Real-world insights on COVID-19 vaccine effectiveness and risk factors for COVID-19 infection from CanPath's SUPPORT-Canada study

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CanPath
Canadian Partnership for Tomorrow's Health
Partenariat canadien pour la santé de demain

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.

- The dominant variants circulating globally are subvariants of Omicron.

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

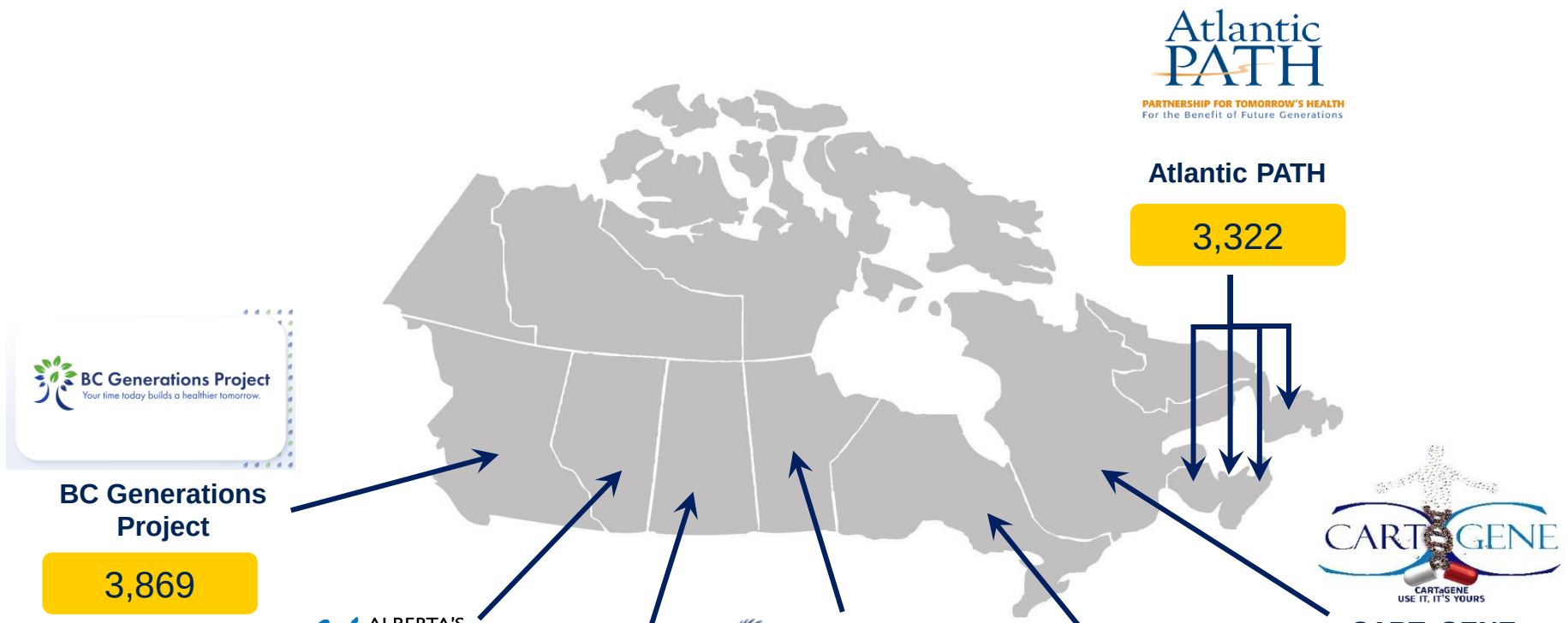
Objectives

1. 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 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, prior infection, and adherence with public health recommendations.

    - We also control for antibody levels in a mediation model.

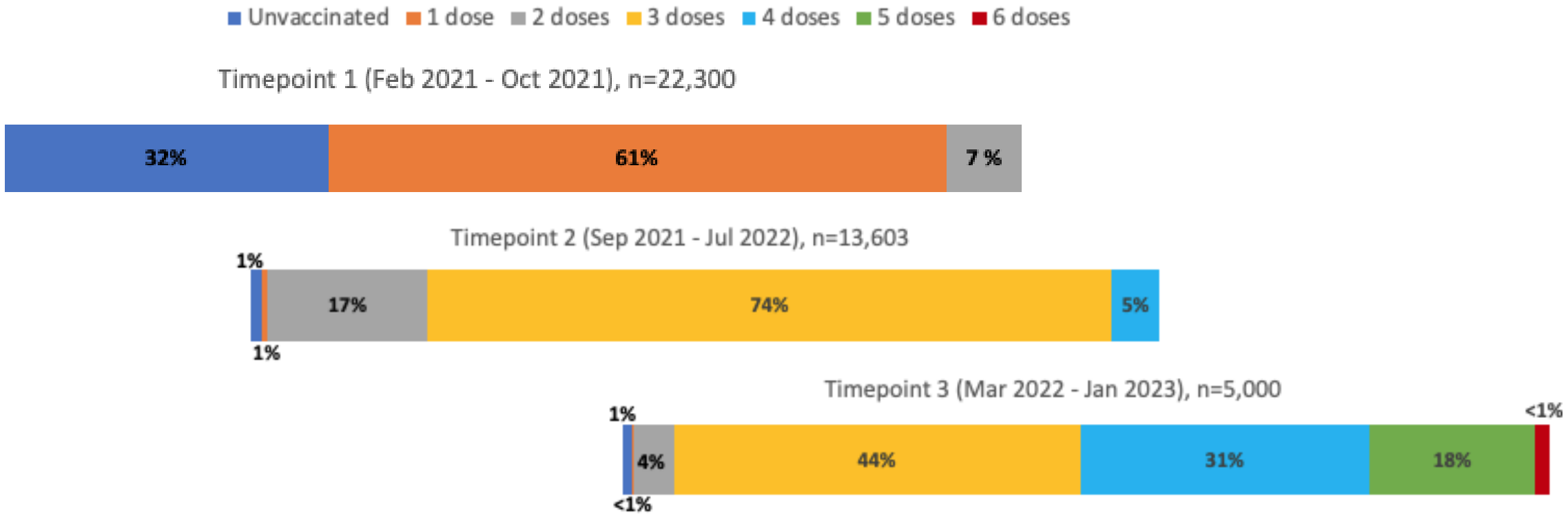
2. To evaluate the association between participant characteristics and risk of infection.

Antibody study population: 22,300 CanPath participants



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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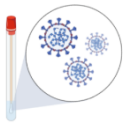
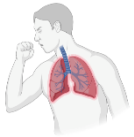
Comprehensive study questionnaire

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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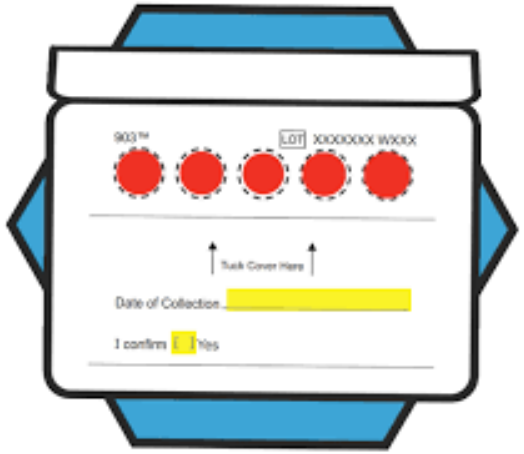
Anti-N IgG serology results capture unconfirmed infections



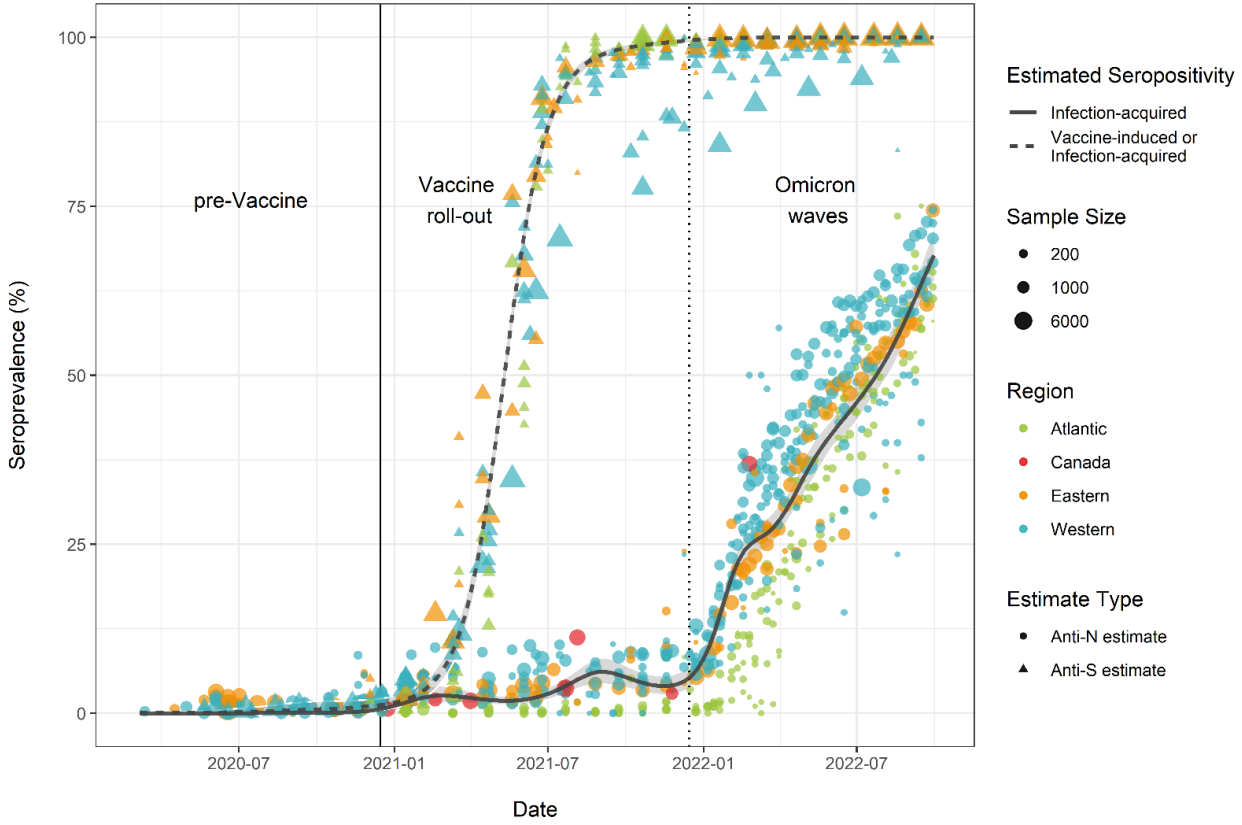
- Measured three antibody levels:
  - Anti-spike (S) IgG : marker of vaccination or natural infection
  - Anti-receptor binding domain (RBD) IgG : marker of vaccination or natural infection
  - Anti-nucleocapsid (**N**) IgG: marker of **natural** infection

- Used anti-N IgG serology results to capture asymptomatic and unconfirmed infections
  - Two distinct thresholds for anti-N positivity were set to reduce false negatives:
    - at low seroprevalence (timepoint 1) , specificity=0.995, sensitivity=0.629
    - at higher seroprevalence (timepoints 2 and 3), specificity=0.904, sensitivity=0.876
  - Adequately assigned participants to the respective groups

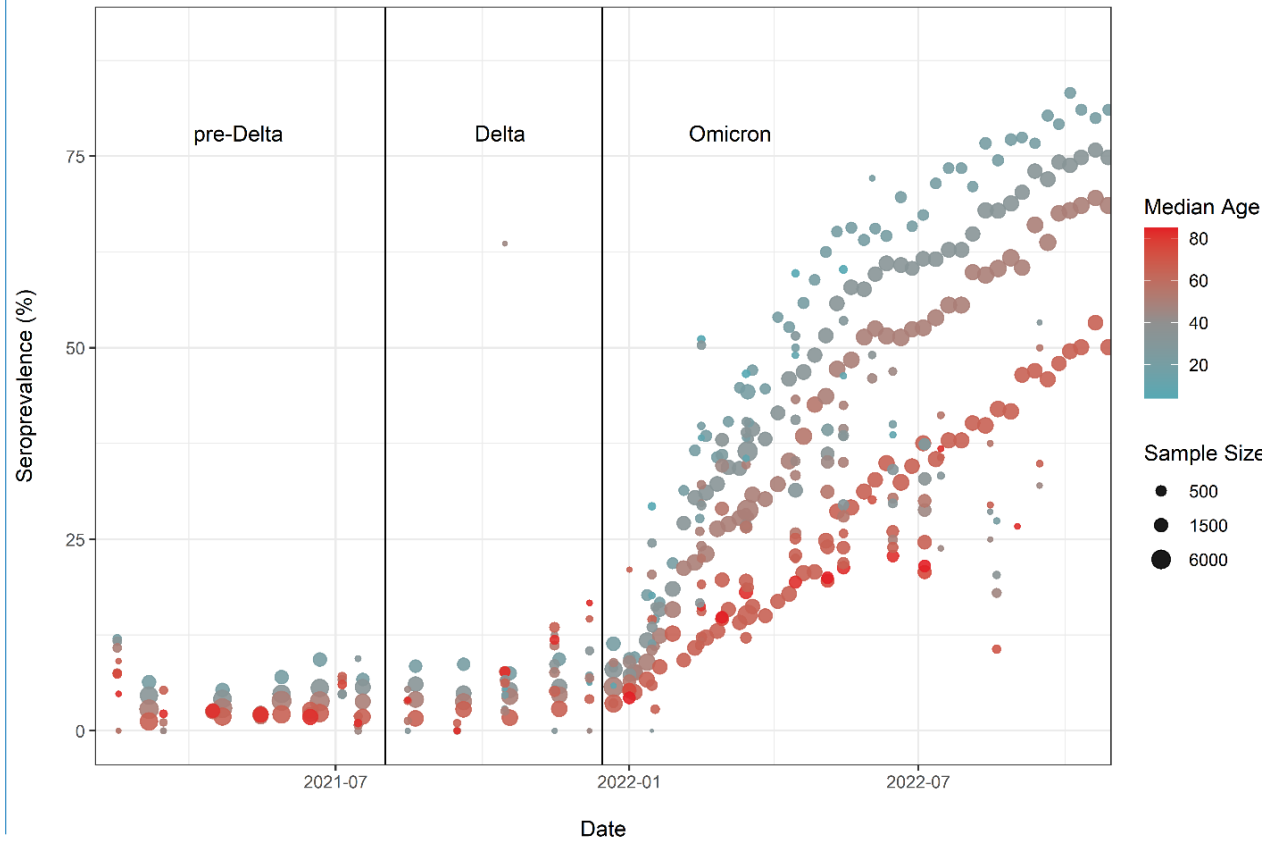
- Determined whether anti-S and anti-RBD antibody levels are correlates of vaccine-induced protection

SARS-CoV-2 seroprevalence (Mar 2020 - Sep 2022)

Vaccine-induced and infection-acquired seropositivity for all age groups, by region:



Infection-acquired seropositivity, by age:



Source: Murphy T et al. The Evolution of Population Immunity to SARS-CoV-2 – A Time-Series Study of Seroprevalence in Canada, 2020-2022. CMAJ (*in submission*).

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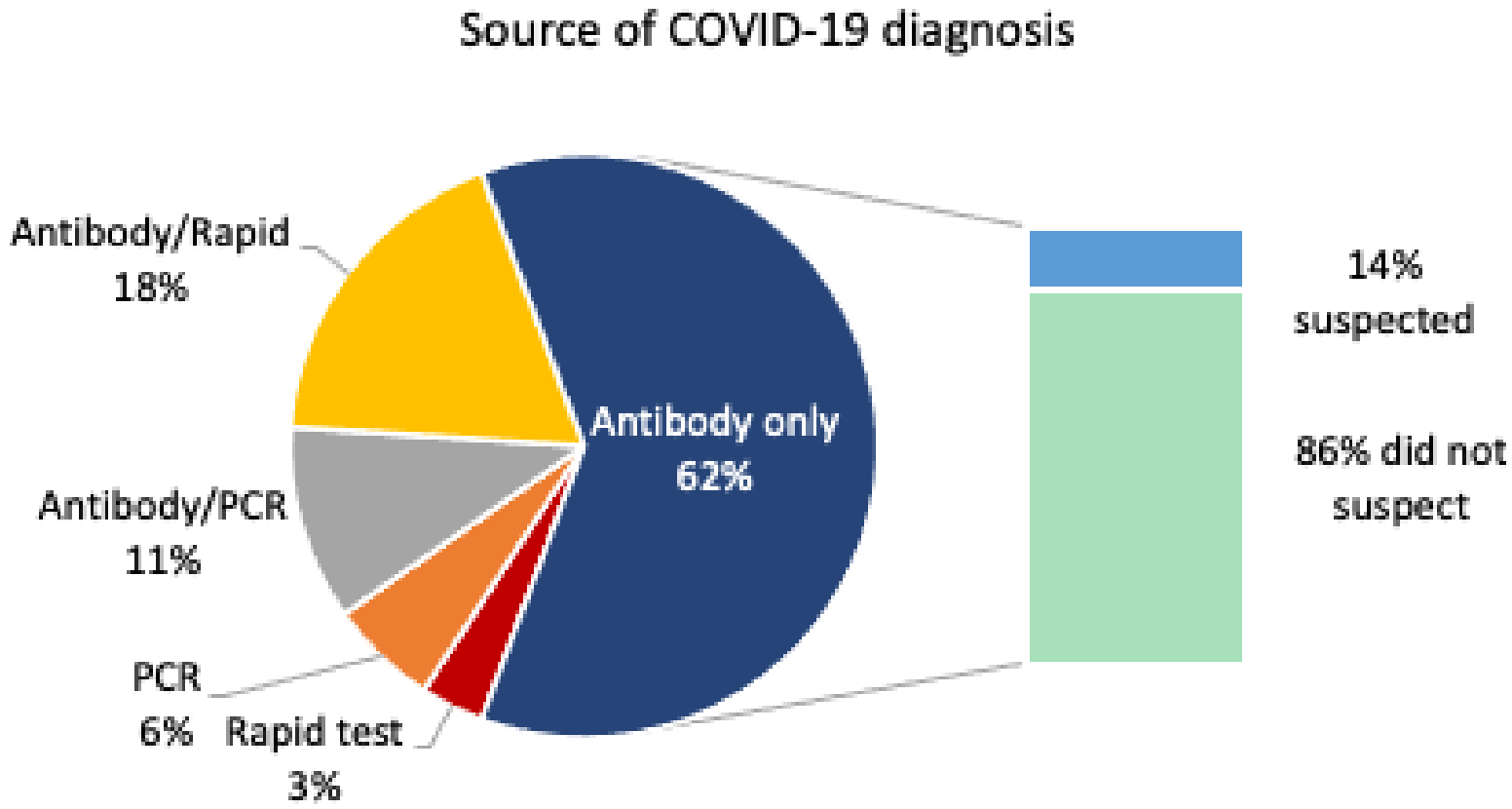
More than half of COVID-19 diagnoses were among those who neither knew nor suspected they were infected



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
  - Cumulative number of SARS-CoV-2-positive tests

- 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 infection

- Time to the 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 continued to be at risk after their first positive test
  - Noninfected participants were censored at the time of the last available follow-up questionnaire

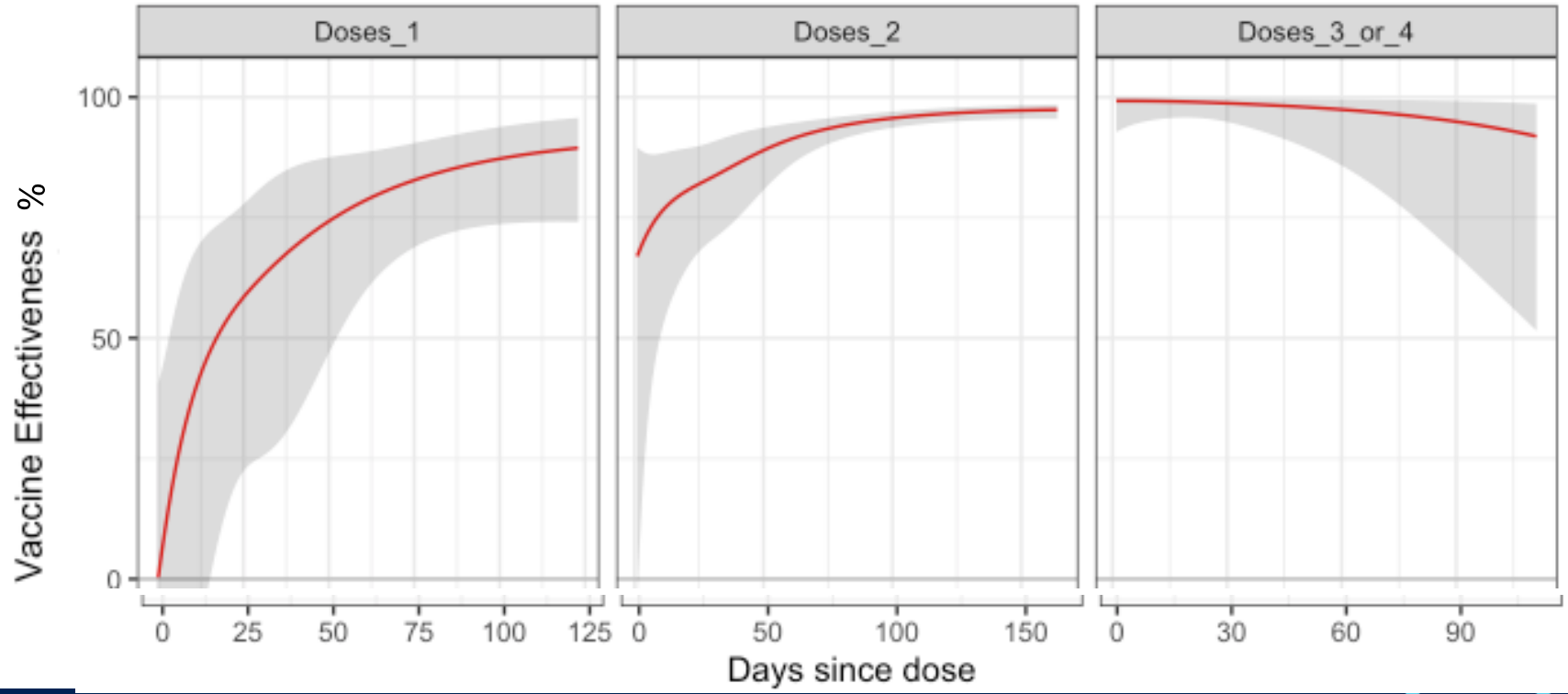
- Cases included irrespective of symptoms or severity (n=2533)

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

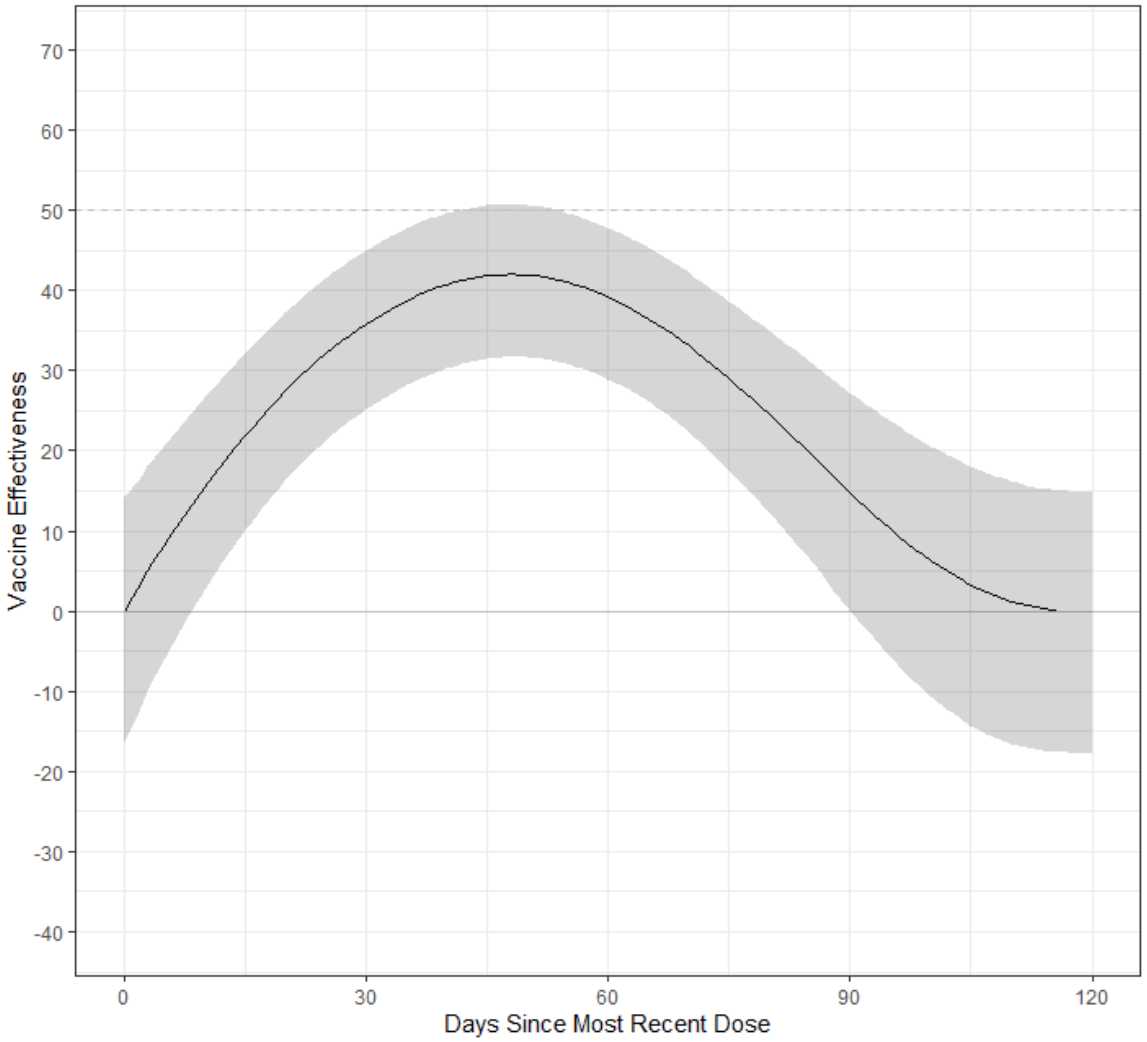
- Vaccine effectiveness (VE) = (1- hazard ratio (HR)) x100%

Vaccine effectiveness robust pre-Omicron

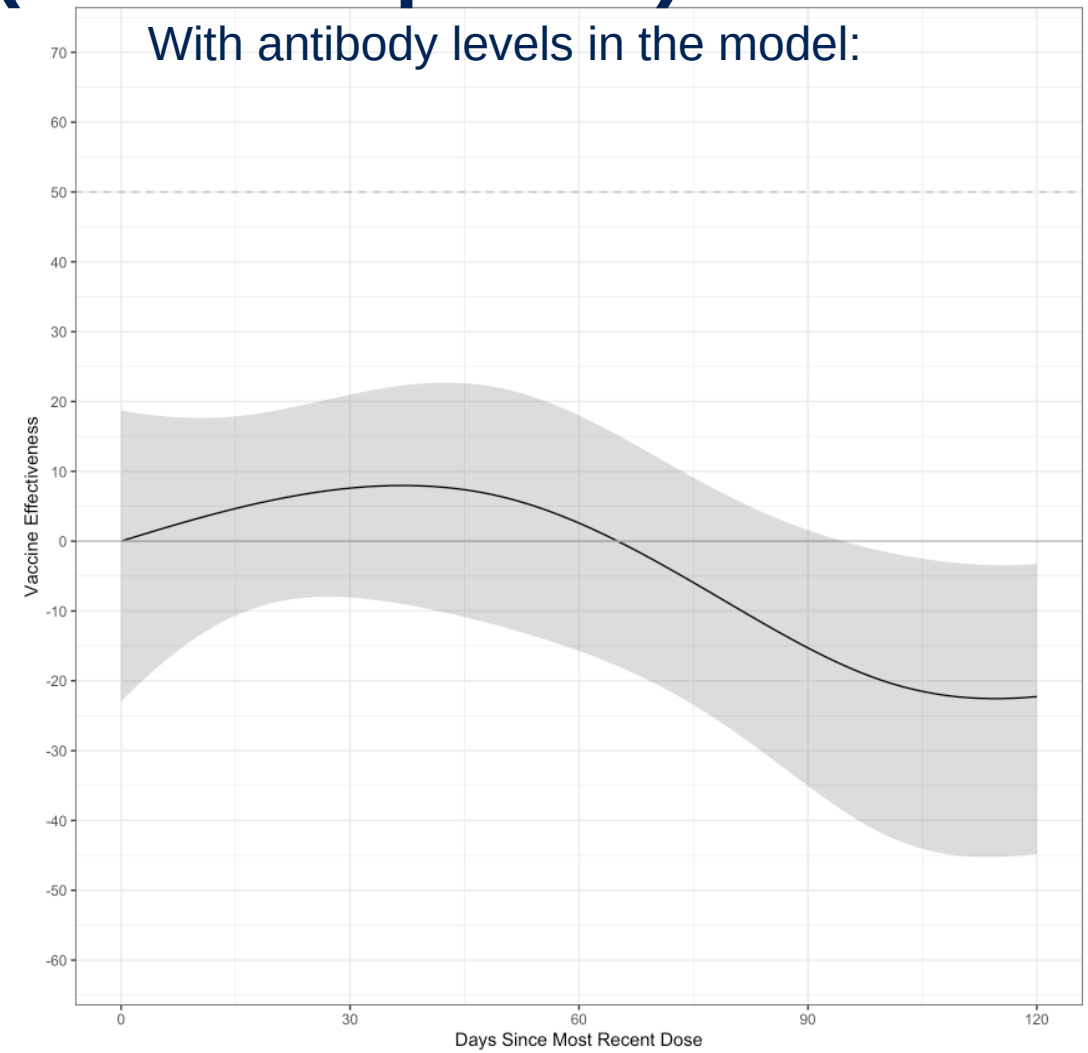
- Evidence of robust immunity:
  - After an initial delay to vaccine effectiveness taking effect



Average vaccine effectiveness (Omicron period)



With antibody levels in the model:



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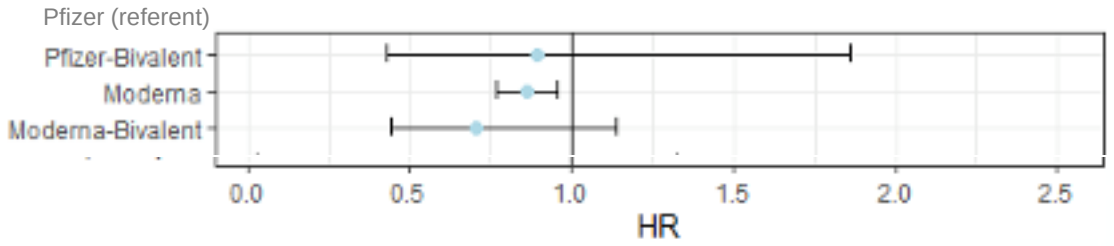
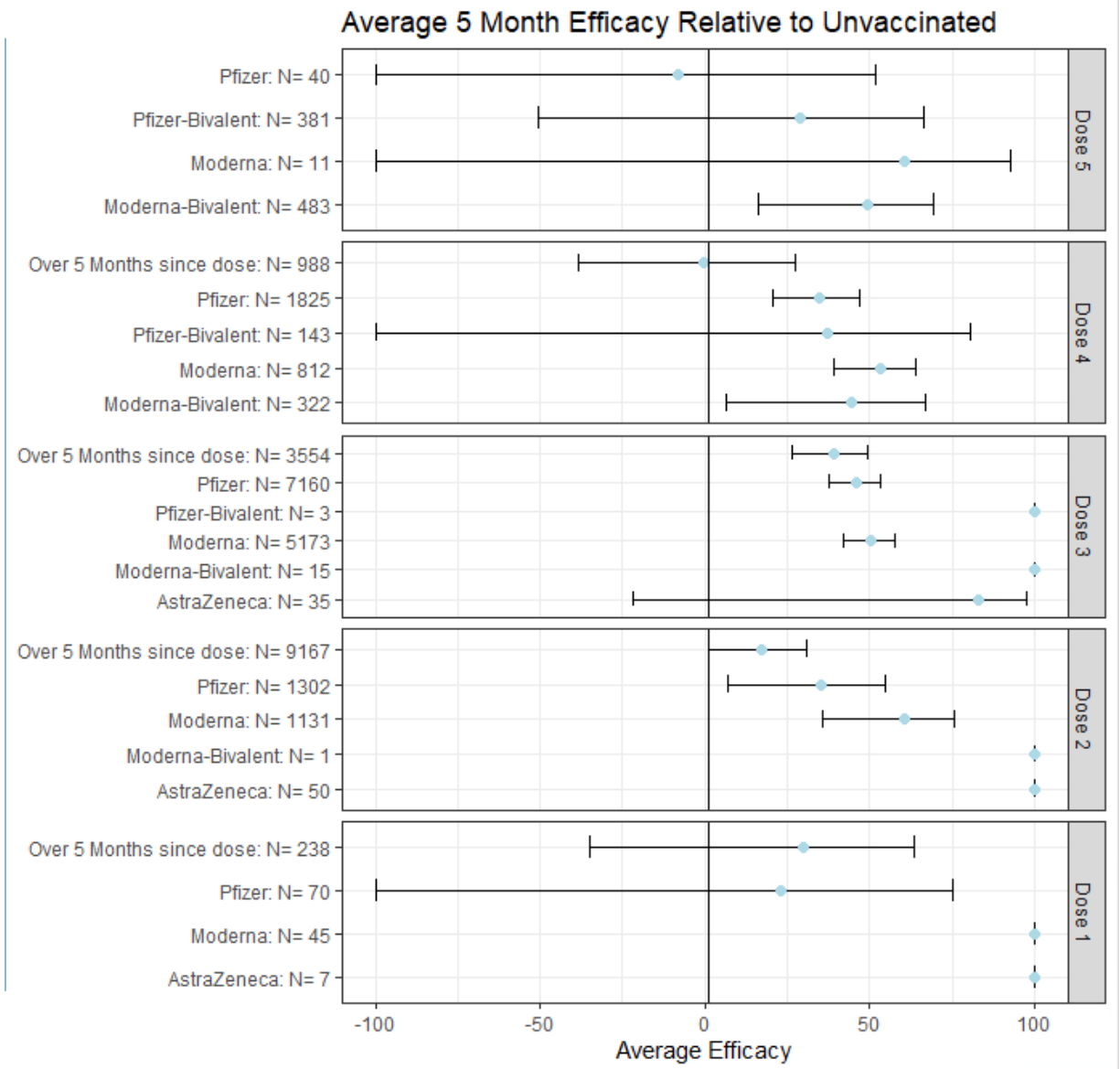
Vaccine effectiveness, by dose number and brand

- At every dose number, the risk of infection was lower among those who received Moderna compared to those who received Pfizer:
  - 14% lower risk, on average
- Bivalent boosters restore waning protection and may broaden protection





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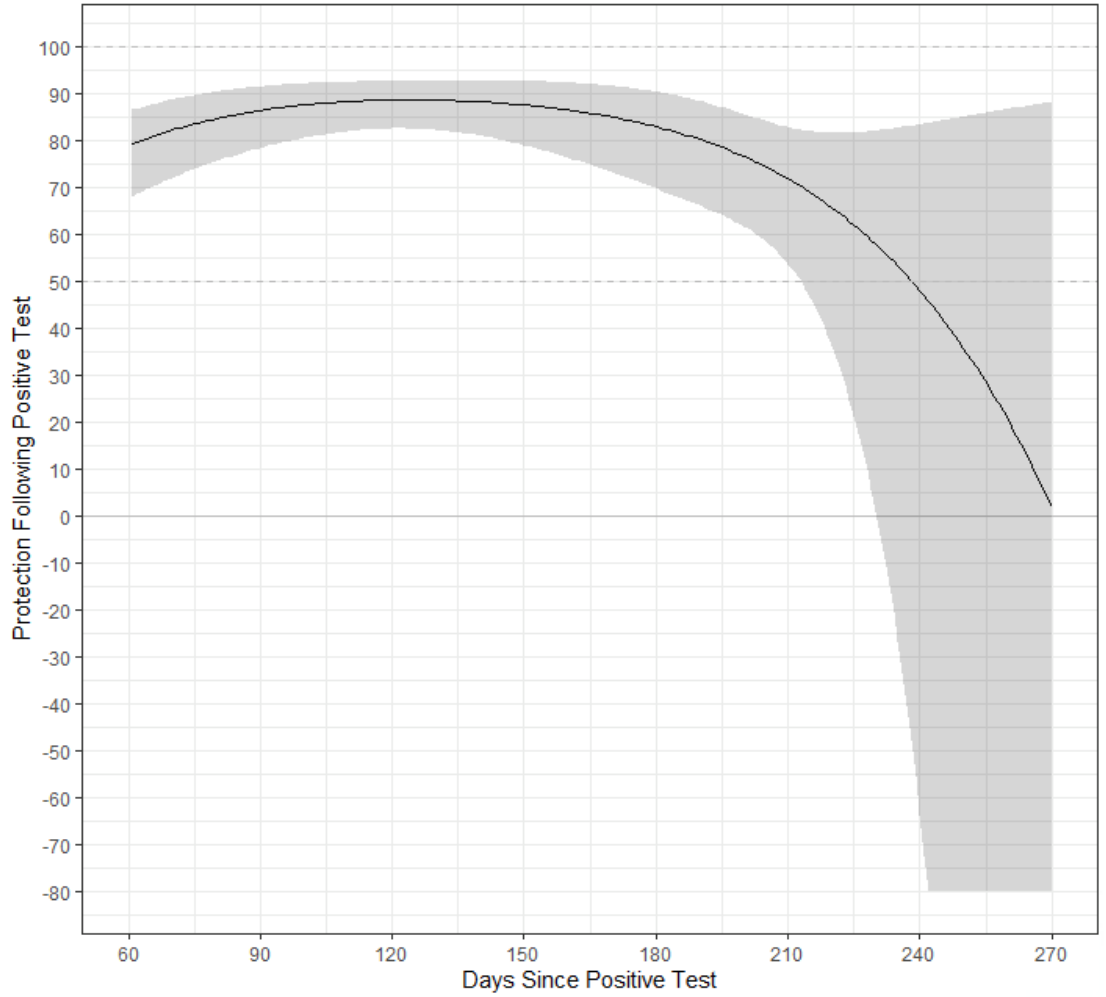
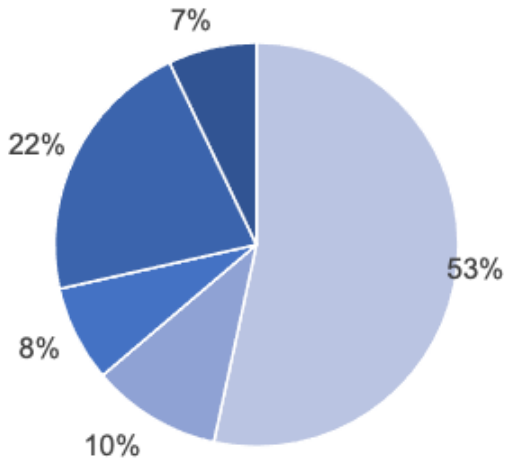
Average protection after a positive test

- Prior COVID infection more protective than vaccination during Omicron surge
  - The risk of reinfection was reduced by ~90% for 6 months and by 50% at 8 months

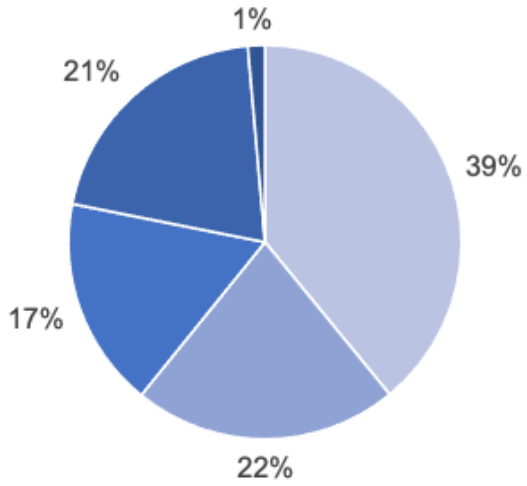


Severity of infection

Pre-Omicron



Omicron



- Asymptomatic
- Runny nose, headache, dry cough, fatigue, or loss of smell
- Fever, or mild shortness of breath
- Severe confusion, severe shortness of breath, vomitting, diarrhea, or mild chest pain
- Severe chest pain or hospitalization

Symptoms by viral variant: Wild-type and Alpha

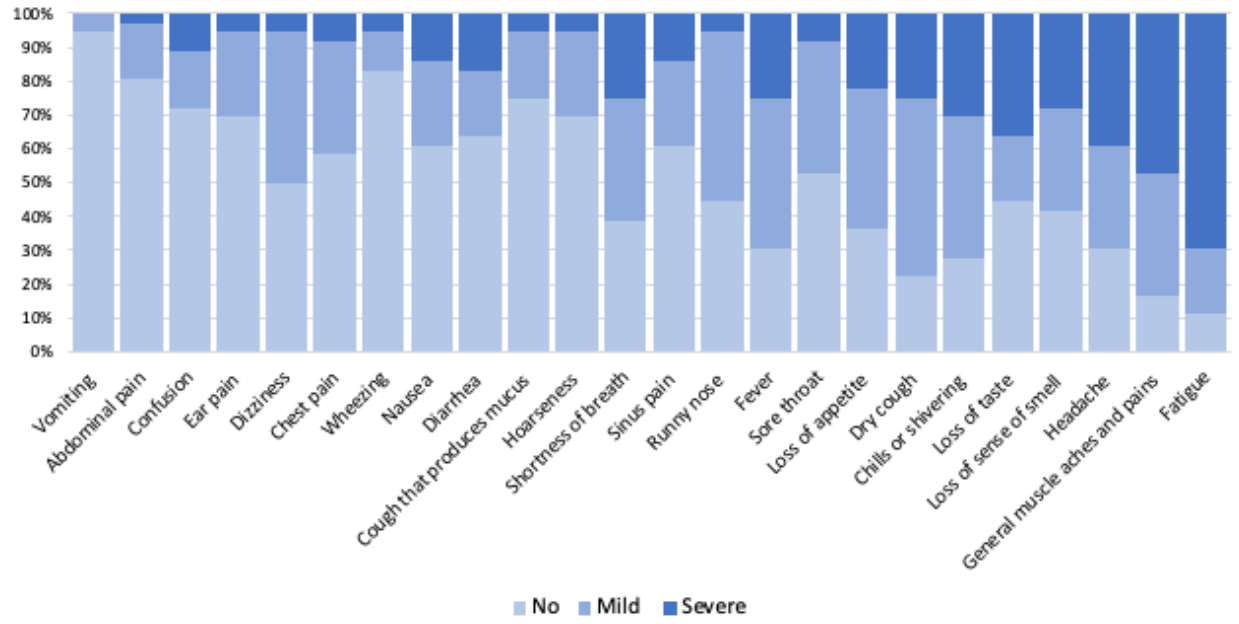
Wild-type (Wuhan) presented with symptoms more likely to be severe than subsequent variants:

- loss of smell and taste were much more common than for subsequent variants
- fatigue, general aches, headache and dry cough were common, and often severe

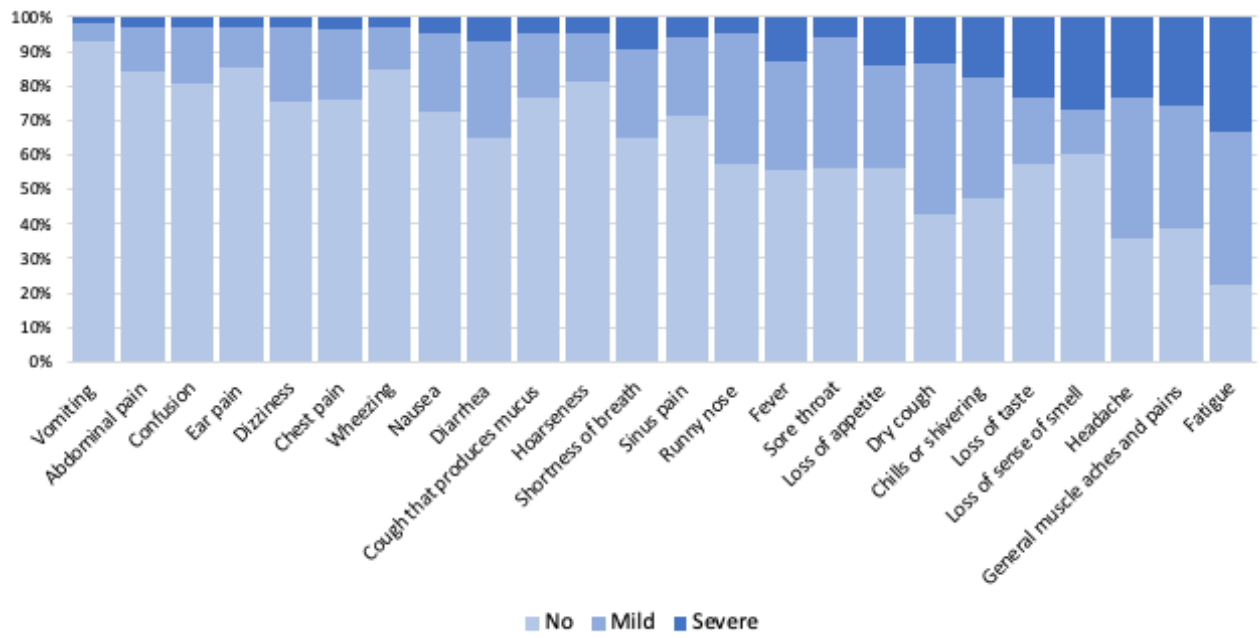
Alpha presented with fewer symptoms, and they were likely to be mild

- fatigue, general aches, headache, shivering and dry cough were reported in ~50%, but most often mild

Wild-type, Jan 11, 2020 to Apr 4, 2020



Alpha, Apr 5, 2020 to Jun 27, 2020



Symptoms by viral variant: Delta and Omicron

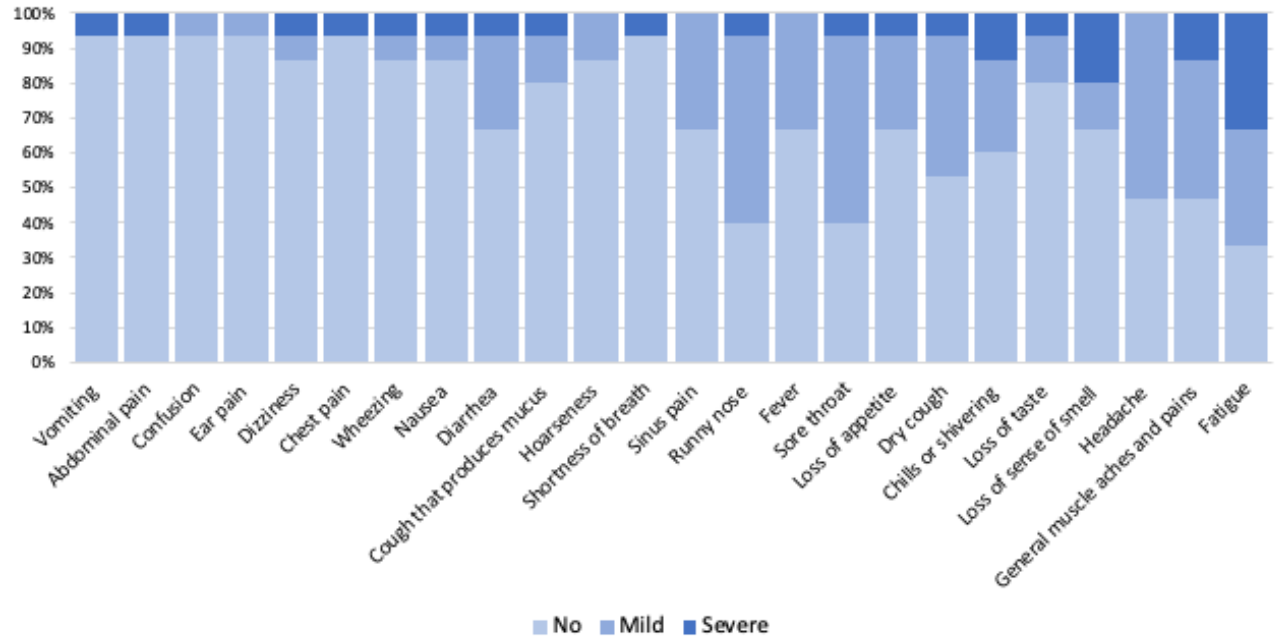
Delta:

- cough and loss of smell are less common than for previous variants
- headache, sore throat, runny nose, fever, and fatigue are common, but mild

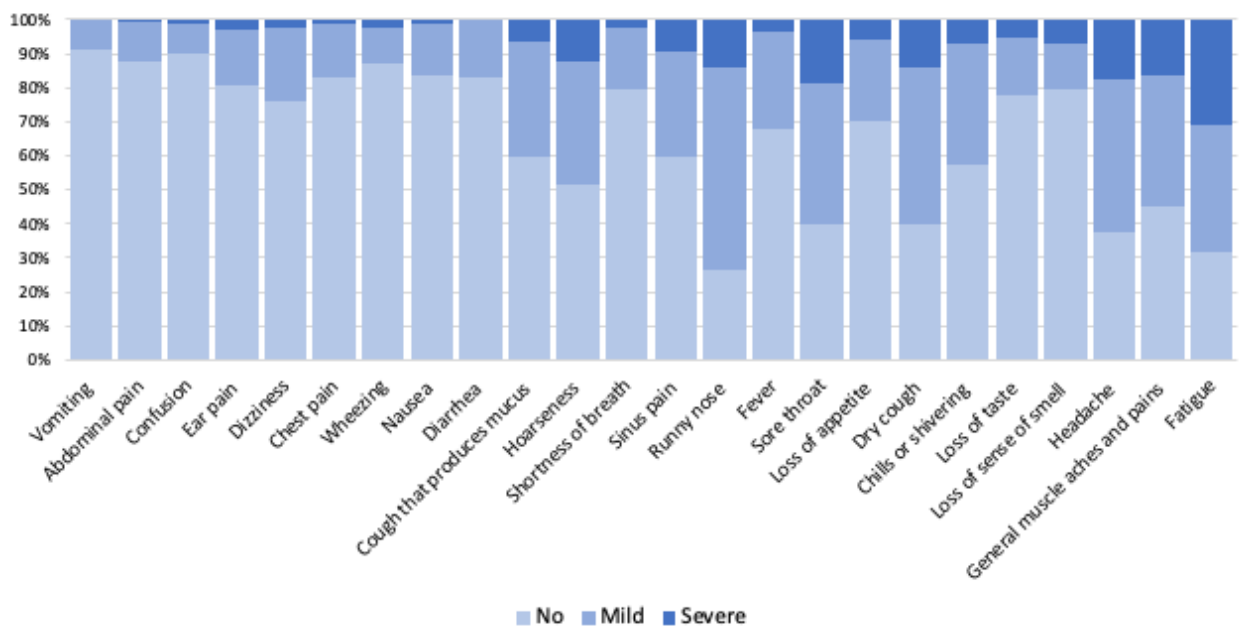
Omicron symptoms were relatively mild in our vaccinated study population:

- upper respiratory or cold like symptoms such as a runny nose, congestion, sneezing, sore throat, headaches, and fatigue were common

Delta, Jun 28, 2020 to Dec 1, 2020



Omicron, Dec 2, 2020 to current



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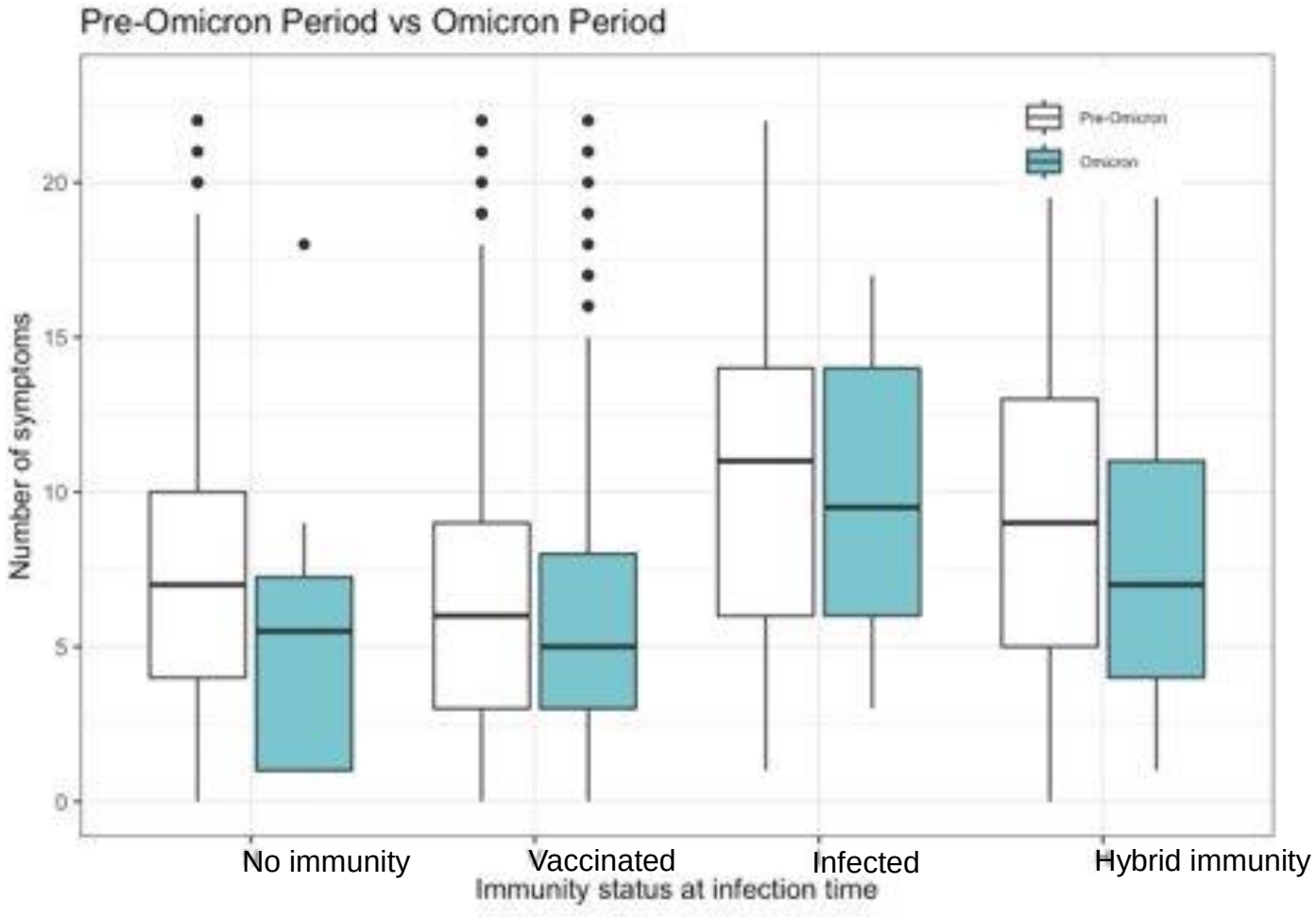
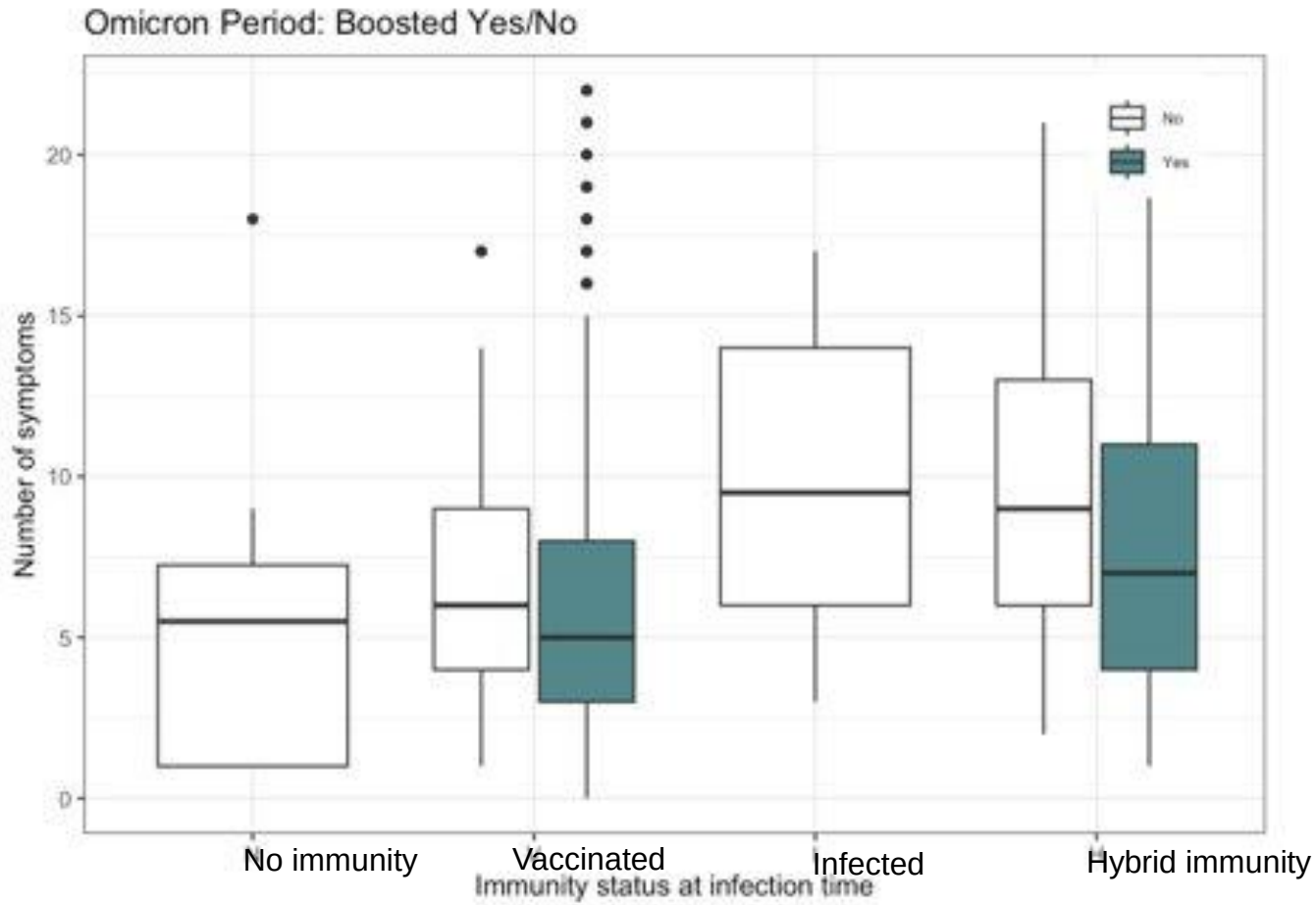
Symptoms according to immune status and time period

- Within each category of immune status, those infected during the Omicron period reported fewer symptoms.
- Participants reported a median of 5 symptoms in the pre-Omicron period, and 6 in the Omicron period
- The vaccinated group reported fewer symptoms than the infected group.
- Those with hybrid immunity did not report fewer symptoms than the vaccinated group



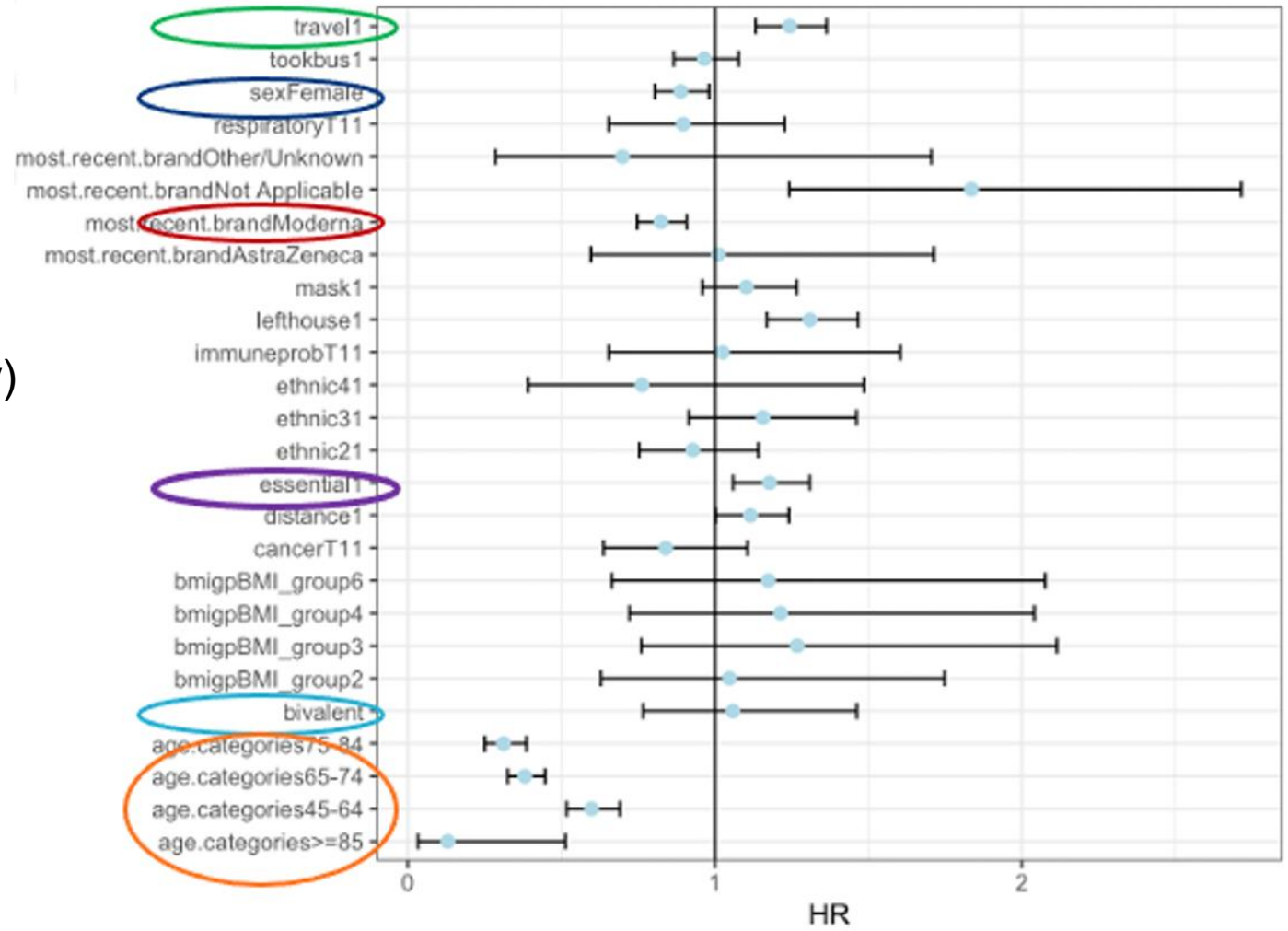
Symptoms according to immune status and receipt of booster vaccination

- Booster vaccination is associated with a reduced symptom number, regardless of whether individuals were previously infected or not.



Risk of infection during the Omicron period

- Women at lower risk of infection
  HR=0.89 (95% CI, 0.80 - 0.98)
- Risk decreases with increasing age
  - HR= 1.00, 0.60, 0.38, 0.31, 0.13 (ages, <45, 45-64, 65-74, 75-84, ≥85, respectively)
- Essential workers at increased risk
  HR= 1.12 (95% CI, 1.06 - 1.31)
- Those who travelled at increased risk
  HR=1.24 (95% CI, 1.13 - 1.37)
- Visible minority groups not at increased risk



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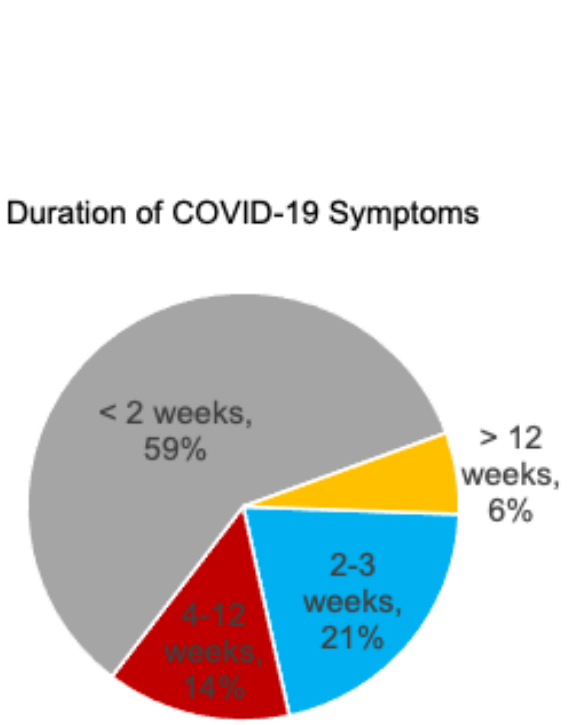
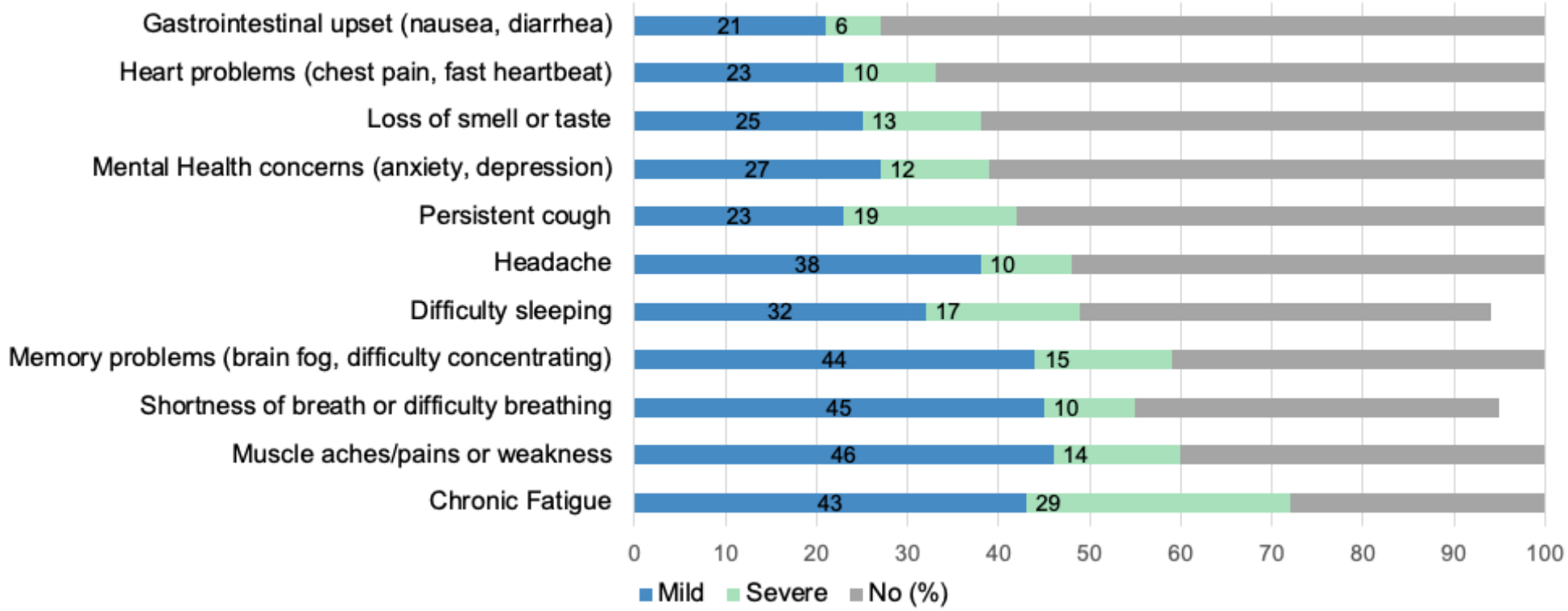
Post Covid-19 Condition (*long COVID*)

- When the symptoms of COVID-19 persist for more than 12 weeks after infection
- Prevalence of 6% infected
- Those with the most serious illness were more likely to experience long COVID
- Those with mild illness still experience long COVID





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Conclusions

- More than half of the COVID-19 diagnoses were among those who neither knew nor suspected they were infected.
- Risk of infection was increased among younger individuals, men, essential workers and those who travelled.
- There were no ethnic differences in risk.
- The effectiveness of full or booster vaccination in preventing SARS-CoV-2 Omicron infection is short-term, lasting **4 months.**
- Antibody levels are correlates of vaccine-induced protection.
- Prior infection protects against reinfection for **8 months.**
- Booster campaigns could be strategically used to rapidly boost population immunity before upcoming waves of infections.

Accessing CanPath Data

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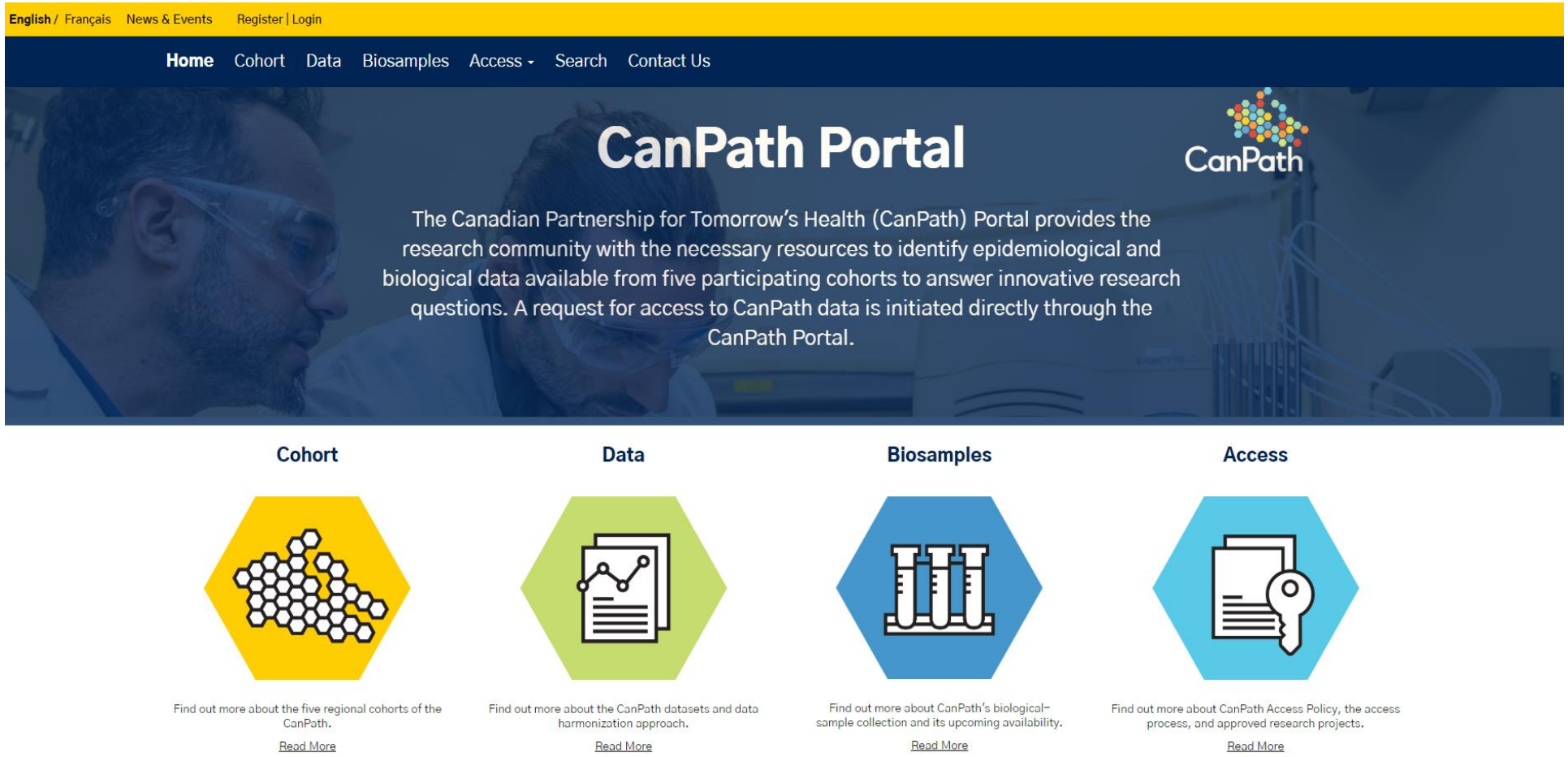

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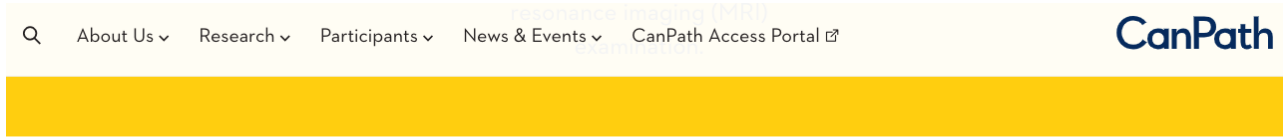


Datasets

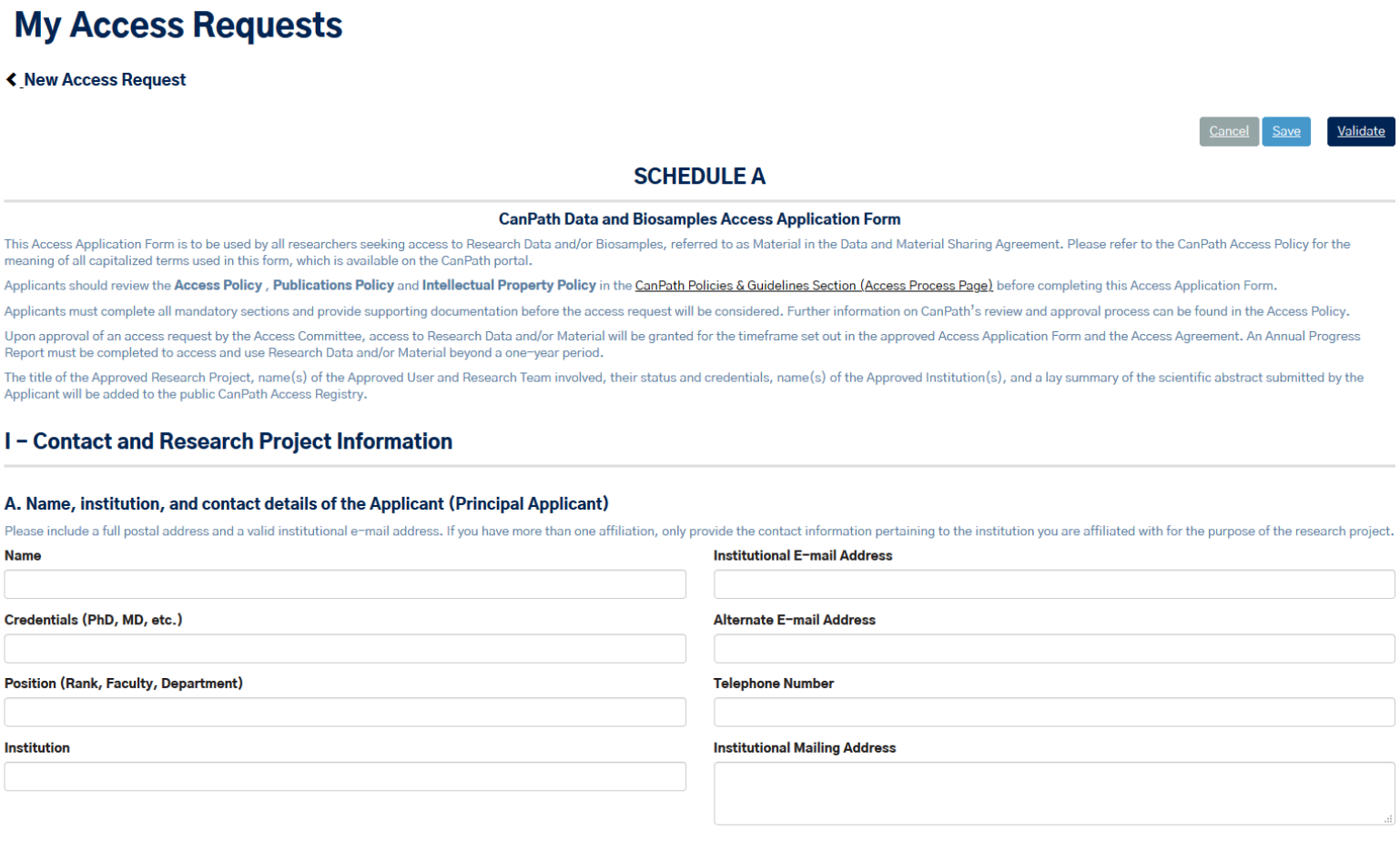
All CanPath participants completed a detailed questionnaire at the time of recruitment (baseline) and continue to provide updated health and lifestyle information through follow-up questionnaires.

Nationally harmonized datasets include data collected by the five mature cohorts: BC Generations Project, Alberta's Tomorrow Project, Ontario Health Study, CARTaGENE and the Atlantic PATH. Data from the Manitoba Tomorrow Project will be made available once participant recruitment is complete.

Harmonized datasets available include:

- Baseline Health and Risk Factors Questionnaire
- Baseline Health and Risk Factors Questionnaire with Additional Diseases
- Baseline Mental Health Questionnaire
- Baseline Physical Measures
- Follow-up Health and Risk Factors Questionnaire
- Pre-analytical Data Related to Biological Samples
- Genotyping Data
- CANUE Environmental Exposure Data
- COVID-19 Questionnaire – ***Now Available***

Accessing CanPath Data



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Applicants should review the **Access Policy** , **Publications Policy** and **Intellectual Property Policy** in the CanPath Policies & Guidelines Section (Access Process Page) before completing this Access Application Form.

Applicants must complete all mandatory sections and provide supporting documentation before the access request will be considered. Further information on CanPath's review and approval process can be found in the Access Policy.

Upon approval of an access request by the Access Committee, access to Research Data and/or Material will be granted for the timeframe set out in the approved Access Application Form and the Access Agreement. An Annual Progress Report must be completed to access and use Research Data and/or Material beyond a one-year period.

The title of the Approved Research Project, name(s) of the Approved User and Research Team involved, their status and credentials, name(s) of the Approved Institution(s), and a lay summary of the scientific abstract submitted by the Applicant will be added to the public CanPath Access Registry.

I – Contact and Research Project Information

A. Name, institution, and contact details of the Applicant (Principal Applicant)

Please include a full postal address and a valid institutional e-mail address. If you have more than one affiliation, only provide the contact information pertaining to the institution you are affiliated with for the purpose of the research project.

Name

Institutional E-mail Address

Credentials (PhD, MD, etc.)

Alternate E-mail Address

Position (Rank, Faculty, Department)

Telephone Number

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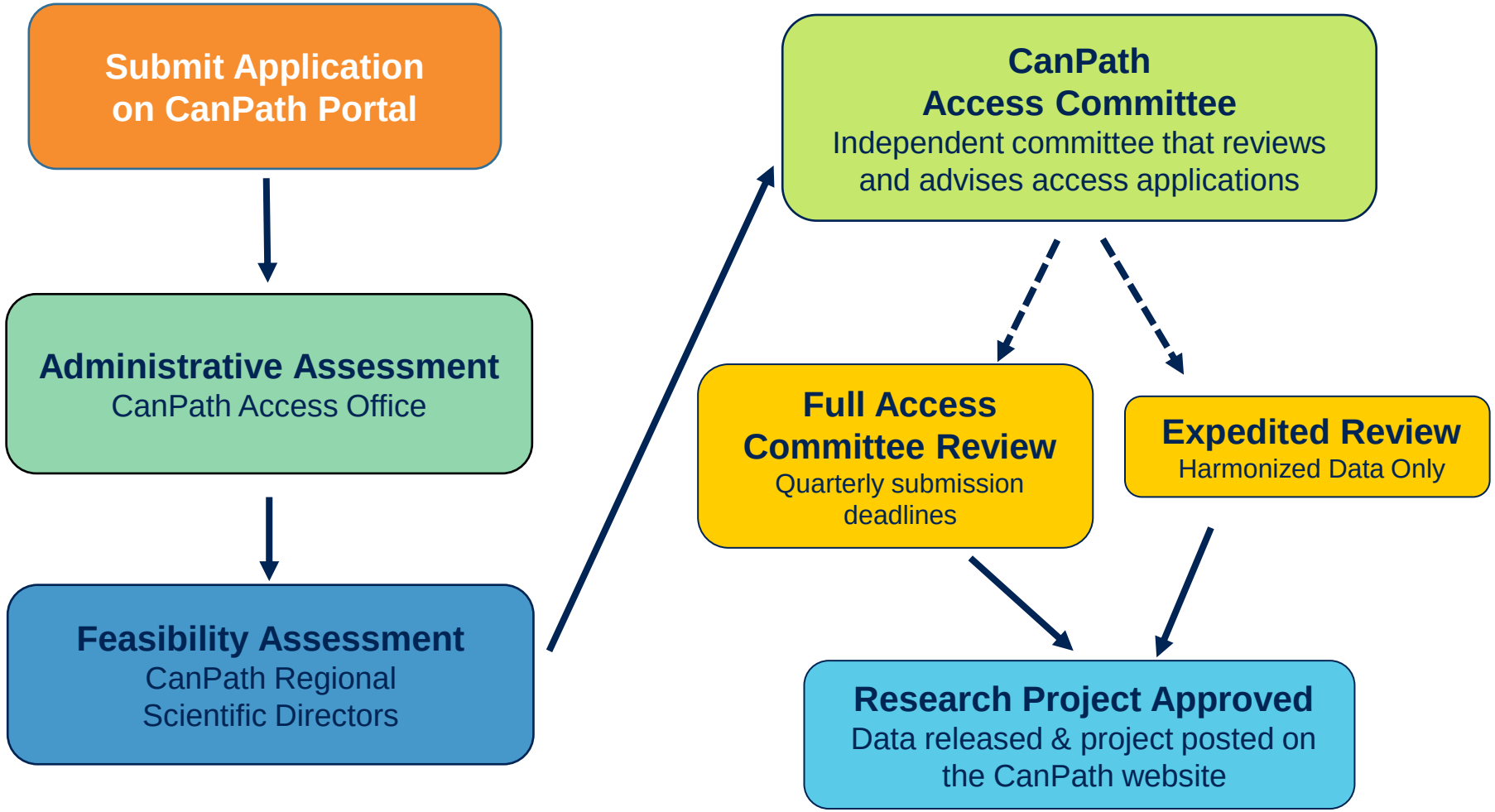
Access Process Overview



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Thank you to the sponsors and hosts of CanPath's antibody study and to the participants across the regional cohorts who generously donated their time, information and biological samples.

OICR Ontario Institute for Cancer Research

CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

COVID-19 IMMUNITY TASK FORCE

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

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