Real-world COVID-19 vaccine effectiveness

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Disclaimer

I have no conflicts of interest to declare related to this study.

Background

- Weak or waning humoral response in tandem with the emergence of new viral variants, capable of potentially escaping immune response, lead to a continued risk of SARS-CoV-2 infection.

- Omicron is currently the dominant variant circulating globally.

- Prior vaccination:
  - Effective against severe COVID-19 and hospitalization due to Omicron variants
  - Less effective against asymptomatic and symptomatic, mild breakthrough infections.

Objective

To measure vaccine effectiveness in a real-world setting over the course of the pandemic.

Our aim is to untangle the relationship between vaccination status (how many doses, of which brands, and elapsed time following each dose) and risk of new COVID-19 infections, while controlling for base infection rates that may vary over the follow-up and by geographic region; as well as participant demographics, and adherence with public health recommendations.

Study population: 22,300 CanPath participants

BC Generations Project
3,869

Alberta's Tomorrow Project
n/a

Saskatchewan PATH
n/a

Manitoba Tomorrow Project
667

Ontario Health Study
9,942

Atlantic PATH
3,322

CARTaGENE (Quebec)
4,500

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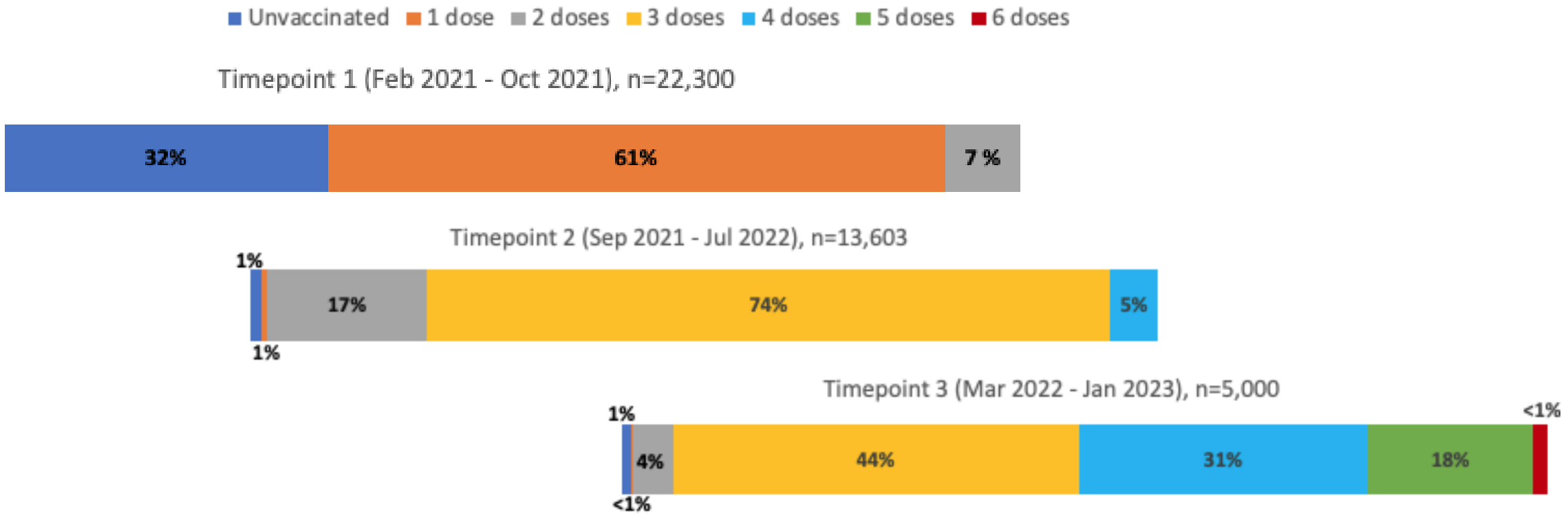
Dried blood spots collected at up to 3 time points

- Study population
  - Aged ≥ 19 years, 66% female
  - Completed questionnaires and provided dried blood spots using mailed kits at up to 3 time points during the vaccine rollout



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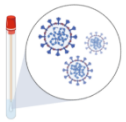
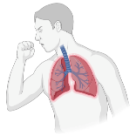
Comprehensive study questionnaire

Vaccination status (brand and date received)



COVID-19 test results and dates / suspected infection and dates



Symptoms experienced (if any)

Care/hospital related information

Comorbidities, smoking status, BMI, influenza vaccination

Preventive measures taken

Potential source and date of exposure

Job classifications for front-line workers

Impact of the pandemic on mental, emotional, social and financial wellbeing

COVID-19 long-term effects

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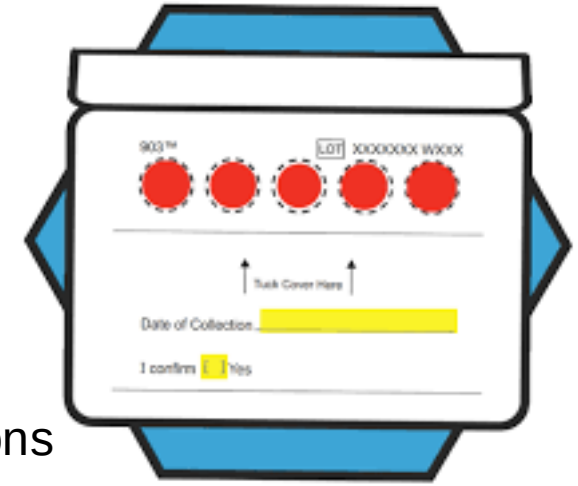
Anti-N IgG serology results capture unconfirmed infections

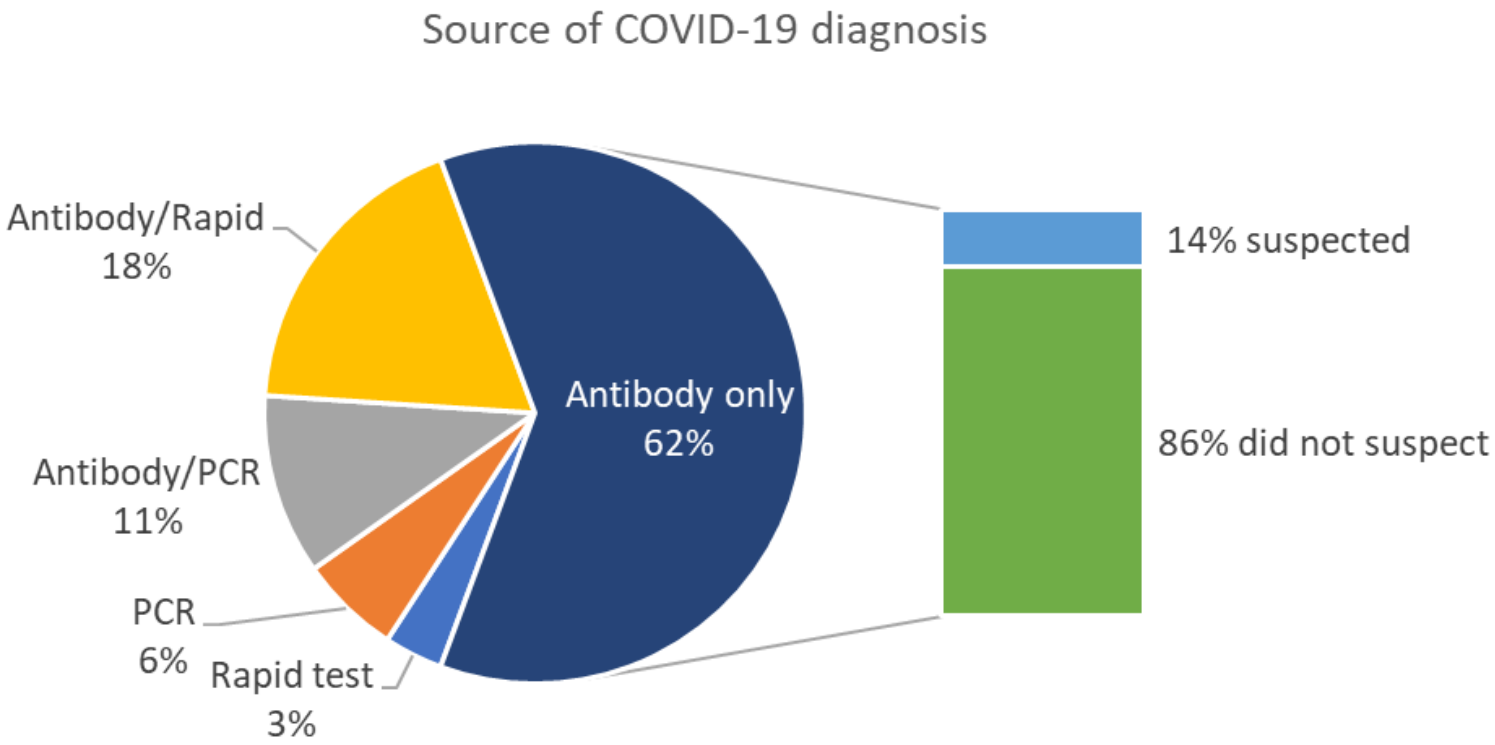


- Measured three antibody levels:
  - Anti-spike (SmT1) IgG : marker of vaccination
  - Anti-receptor binding domain (RBD) IgG : marker of vaccination
  - Anti-nucleocapsid (N) IgG: marker of vaccination or natural infection

- Used anti-N IgG serology results to capture asymptomatic and unconfirmed infections
  - Two distinct thresholds for N were set to reduce false negatives:
    - at low seroprevalence (timepoint 1) , specificity=0.995, sensitivity=0.998
    - at higher seroprevalence (timepoints 2 and 3), specificity=0.904, sensitivity=0.876
  - Adequately assigned participants to the respective groups

- Determined whether anti-SmT1 and anti-RBD antibody levels are associated with risk of infection

More than half of COVID-19 diagnoses were among those who neither knew nor suspected they were infected



Model includes time-varying vaccine-related variables

- Time-varying exposures
  - Vaccination number (0-6)
  - Vaccine brand most recently received (Moderna, Pfizer, AstraZeneca, other)
  - Bivalent vaccine (yes, no)
    - Assumptions were based on Health Canada's approval dates of:
      1 Sep 2022 for the new bivalent Moderna vaccine and
      7 Oct 2022 for the new bivalent Pfizer vaccine

- Covariates
  - Age, sex, ethnicity, geographic region (cohort)
  - Cancer history, immunocompromised status, body mass index
  - Essential worker status
  - Preventive measures: travel, mask use, use of public transportation, avoidance of indoor gatherings

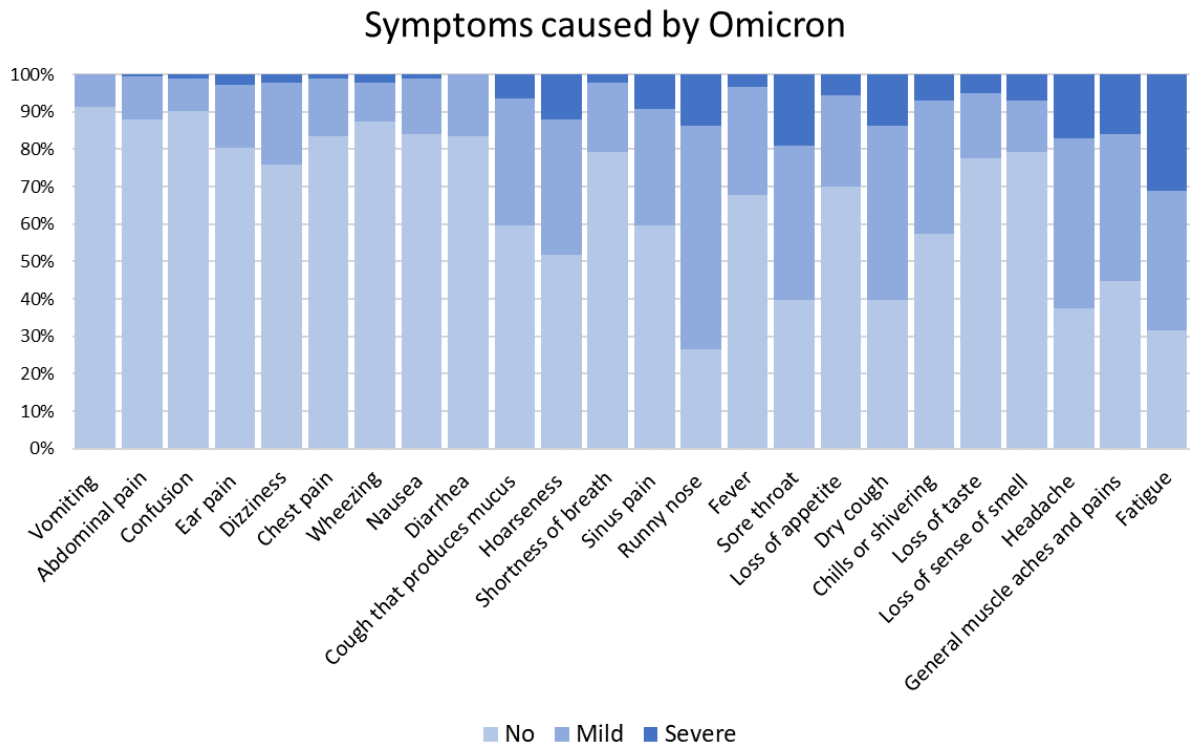
Main outcome is time to first SARS-CoV-2 infection

- Time to the first SARS-CoV-2-positive test during 2 periods:
  - Omicron period (2 Dec 2021 to Jan 2023)
  - Pre-Omicron period (11 Jan 2020 to 1 Dec 2021)
  - Participants were no longer at risk after their first positive test
  - Noninfected participants were censored at the time of the last available follow-up questionnaire

- Cases included irrespective of symptoms or severity (n=2533)

- Excluded those anti-N IgG positive with unknown infection dates (n=2099)

- Vaccine effectiveness (VE) = (1- hazard ratio (HR)) x100%



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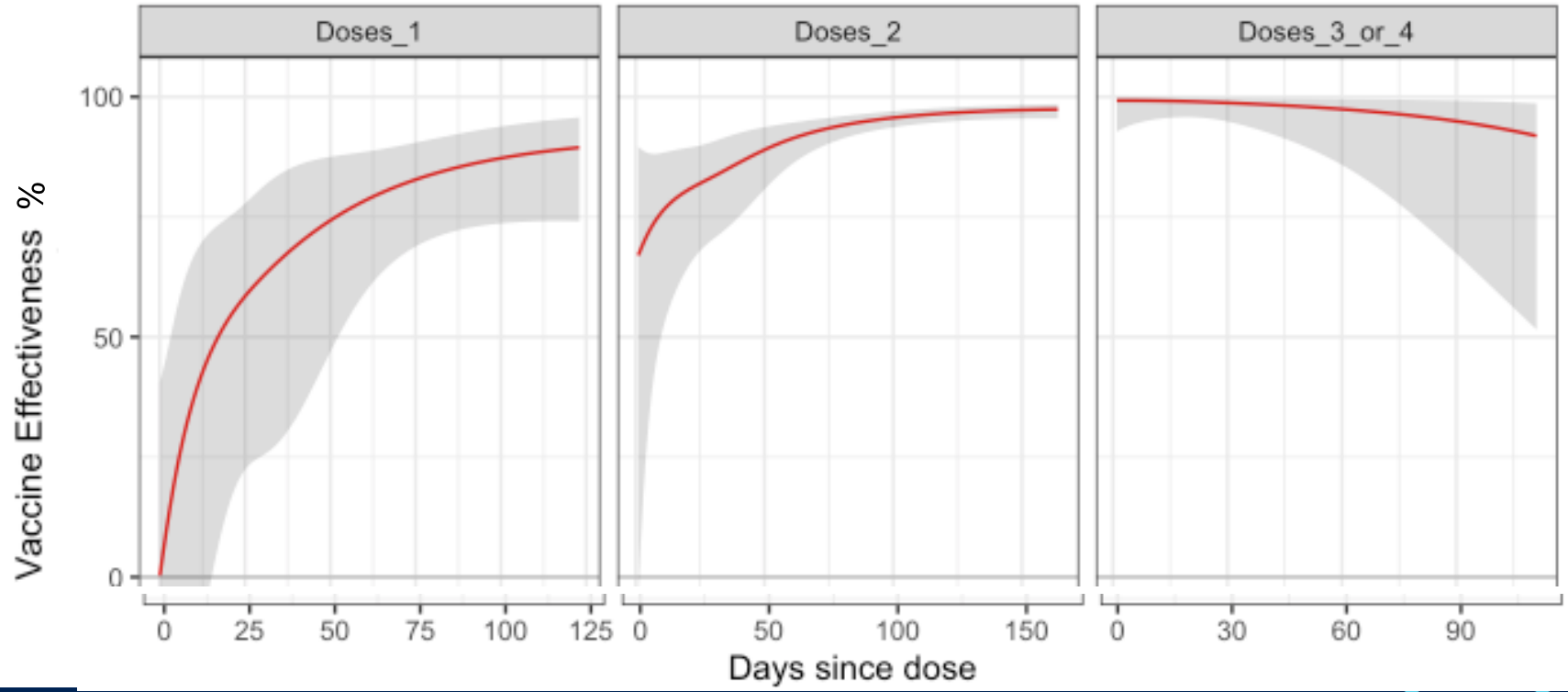
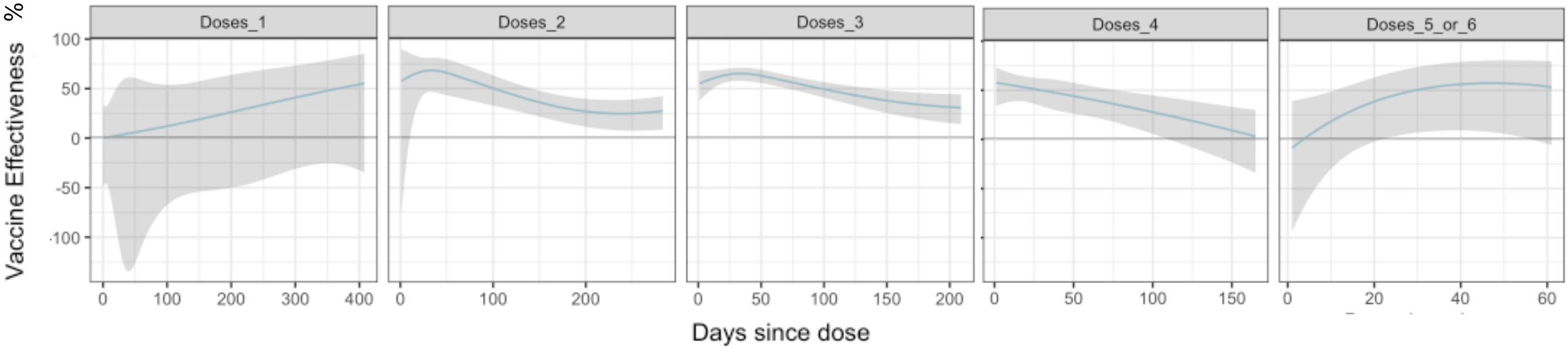
VE robust pre-Omicron

- Evidence of robust immunity:
  - After an initial delay to vaccine effectiveness taking effect

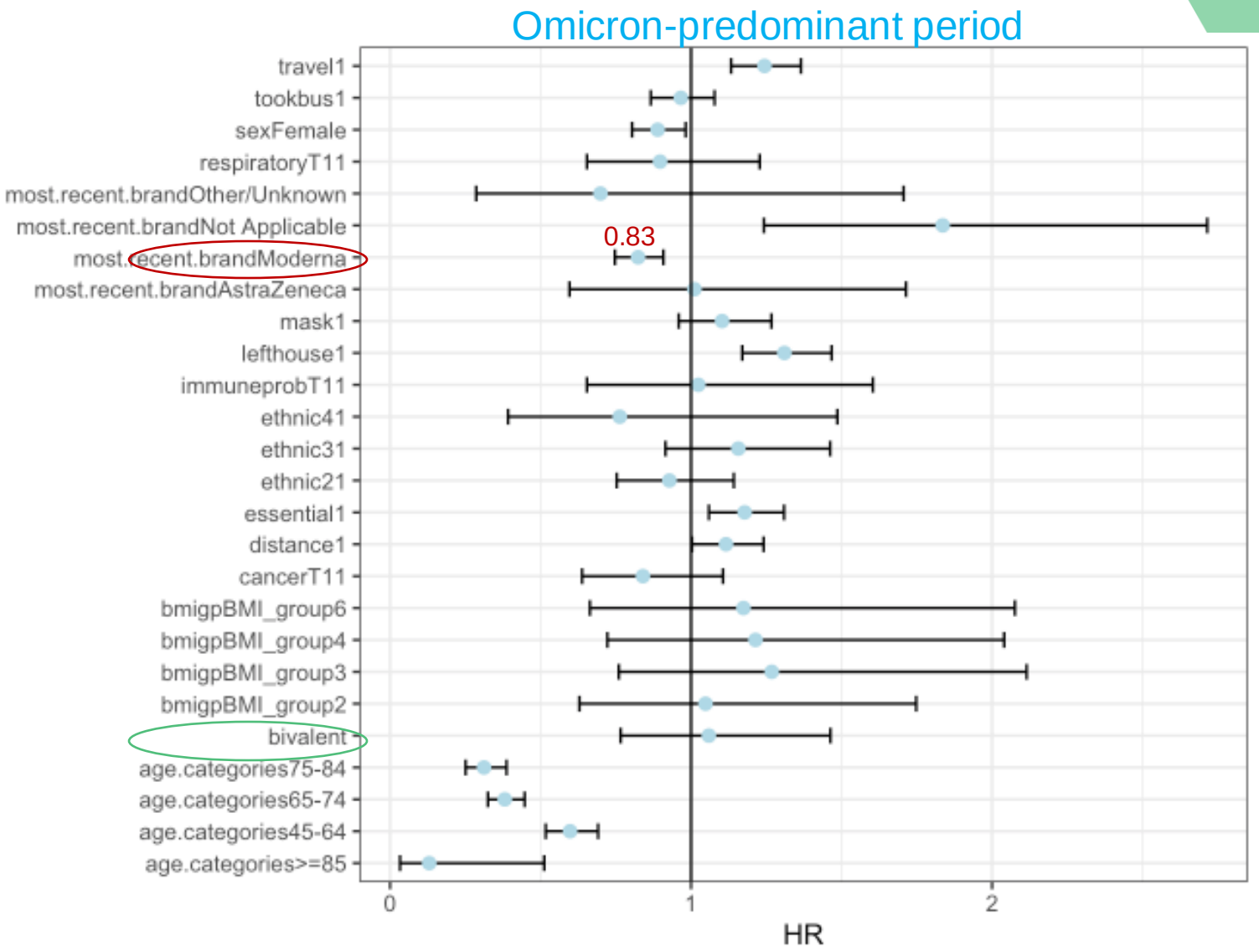


VE against Omicron infections waning

- Evidence of waning immunity after being fully vaccinated or boosted:
  - from a high of 56-68% at one or two months
  - to a low of 3-30% at five months or longer



Highest VE among Moderna recipients; boosting with a bivalent vaccine has similar effect as boosting with monovalent



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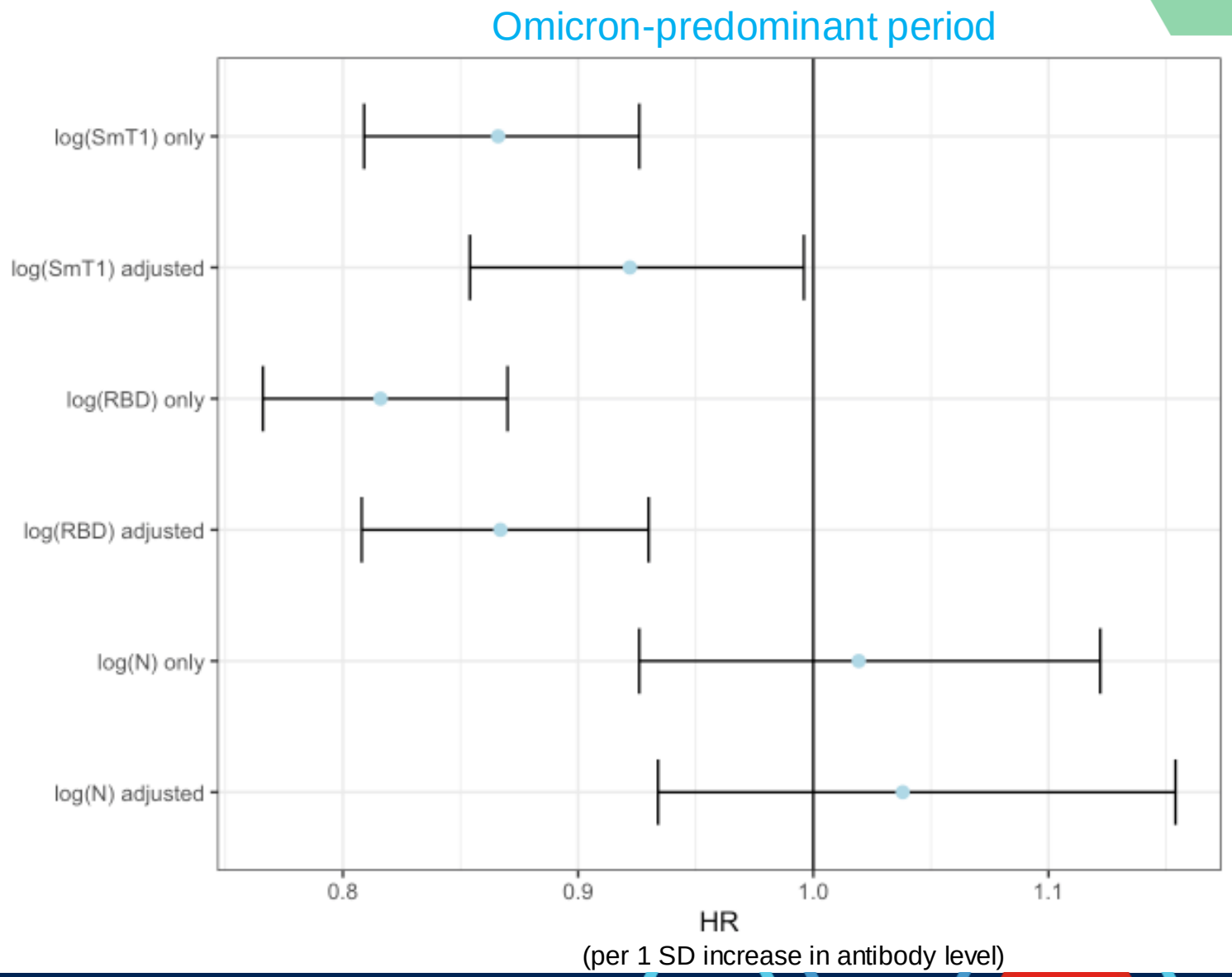
An increase in predicted anti-SmT1 and anti-RBD antibody levels is associated with a decreased risk of infection



Learnings/challenges

- Time since vaccination by dose number and calendar time are inextricably confounded: two years into the pandemic, infection rates increased dramatically
  - Stratified analyses by pre-Omicron and Omicron predominant periods

- Access to PCR testing varied over time
  - Incorporated baseline serology results
  - Adapted questionnnaires to capture use of at-home rapid antigen tests

- Must take measures to avoid misclassification of non-cases as cases

Conclusions

- Our results indicate the short-term effectiveness of full or booster vaccination in preventing SARS-CoV-2 Omicron infection.

- Booster campaigns could be strategically used to rapidly boost population immunity before upcoming waves of infections.

Study Team

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COVID-19 IMMUNITY TASK FORCE

GROUPE DE TRAVAIL SUR L'IMMUNITÉ FACE À LA COVID-19

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