Public Health Ontario | Santé publique Ontario

Effectiveness of mRNA COVID-19 monovalent and bivalent vaccine booster doses against Omicron severe outcomes among adults aged ≥50 years in Ontario, Canada: a Canadian Immunization Research Network (CIRN) study

Authors: Ramandip Grewal, Lena Nguyen, Sarah A Buchan, Sharifa Nasreen, Peter C Austin, Kevin A Brown, Jonathan Gubbay, Nelson Lee, Kevin L Schwartz, Mina Tadrous, Kumanan Wilson, Sarah E Wilson, Jeffrey C Kwong (PI)

Presented by: Ramandip Grewal, PhD

Scientist, Public Health Ontario

CITF Scientific Meeting

March 9, 2023

No conflicts of interest to declare.

Background

- Moderna Spikevax BA.1 bivalent vaccine was introduced to Ontario's COVID-19 vaccination program for adults at highest risk, including adults aged ≥70 years, on September 12, 2022, and was expanded to all adults on September 26, 2022
- Pfizer-BioNTech Comirnaty BA.4/BA.5 bivalent vaccine was introduced to the program on October 17, 2022
- Bivalent products are the preferred products for booster doses as outlined by NACI, but monovalent vaccines are still available and accessible in Ontario

Reference: https://www.canada.ca/content/dam/phac-aspc/documents/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-bivalent-Omicron-containing-mrna-covid-19-vaccines.pdf

SARS-CoV-2 seroprevalence in Ontario

- Significant increase in infection since the emergence of the Omicron variant
- By January 2023, infection-acquired seroprevalence was ~80% in Ontario
- Estimates of seropositivity due to infection are lower among older adults, but still ~60% among Canadian adults aged ≥60 years
- Current and future vaccine effectiveness estimates will be more generalizable to those previously infected than those not

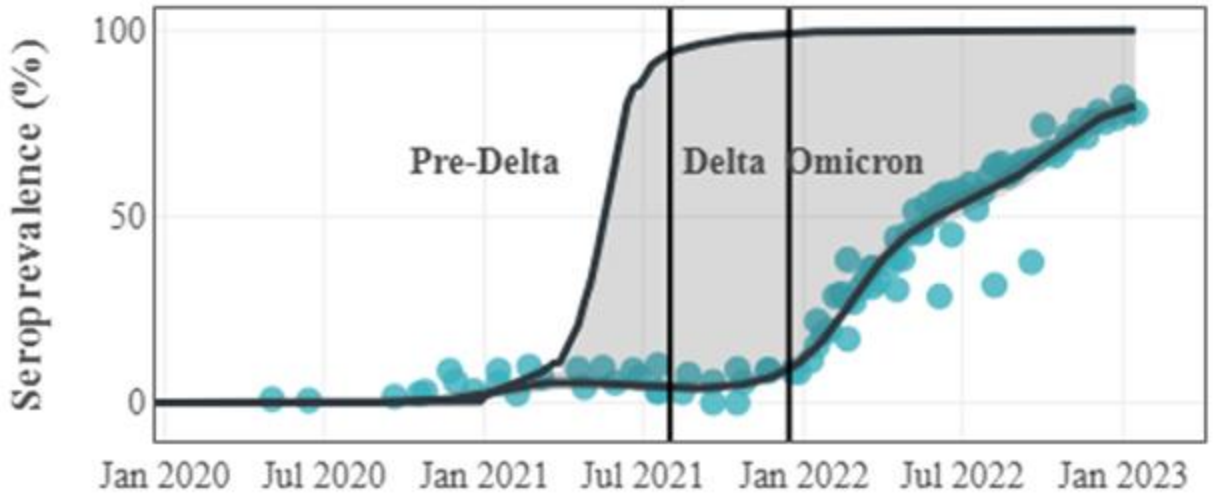
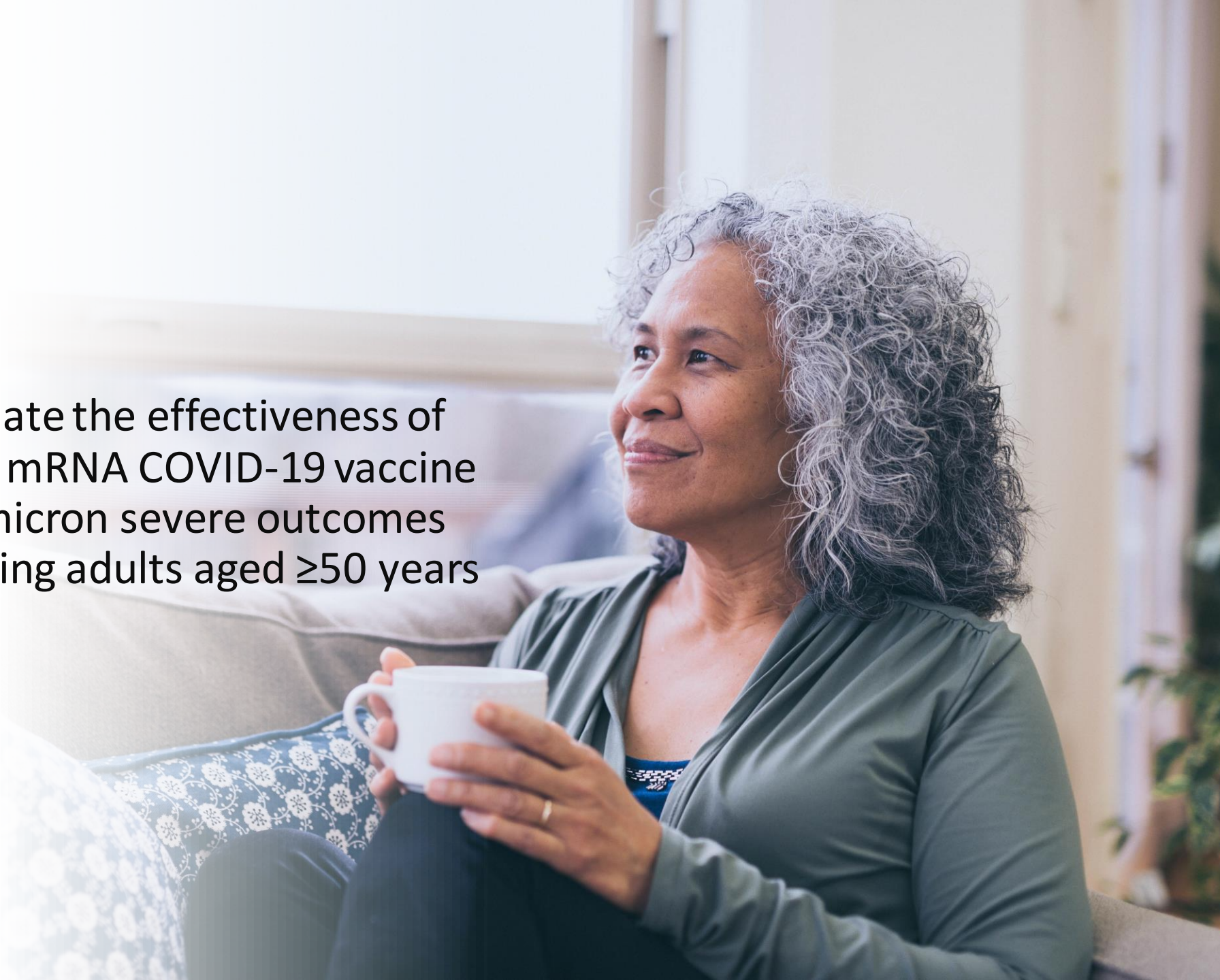


Figure. SARS-CoV-2 seroprevalence among Ontario adults.

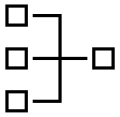
Reference: https://www.covid19immunitytaskforce.ca/seroprevalence-in-canada/

Study objective: to estimate the effectiveness of monovalent and bivalent mRNA COVID-19 vaccine booster doses against Omicron severe outcomes among community-dwelling adults aged ≥50 years



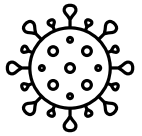
Methods

Study design:



- Test-negative design

Outcomes:

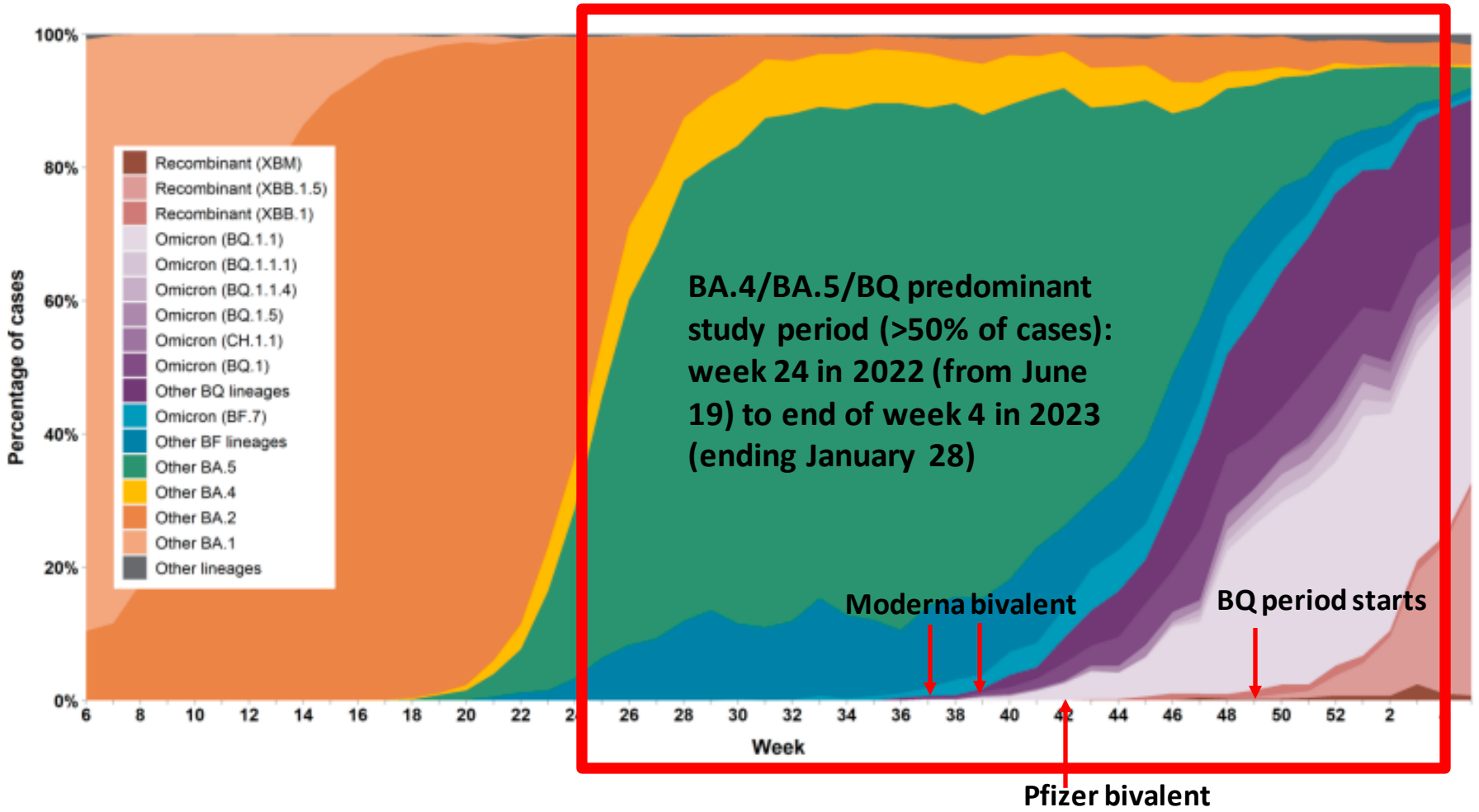


- **Cases:** Severe outcomes (hospitalization or death)
- **Controls:** Symptomatic, tested negative, sampled by week

Study population:

- Community-dwelling adults aged ≥50 years, PCR-tested for SARS-CoV-2 between June 19, 2022 and January 28, 2023 (3,755 cases and 14,338 controls)
- Selected exclusions:
  - Immunocompromised (n=5,944) or third dose before Nov 3, 2021 (n=4,771)
  - Received <4 doses (n=40,422) or received non-authorized vaccines (n=13)
  - Nosocomial infections (n=388)
  - Tested positive within 60 days prior to test (n=36)

Figure 1. Percentage of COVID-19 cases by the most prevalent lineages and week, representative surveillance, Ontario, February 6, 2022 to February 4, 2023



Note: Results may not be representative of Ontario overall, particularly in earlier weeks. Details on the proportion of eligible samples sequenced by the OCGN can be found in the technical notes. Week was assigned based on earliest date available for a sample. If more than one sample was sequenced for a case, the most recent sample was included. Results for recent weeks are incomplete as not all sequencing and bioinformatics analyses were complete at the time of data extraction and will be included in subsequent reports.

Data sources: PHO, Hospital for Sick Children, Kingston Health Sciences Centre, Shared Hospital Laboratory, Hamilton Regional Laboratory Medicine Program

Reference: https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-sars-cov2-whole-genome-sequencing-epi-summary.pdf

Methods: Vaccine effectiveness

Exposure (days since last dose: 7-29, 30-59, 60-89, 90-119 days), restricted to 4+ doses

- Pfizer monovalent
- Moderna monovalent*
- Moderna BA.1 bivalent
- Pfizer BA.4/BA.5 bivalent

Comparator (i.e. non-exposed):

- Unvaccinated

Statistical analysis:

- Multivariable logistic regression
- Secondary analysis stratified by sublineage period (BA.4/BA.5 = June 19, 2022 to December 3, 2022; BQ = December 4, 2022 to January 28, 2023)

*Ontario recommendation was for adults aged ≥70 years to receive a full dose (younger adults recommended to receive half dose) but could not differentiate in data.

Covariates adjusted for in models

- Age, sex
- Geographic region
- Week of test
- Comorbidities (other than immunocompromised)
- Receipt of home care services
- Receipt of recent prior influenza vaccine (proxy for health behaviours)
- # of SARS-CoV-2 tests during 3 months before Dec 14, 2020 (proxy for HCWs)
- Area-level variables: income, % essential workers, household size, % visible minorities

Study population: cases versus controls

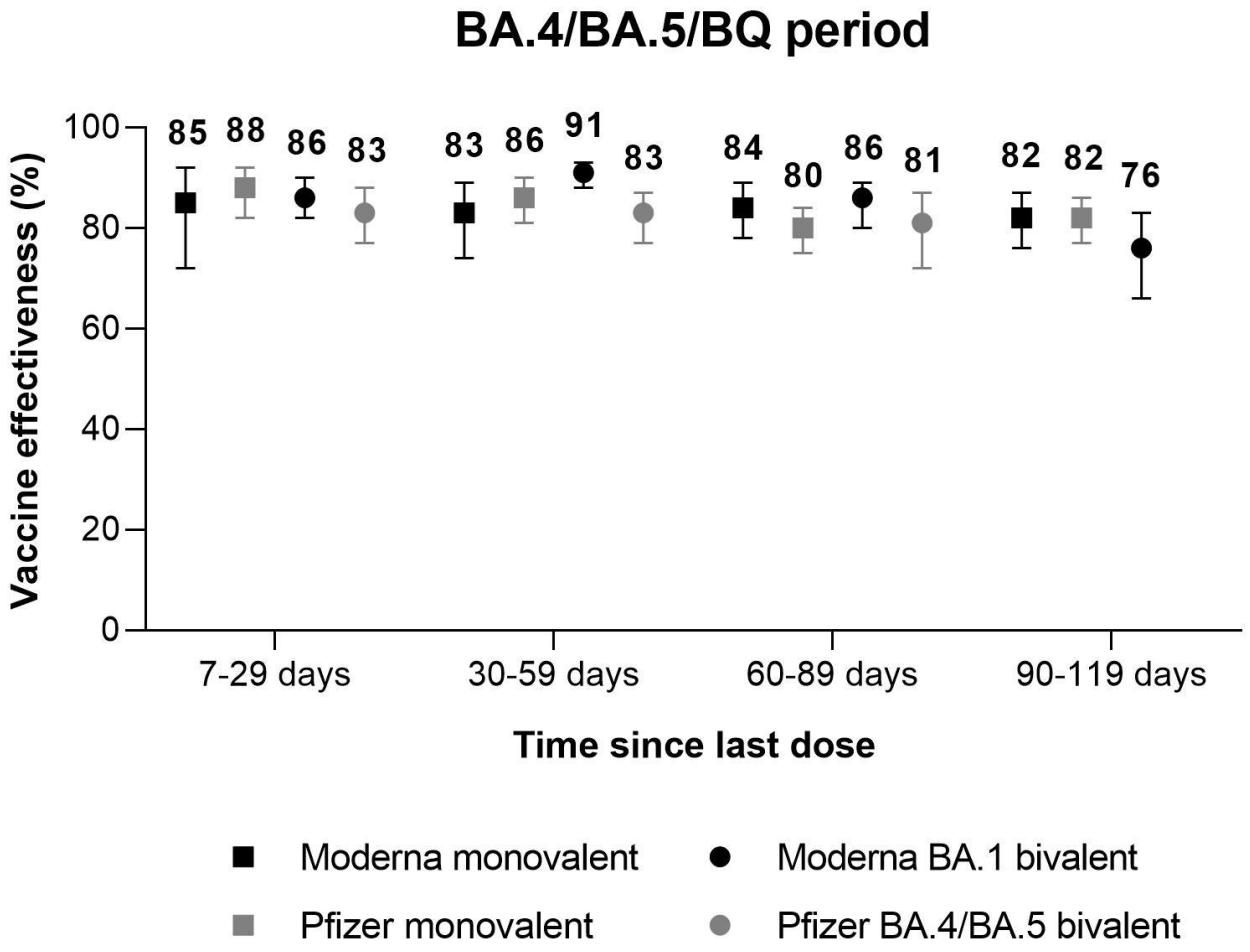
	Omicron-positive cases (n, %)	SARS-CoV-2 negative controls (n, %)
Total	n = 3,755	n = 14,338
Mean age in years (standard deviation)	80.3 (12.0)	72.4 (10.3)
Most recent dose n, (%)* Unvaccinated 4 5	 1,101 (29.3%) 2,143 (57.1%) 509 (13.6%)	 1,578 (10.9%) 9,838 (68.6%) 2,924 (20.4%)
Documented prior infection > 60 days ago	64 (1.7%)	570 (4.0%)

*Very few with 6 doses (~10 people).

Study population: unvaccinated versus vaccinated

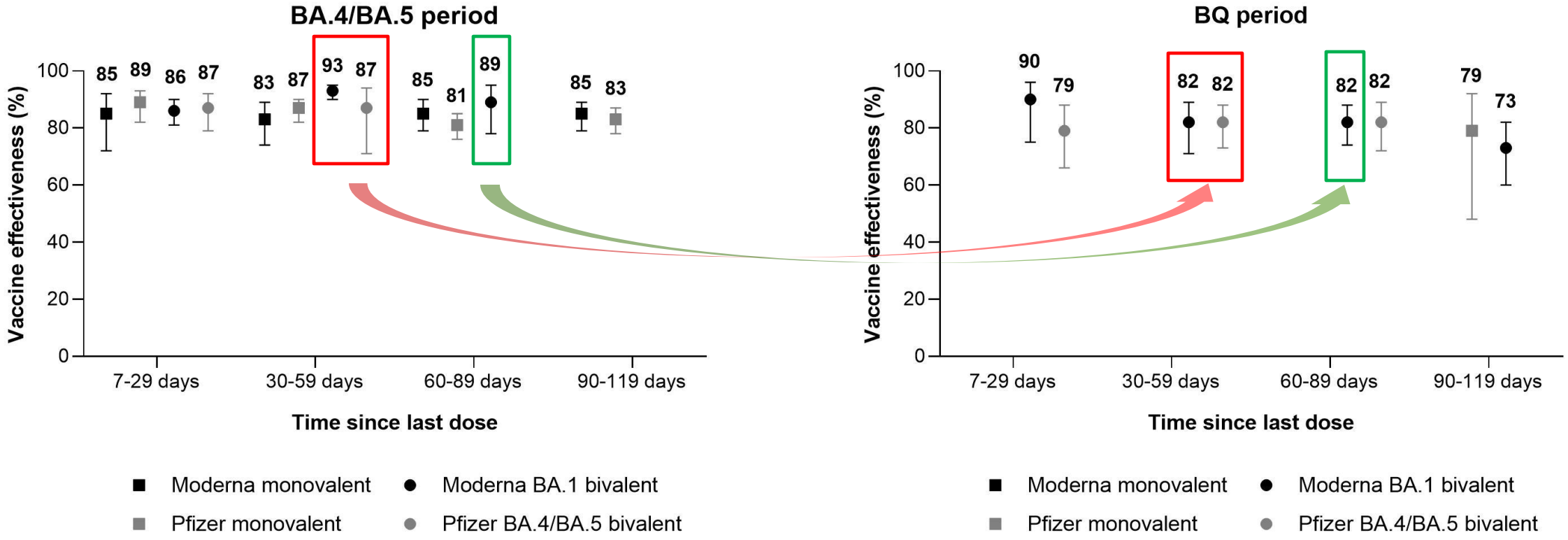
	Unvaccinated (n, %)	4 doses (n, %)	5 doses (n, %)
Total	n = 2,669	n = 11,981	n = 3,433
Mean age in years (standard deviation)	72.5 (12.7)	73.4 (12.1)	77.8 (10.4)
Male sex	1,331 (50.0%)	5,012 (41.8%)	1,501 (43.7%)
Household income quintile			
1 (lowest)	822 (30.8%)	2,388 (19.9%)	688 (20.0%)
2	591 (22.1%)	2,545 (21.2%)	722 (21.0%)
3	475 (17.8%)	2,200 (18.4%)	651 (19.0%)
4	434 (16.3%)	2,291 (19.1%)	673 (19.6%)
5 (highest)	330 (12.4%)	2,509 (20.9%)	684 (19.9%)
Receipt of recent prior influenza vaccine	499 (18.7%)	8,850 (73.9%)	2,888 (84.1%)

Vaccine effectiveness of monovalent and bivalent vaccines relatively similar up to 4 months



Could BQ be diluting estimates?

Vaccine effectiveness may be lower in the BQ period



Limitations

- Most prior infections in Ontario are undocumented, making it difficult to effectively account for prior infection in analyses and determine its influence on estimates.
- Potential for residual confounding since we were limited to the covariates available in the databases used.

Conclusions

- Booster doses of monovalent and bivalent mRNA COVID-19 vaccine products provide similar short-term protection against severe outcomes in community-dwelling adults aged ≥50 years.
- Vaccine effectiveness may be slightly lower during the BQ predominant period compared to the BA.4/BA.5 predominant period.
- Longer follow-up is necessary to determine the longer term protection of bivalent vaccines and the effectiveness against Omicron sublineages such as XBB.

Lessons Learned

- Data linkage facilitates efficient and timely estimation of vaccine effectiveness.
- Findings suggest that a booster dose of any mRNA vaccine is beneficial in the short term.
- Potentially lower vaccine effectiveness against BQ (and possibly newer, more transmissible sublineages such as XBB) make comparing effectiveness of monovalent and bivalent products across a longer term more difficult.
- Estimation of vaccine effectiveness is becoming increasingly difficult over time due to hybrid immunity and the consistent emergence of more immune evasive Omicron sublineages.

Data acknowledgements and disclaimers

We would like to acknowledge Public Health Ontario for access to vaccination data from COVaxON, case-level data from CCM and COVID-19 laboratory data, as well as assistance with data interpretation. We also thank the staff of Ontario's public health units who are responsible for COVID-19 case and contact management and data collection within CCM. We thank IQVIA Solutions Canada Inc. for use of their Drug Information File. The authors are grateful to the Ontario residents without whom this research would be impossible.

This work was supported by the Applied Health Research Questions (AHRQ) Portfolio at ICES, which is funded by the Ontario Ministry of Health (MOH). For more information on AHRQ and how to submit a request, please visit www.ices.on.ca/DAS/AHRQ. This work was also supported by the Ontario Health Data Platform (OHDP), a Province of Ontario initiative to support Ontario's ongoing response to COVID-19 and its related impacts. This work was supported by Public Health Ontario. This study was also supported by ICES, which is funded by an annual grant from the Ontario MOH and the Ministry of Long-Term Care (MLTC). The study sponsors did not participate in the design and conduct of the study; collection, management, analysis and interpretation of the data; preparation, review or approval of the manuscript; or the decision to submit the manuscript for publication. Parts of this material are based on data and/or information compiled and provided by the Canadian Institute for Health Information (CIHI), and by Ontario Health (OH). However, the analyses, conclusions, opinions and statements expressed herein are solely those of the authors, and do not reflect those of the funding or data sources; no endorsement by ICES, MOH, MLTC, OHDP, its partners, the Province of Ontario, Ontario Health, CIHI, or OH is intended or should be inferred.