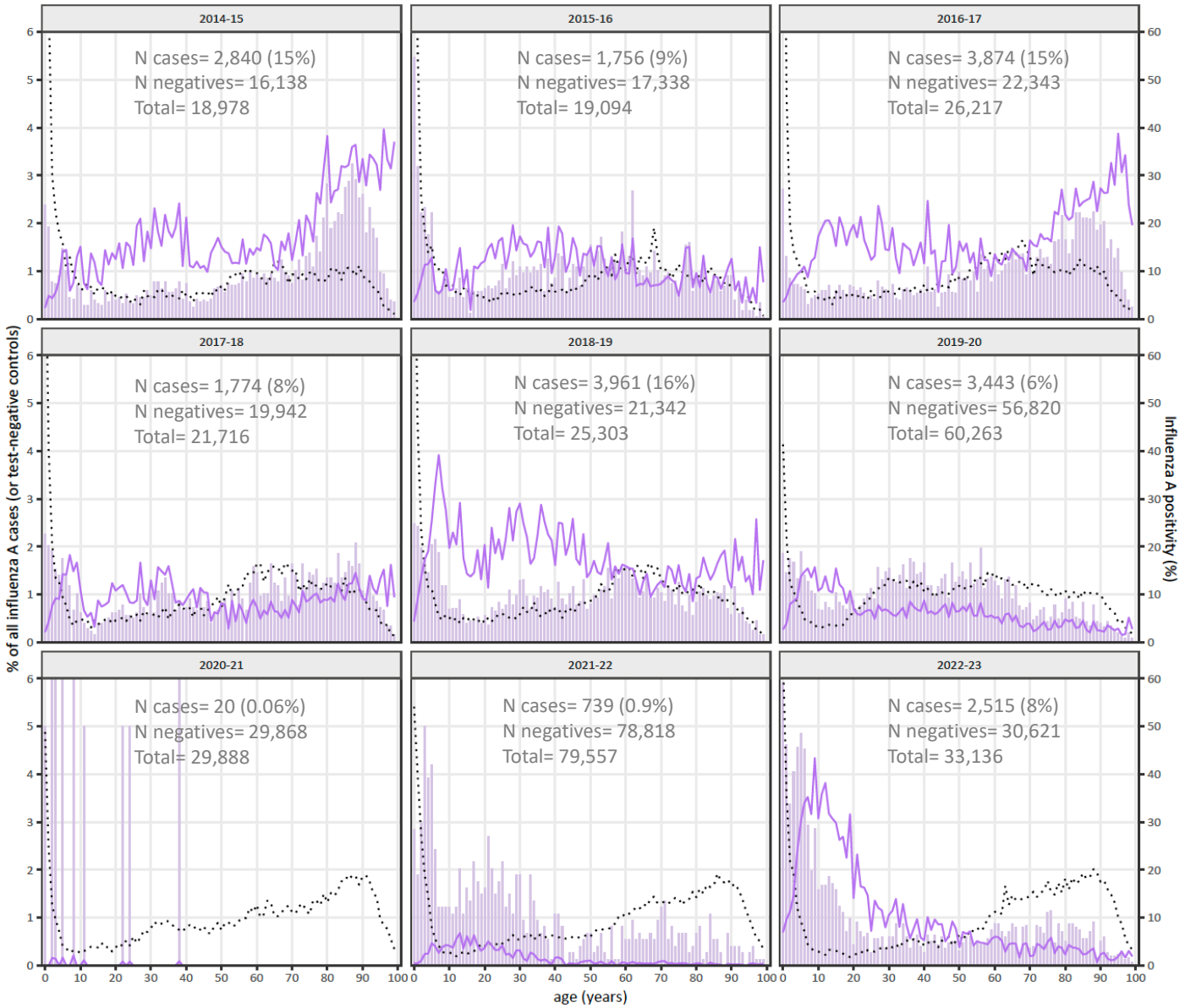
Table 1: Season indicators reported up to week 52 compared to recent pre-pandemic seasons, 2017–2018 to 2019–2020

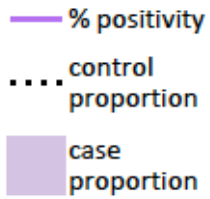
Indicator		2022–2023	2019–2020	2018–2019	2017–2018
Epidemic onset		Week 43	Week 47	Week 43	Week 45
Onset to peak		5 weeks	14 weeks	8 weeks	14 weeks
1st report of localized activity		Week 35	Week 40	Week 38	Week 36
Peak percent positivity week (%)		Week 47 (23.8%)	Week 6 (29.7%)	Week 52 (28.9%)	Week 7 (32.5%)
Dominant circulating influenza type (%)		Influenza A (99%)	Influenza B (51%)	Influenza A (99%)	Influenza A (74%)
Dominant circulating influenza A subtype (%)		H3N2 (94%)	H3N2 (68%)	H1N1 (93%)	H3N2 (96%)
Proportion of detections among ages 65 years and older (%)		26	21	16	44
Proportion of detections among ages 19 years and younger (%)		42	44	41	19
Provincial and territorial severe outcomes[a]	Cumulative hospitalization rate (per 100,000)	41	7	13	19
	Hospitalizations	3,411	618	1,064	1,493
	ICU admissions	301	73	151	114
	Deaths	182	22	27	34
Paediatric severe outcomes[b]	Hospitalizations	1,505	264	414	195
	ICU admissions	12% 183	22% 57	17% 71	18% 35
	Deaths	6	0	fewer than 5	fewer than 5

IMPACT pediatric hospitalizations, weeks 35-52



Influenza A test-positivity by single year of age and season, BC





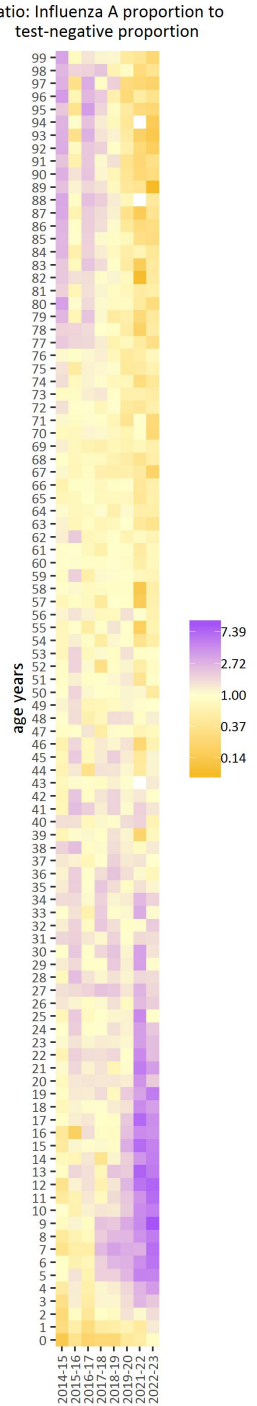
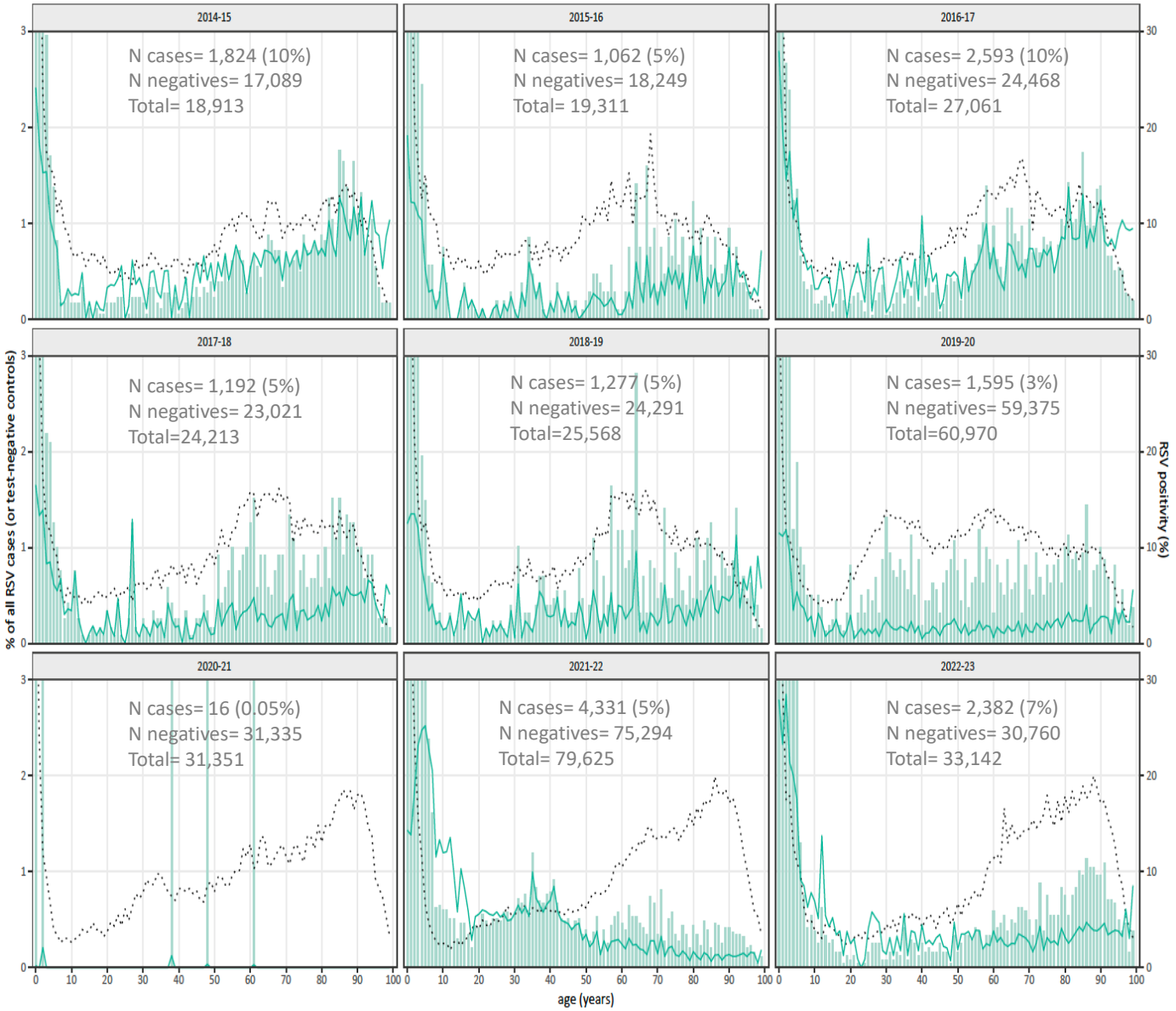
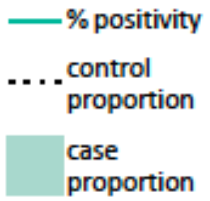


Figure & analyses courtesy: Shinhye Kim, BCCDC; with thanks to Yin Chang, BCCDC PHL for data support

a. Epi-weeks 35-34 each season except 2022-23 (epi-weeks 35-4)
b. VPP test sites: Vancouver Coastal, Providence Healthcare, PHSA test sites

RSV test-positivity by single year of age and season, BC





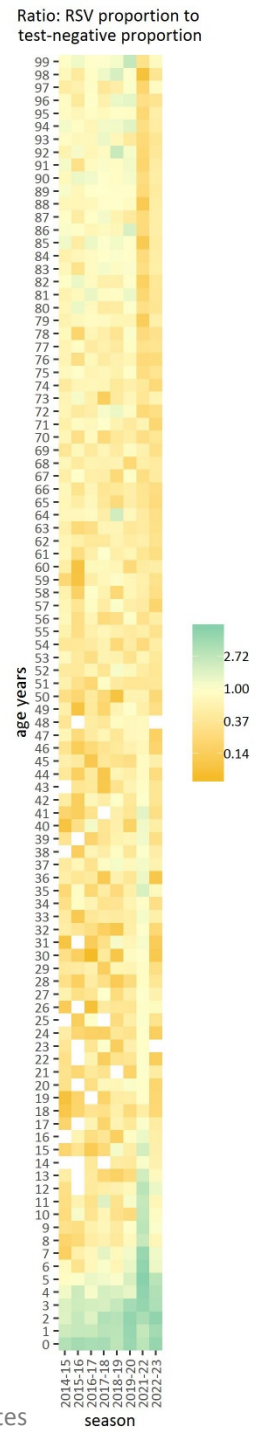


Figure & analyses courtesy: Shinhye Kim, BCCDC; with thanks to Yin Chang, BCCDC PHL for data support

a. Epi-weeks 35-34 each season except 2022-23 (epi-weeks 35-4)
b. VPP test sites: Vancouver Coastal, Providence Healthcare, PHSA test sites

https://www.medrxiv.org/content/10.1101/2022.11.18.22282477v1.full.pdf

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Comparative analysis of pediatric Respiratory Syncytial Virus epidemiology and clinical severity before and during the COVID-19 pandemic in British Columbia, Canada

Posted November 19, 2022.

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Supplemental table 3: Hospitalization and severity outcomes by age groups and annual periods, for children with RSV at BCCH.

	September 1st to August 31st period (number of RSV cases; n = 1,436)				
Age group / **Severity outcomes**	**2017-18** (n = 259)	**2018-19** (n = 273)	**2019-20** (n = 219)	**2017-20 periods combined** (n = 250)[1]	**2021-22** (n = 685)
<6 months old, n (%)[2]	135 (52.1)	133 (48.7)	103 (47.0)	124 (49.4)	241 (35.2)
Hospitalized, n (% age group)[3]	74 (54.8)	57 (42.9)	52 (50.5)	61 (49.3)	63 (26.0)
Length of in-hospital stay, median days (IQR)	4 (2 - 6)	4 (2 - 5)	4 (2 - 7)	4 (2 - 6)	3 (2 - 6)
Received supplemental O_2, n (% hospitalized)	49 (66.2)	39 (68.4)	39 (75.0)	43.25 (70.3)	46 (73.0)
ICU admission, n (% hospitalized)	18 (24.3)	10 (17.5)	13 (25.0)	14.25 (23.2)	16 (25.4)
6 to <12 months old, n (%)[2]	41 (15.8)	40 (14.7)	33 (15.1)	38 (15.2)	106 (15.5)
Hospitalization, n (% age group) [3]	25 (61.0)	16 (40.0)	20 (60.6)	20 (53.5)	13 (12.3)
Length of in-hospital stay, median days (IQR)	3 (1 - 5)	4 (3 - 5)	3 (2 - 4)	3 (2 - 5)	4 (3 - 6)
Received supplemental O_2, n (% hospitalized)	18 (72.0)	11 (68.8)	13 (65.0)	13 (70.3)	10 (76.9)
ICU admission, n (% hospitalized)	4 (16.0)	4 (25.0)	1 (5.0)	3 (16.2)	3 (23.1)
12 to <24 months old, n (%)[2]	53 (20.5)	69 (25.3)	57 (26.0)	60 (23.8)	188 (27.4)
Hospitalization, n (% of age group) [3]	32 (60.4)	48 (69.6)	32 (56.1)	37 (62.6)	23 (12.2)
Length of in-hospital stay, median days (IQR)	3 (2 - 6)	3(2 - 5)	3 (2 - 4)	3 (2 - 5)	2 (2 - 4)
Received supplemental O_2, n (% hospitalized)	22 (68.8)	31 (64.6)	18 (56.2)	22.25 (65.9)	18 (78.3)
Intensive care admission, n (% hospitalized)	7 (21.9)	7 (14.6)	7 (21.9)	6.25 (18.5)	4 (17.4)
24 to <36 months old, n (%)[2]	30 (11.6)	31 (11.4)	26 (11.9)	29 (11.6)	150 (21.9)
Hospitalization, n (% age group) [3]	22 (73.3)	17 (54.8)	11 (42.3)	17 (57.5)	24 (16.0)
Length of in-hospital stay, median days (IQR)	4 (3 - 9)	4 (3 - 6)	3 (2 - 6)	4 (3 - 7)	3 (2 - 4)
Received supplemental O_2, n (% hospitalized)	13 (59.1)	12 (70.6)	5 (45.5)	11.75 (63.5)	17 (70.8)
ICU admission, n (% hospitalized)	8 (36.4)	4 (23.5)	1 (9.1)	4.25 (23.0)	4 (16.7)
Total hospitalized (SD)	153	138	115	135 (15.6)	123

Why more respiratory illness in children in 2021-22 and 2022-23?

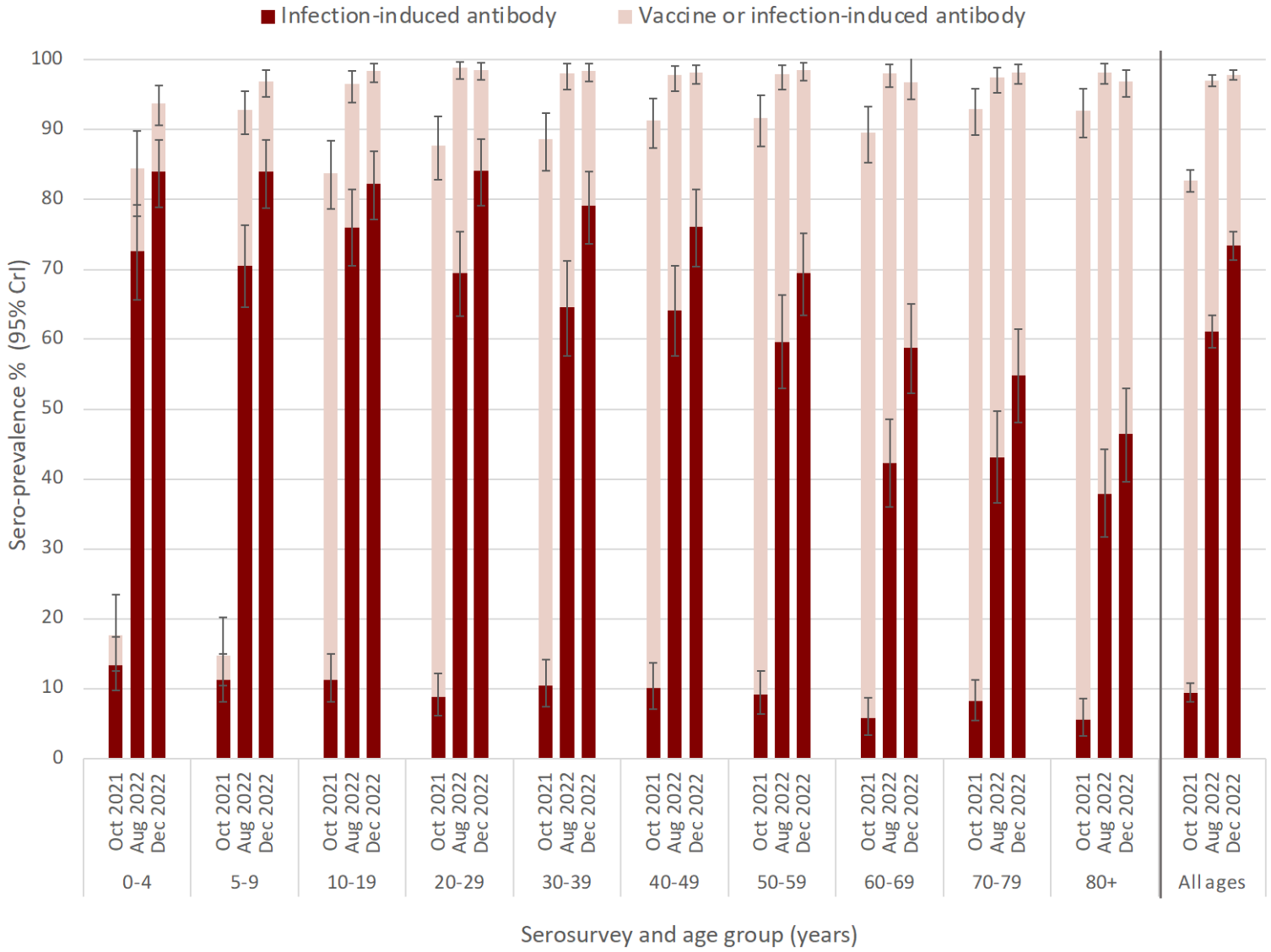
- **Most likely explanation is a temporary, non-specific cohort effect**
  - While COVID-19 mitigation measures were in place respiratory virus circulation was paused
  - During those years, children were spared infections they would have normally got earlier in life
    - Accumulation of several cohorts of children remaining susceptible
    - Typically those infections (and reinfections) would have occurred over a longer and staggered period
    - With reopening a large pool of susceptible children fueled simultaneous infections
    - Applied to multiple different respiratory viruses at the same time
    - Accompanied by a shift in the age distribution toward older children
  - It doesn't mean the viruses became more virulent or we became weaker
    - Even with the same low per case risk of severe outcome, when there are more cases it means more severe outcomes also (and strain on health care systems)

      Total number of severe outcomes = number of cases x per case risk of severe outcome

- **Should be a temporary cohort effect**
  - Should subside once susceptible cohorts get the infections they missed out on during the pandemic

Update: COVID-19 sero-prevalence & implications for booster dose recommendations

Updated seroprevalence estimates, Lower Mainland, BC, Dec 2022



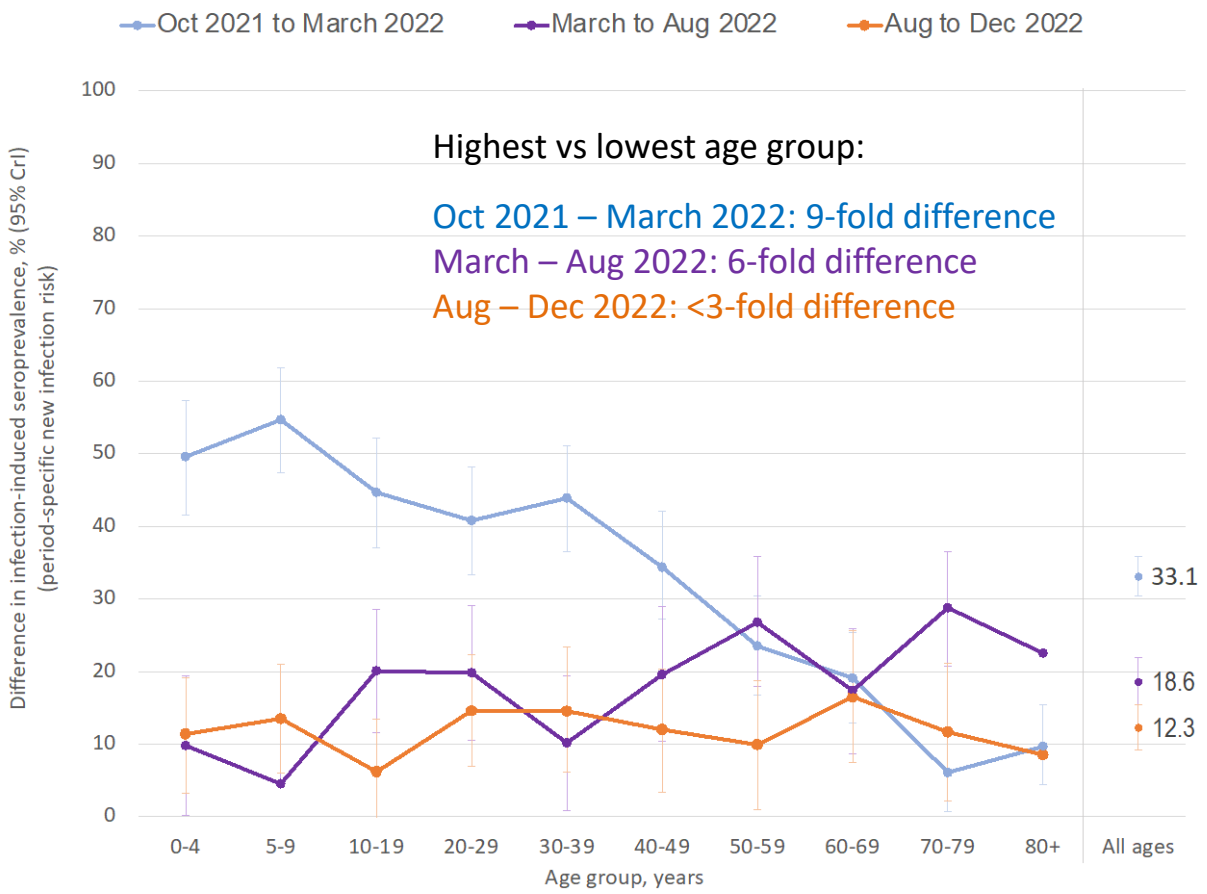
By end of the 3rd pandemic year:

- In addition to high vaccine coverage in all but the very young:
  - Three quarters have evidence of prior infection
    - >80% of children & young adults
    - Gradual decrease by age
    - <50% of older adults ≥80 years

Figure & analyses courtesy: Samantha Kaweski

The risk of new infection has become more similar by age

Risk of new infection, by age group, between serosurveys



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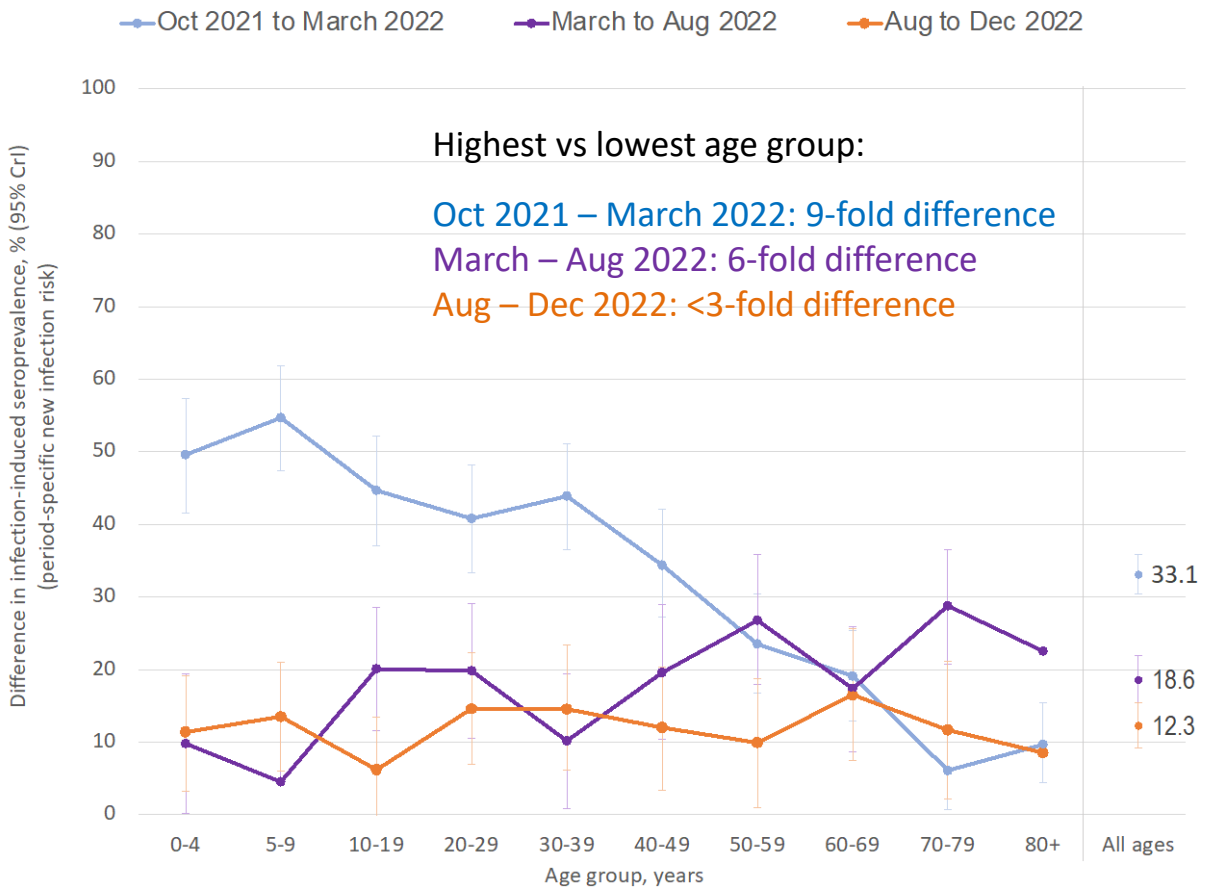


Older adults ≥70 years are 12% of the population, but 60-75% of all the SARS-CoV-2 hospitalizations

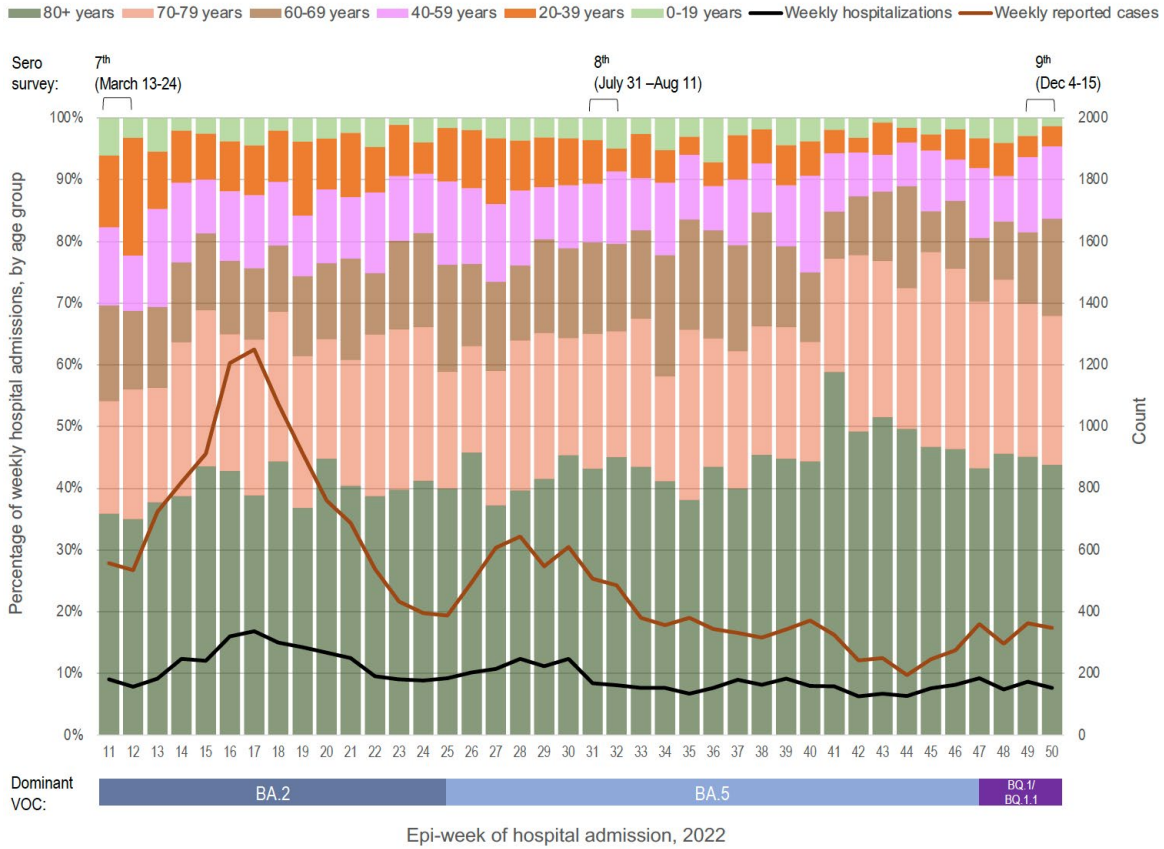


Figure & analyses courtesy: Samantha Kaweski

Hospitalization data courtesy: Hannah Caird
Figure courtesy: Samantha Kaweski

Preliminary estimates: hospitalization risk (for COVID-19) by age

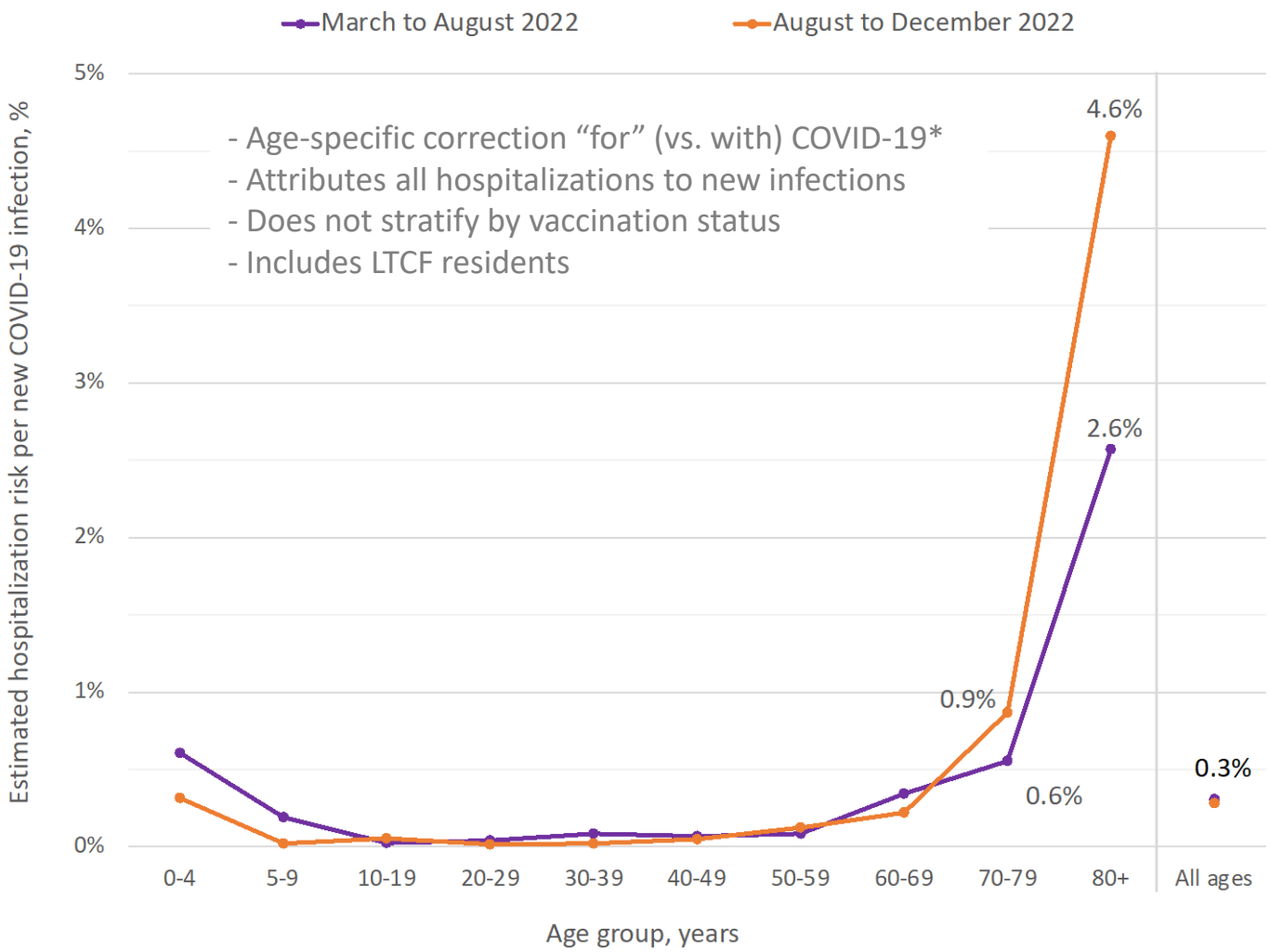


Figure & analyses courtesy: Samantha Kaweski

*Correction factors, personal communication Dr. Kate Smolina, Interim Scientific Director, Data & Analytic Services and Knowledge Translation, BCCDC. These were estimated March to August 2022, and were applied to each period. Potential variation by period could influence findings.

Preliminary estimates: hospitalization risk (for COVID-19) by age

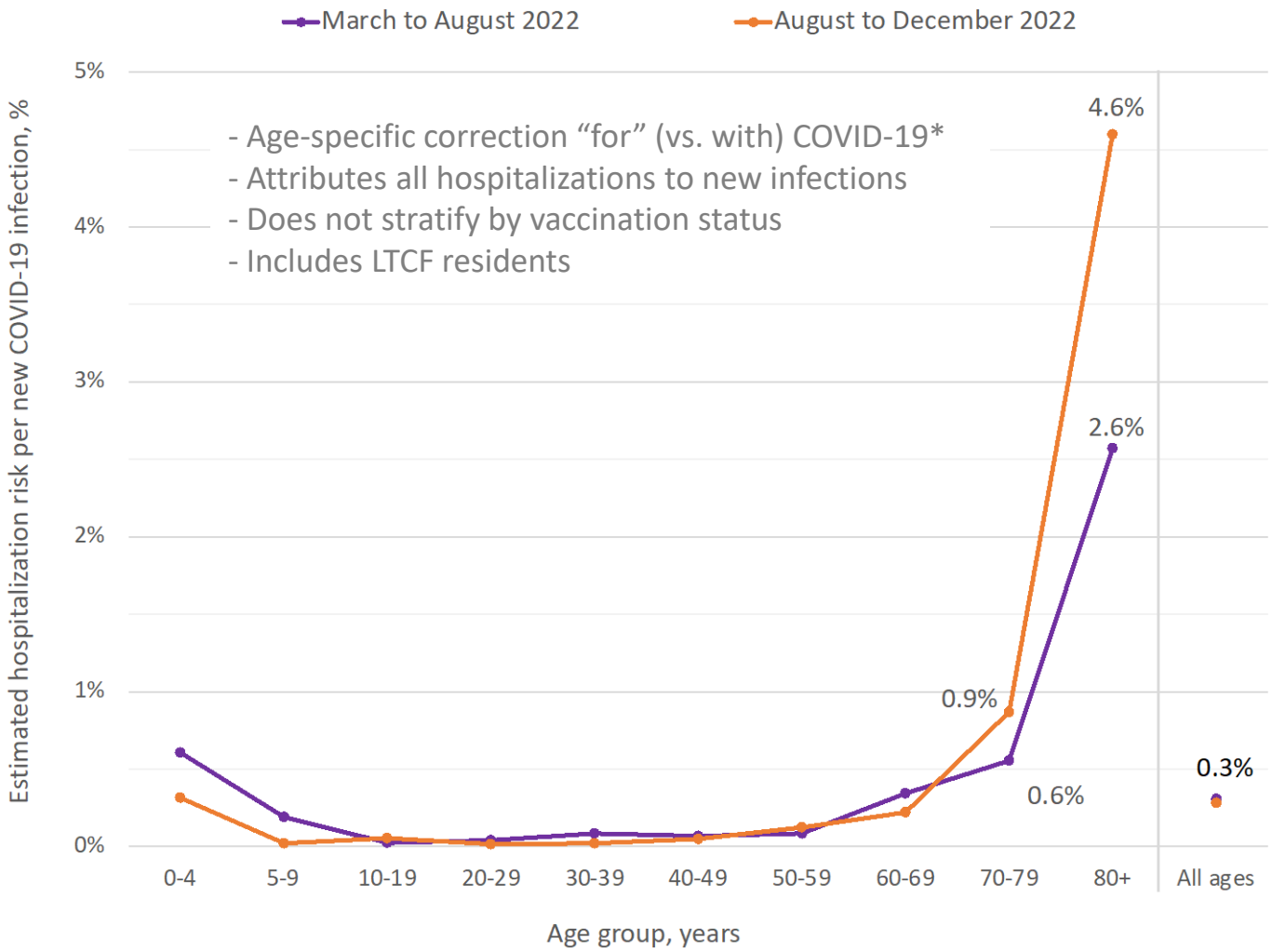
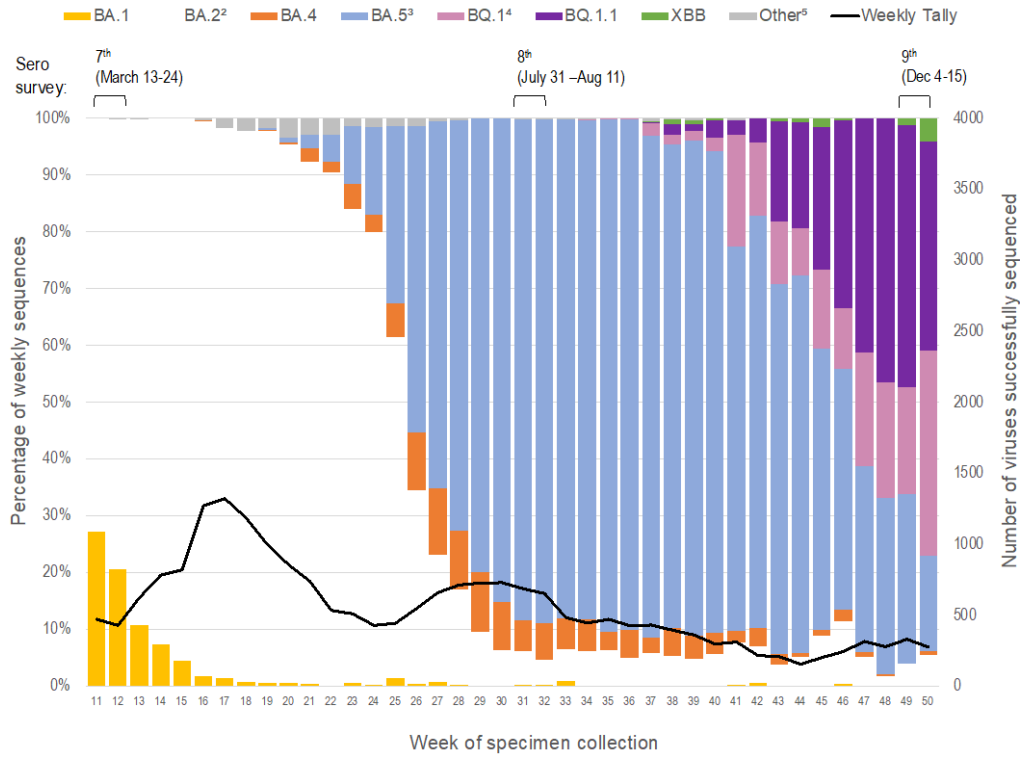


Figure & analyses courtesy: Samantha Kaweski

Contribution of BQ.1 during autumn 2022?



Genomic data courtesy: Dr. Hind Sbihi
Figure courtesy: Samantha Kaweski

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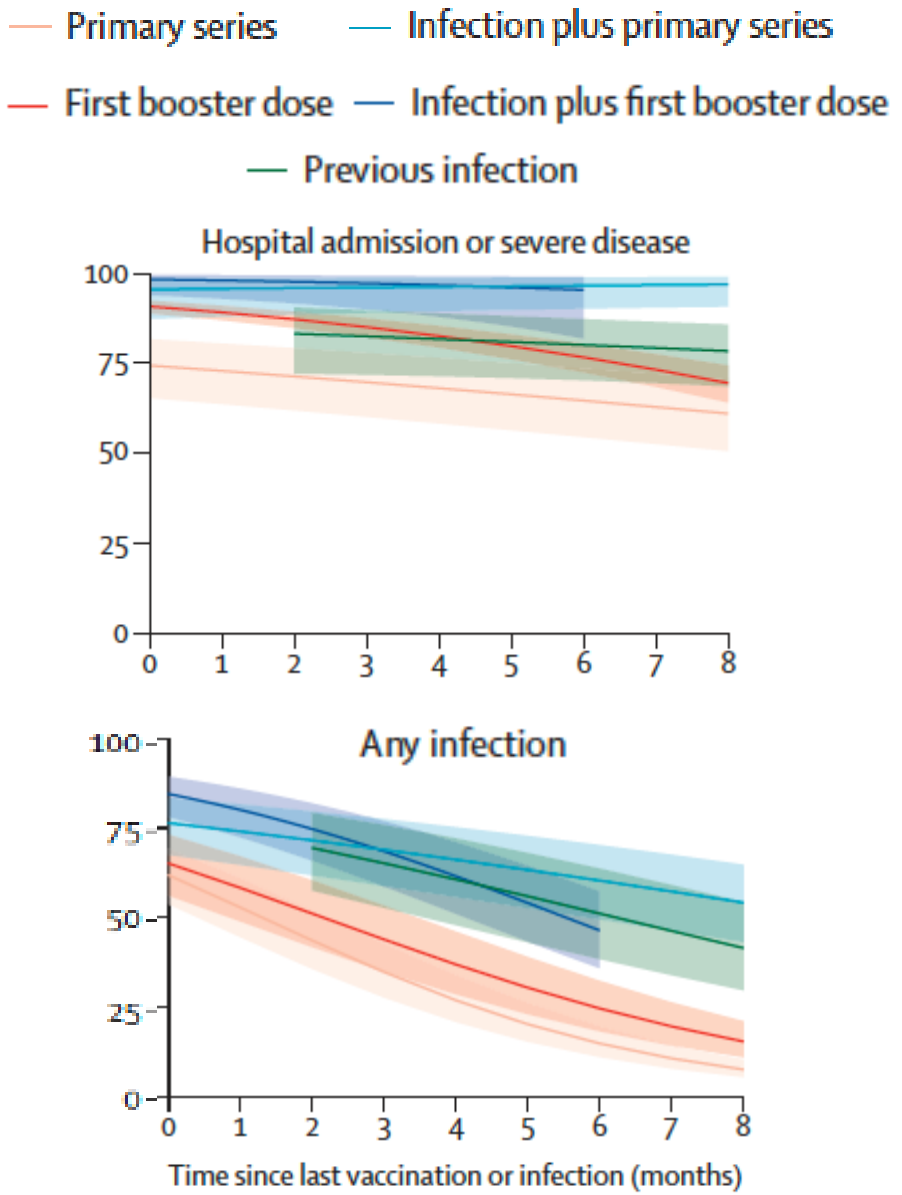
Protective effectiveness of previous SARS-CoV-2 infection and hybrid immunity against the omicron variant and severe disease: a systematic review and meta-regression

Niklas Bobrovitz, Harriet Ware, Xiaomeng Ma, Zihan Li, Reza Hosseini, Christian Cao, Anabel Selemon, Mairead Whelan, Zahra Premji, Hanane Issa, Brianna Cheng, Laith J Abu Raddad, David L Buckeridge, Maria D Van Kerkhove, Vanessa Piechotta, Melissa M Higdon, Annelies Wilder-Smith, Isabel Bergeri, Daniel R Feikin, Rahul K Arora, Minal K Patel*, Lorenzo Subissi**

Publications spanning Jan 1, 2020 to June 6, 2022; pre-Omicron vs. BA.1 or BA.2

Table 2: Protection conferred by previous infection and hybrid immunity compared to immune-naive individuals

	Number of studies	Number of estimates	Month 1*	Month 2†	Month 3	Month 4	Month 6	Month 9	Month 12	Month 15
Previous infection										
Hospital admission or severe disease	6	16	NA	83·2% (72·1 to 90·5)	82·5% (71·8 to 89·7)	81·7% (71·4 to 88·9)	80·1% (70·3 to 87·2)	77·5% (67·5 to 85·1)	74·6% (63·1 to 83·5)	71·6% (57·1 to 82·6)
Any infection§	10	64	NA	69·5% (57·6 to 79·2)	65·2% (52·9 to 75·9)	60·7% (48 to 72·1)	51·2% (38·6 to 63·7)	37·0% (26 to 49·6)	24·7% (16·4 to 35·5)	15·5% (9·9 to 23·6)
Hybrid immunity (primary series vaccination)										
Hospital admission or severe disease	5	23	95·7% (88·0 to 98·5)	95·9% (88·5 to 98·6)	96·0% (89·0 to 98·6)	96·2% (89·4 to 98·7)	96·5% (90·2 to 98·8)	97·0% (90·9 to 99)	97·4% (91·4 to 99·2)¶	NA
Any infection	7	55	74·1% (64·8 to 81·6)	71·6% (61·9 to 79·6)	69·0% (58·9 to 77·5)	66·2% (55·8 to 75·3)	60·4% (49·6 to 70·3)	51·1% (40·2 to 61·9)	41·8% (31·5 to 52·8)¶	NA
Hybrid immunity (first booster vaccination)										
Hospital admission or severe disease	4	17	98·0% (92·9 to 99·5)	97·6% (91·6 to 99·4)	97·2% (90·0 to 99·3)	96·7% (87·9 to 99·1)	95·3% (81·9 to 98·9)¶	NA	NA	NA
Any infection	6	24	80·1% (72·5 to 86)	74·8 (66·0 to 81·9)	68·6% (58·8 to 76·9)	61·6% (51·2 to 71·1)	46·5% (36·0 to 57·3)¶	NA	NA	NA



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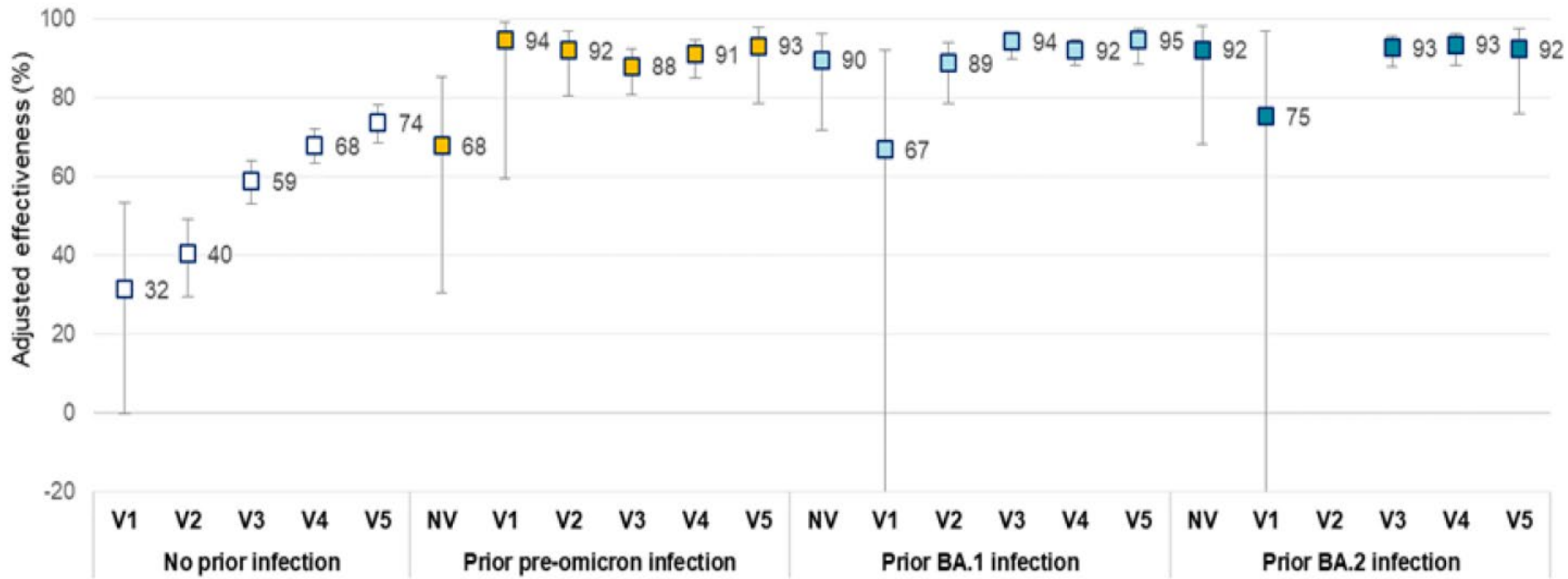
Prior infection- and/or vaccine-induced protection against Omicron BA.1, BA.2 and BA.4/BA.5-related hospitalisations in older adults: a test-negative case-control study in Quebec, Canada

Sara Carazo, Danuta M. Skowronski, Marc Brisson, Chantal Sauvageau, Nicholas Brousseau, Judith Fafard, Rodica Gilca, Denis Talbot, Manale Ouakki, Yossi Febriani, Geneviève Deceuninck, Philippe De Wals, Gaston De Serres

doi: https://doi.org/10.1101/2022.12.21.22283740

Protection against BA.4/BA.5 hospitalization in older adults, by prior vaccine and/or infection status



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Prior (pre-Omicron or Omicron) infection and/or vaccine-induced protection against BA.4/BA.5

	Adjusted effectiveness[a], % (95% confidence intervals)				
Interval since vaccination or time since primary infection	**<3 months[b]**	**3 to 5 months**	**6 to 8 months**	**9 to 11 months**	**12 to 14 months**
1. When vaccination is last event:					
Vaccination without PI					
2 doses	55 (-95, 89)	40 (-5, 66)	40 (5, 62)	36 (17, 51)	47 (35, 57)
3 doses	82 (68, 90)	67 (60, 74)	56 (49, 62)	56 (45, 66)	NA
4 doses	80 (76, 83)	64 (58, 69)	52 (38, 63)	75 (-7, 94)	NA
5 doses	73 (67, 78)	57 (11, 79)	NA	NA	NA
Vaccination after PI					
2 to 5 doses and pre-omicron PI	95 (90, 98)	89 (81, 93)	90 (79, 95)	82 (54, 93)	NA
2 to 5 doses and omicron PI	94 (90, 96)	94 (90, 97)	95 (65, 99)	NA	NA
2. When PI is last event:					
PI without vaccination					
Pre-omicron PI	NE	NE	NE	NE	NE
Omicron PI	90 (30, 99)	93 (71, 98)	84 (57, 94)	NA	NA
PI after vaccination					
2 to 5 doses and pre-omicron PI	NE	NE	NE	NE	NE
2 to 5 doses and omicron PI	91 (85, 95)	94 (90, 96)	92 (86, 96)	88 (51, 97)	NA

Summary, COVID-19 seroprevalence & hybrid immunity

- Three years into the pandemic, most British Columbians have been vaccinated and most also have serological evidence of prior infection

- Accumulating evidence shows those who have received the primary vaccines series and have a history of prior infection have strong and long-lasting protection against severe COVID-19 outcomes

- Additional vaccine doses should be prioritized toward high-risk individuals without a history of prior SARS-CoV-2 infection
  - Older adults remain least likely to have acquired infection and at greatest risk of severe outcome

- Consider lessons learned from influenza
  - Avoid making assumptions, projections or premature recommendations beyond what is clearly indicated or that the evidence can support

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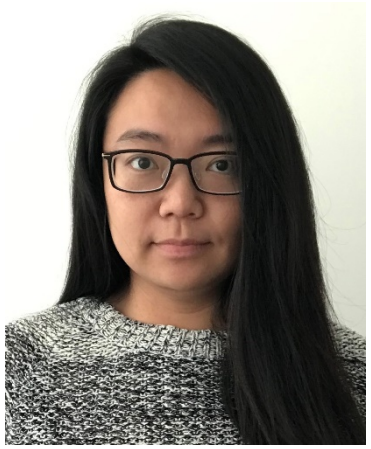

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