CanPath Covid-19 Antibody Study

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Webinar: March 23, 2022

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

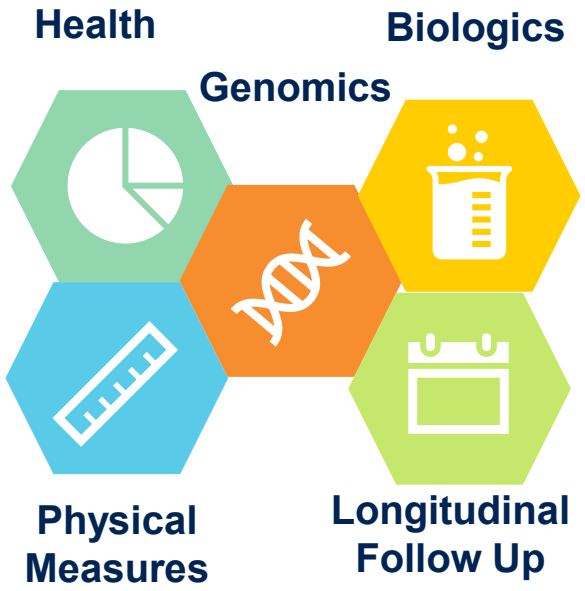
Canada's largest population health research platform

- CanPath is a **population-health research platform** for assessing the effect of genetics, behaviour, family health history and environment on chronic diseases.
- CanPath brings together seven cohorts across ten provinces
- The study is jointly housed at the University of Toronto & The Ontario Institute for Cancer Research

330,000+ Canadians

+

+



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330,000 Canadians are followed longitudinally

National Leadership Team

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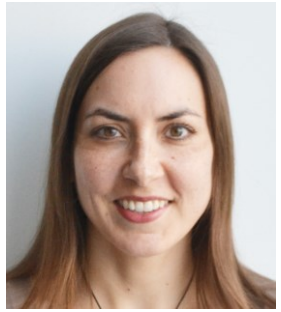

Kelly McDonald
Ontario Health
Study

Ellen Sweeney
Atlantic Path

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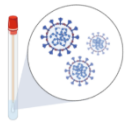
CanPath COVID-19 Initiatives

- COVID-19 Questionnaire (launched in March 2020)
  - Leverages existing infrastructure to determine **population-level prevalence** of COVID-19;
  - Determine **biological, societal and behavioural factors** that affect susceptibility to COVID-19;
  - Capture the **socio-economic and mental health and long-term health outcomes** of COVID-19

- COVID-19 Antibody Study (launched in March 2021 and ongoing)
  - Collection of **dried blood spots** using kits mailed to participants, which are then tested for infection-acquired antibodies and vaccine-induced antibodies, along with a supporting questionnaire.

CanPath COVID-19 questionnaire was designed to align with international efforts



COVID-19 test result/ suspected infection

Symptoms experienced (if any)

Participant hospitalized or received medical care

Current health status and risk factors for COVID-19

Potential source of exposure

Impact of pandemic on job status

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

101,595

COVID-19 Questionnaires Completed

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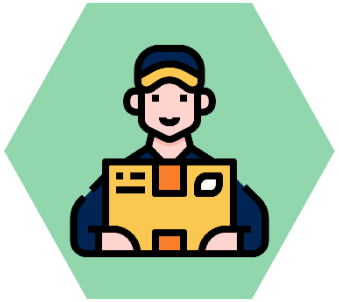
Antibody study questionnaire (launched in March 2021 and ongoing…)

Unique variables not collected in initial COVID-19 Questionnaire

- More detailed job classifications for front-line workers likely to have occupational exposures:
  - Passenger and delivery drivers, including taxi/uber drivers, restaurant and package delivery drivers
  - Services requiring entry into private homes, including Personal Support Workers, nurses, community aid/shelter workers, tradespeople, movers and cleaners

- COVID-19 Vaccines:
  - Participant vaccination status (which one and date), vaccine availability, and willingness to receive COVID-19 vaccine



SUPPORT-Canada: A national COVID-19 serological surveillance study

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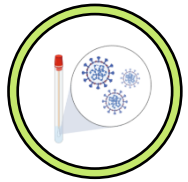
Canadian Partnership for Tomorrow's Health

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

Public Health Agency of Canada
Agence de la santé publique du Canada

COVID-19 IMMUNITY TASK FORCE

Collection of COVID-19 related data and outcomes from over 20,000 Canadians



Longitudinal serological surveillance of SARS-CoV-2 antibodies in diagnosed, symptomatic, asymptomatic and susceptible Canadians

Deep sequencing to support functional immuno-genomics studies

CanPath COVID-19 Antibody Studies

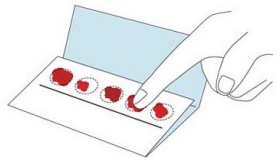
CIHR-funded study

- Seroprevalence of SARS-CoV-2 antibodies in 3,000 randomly selected CanPath participants at 3 time points (500 per regional cohort)
- Developing capacity for immunogenomics through blood collection from 4,000 participants

COVID-19 Immunity Task Force- and PHAC-funded Study

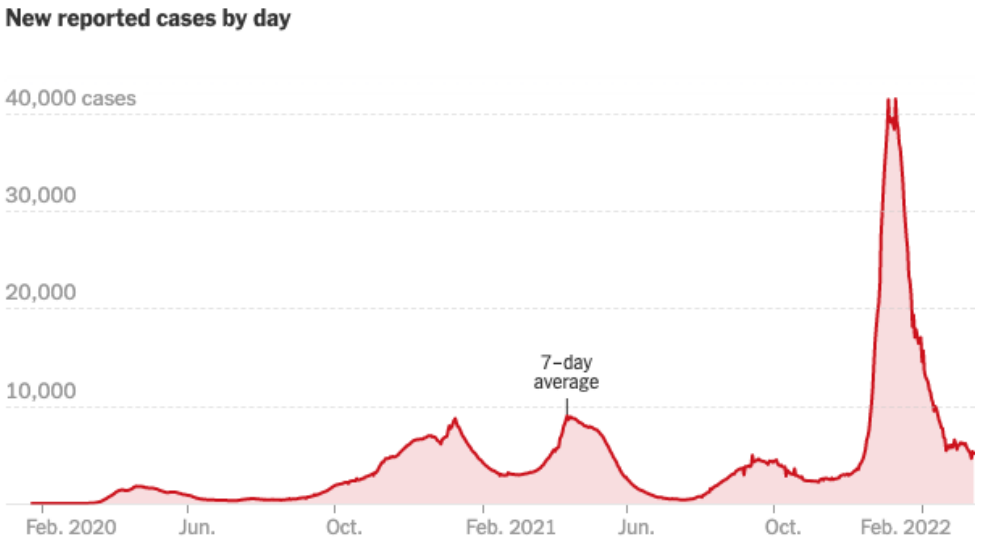
- Seroprevalence of SARS-CoV-2 antibodies in 25,000 CanPath participants at 2 time points
- Includes populations that are traditionally not included in studies or are among the highest risk of exposure to COVID-19, such as residents of long-term care homes and people living in under-served urban and rural communities with high prevalence of COVID-19, and those with underlying conditions

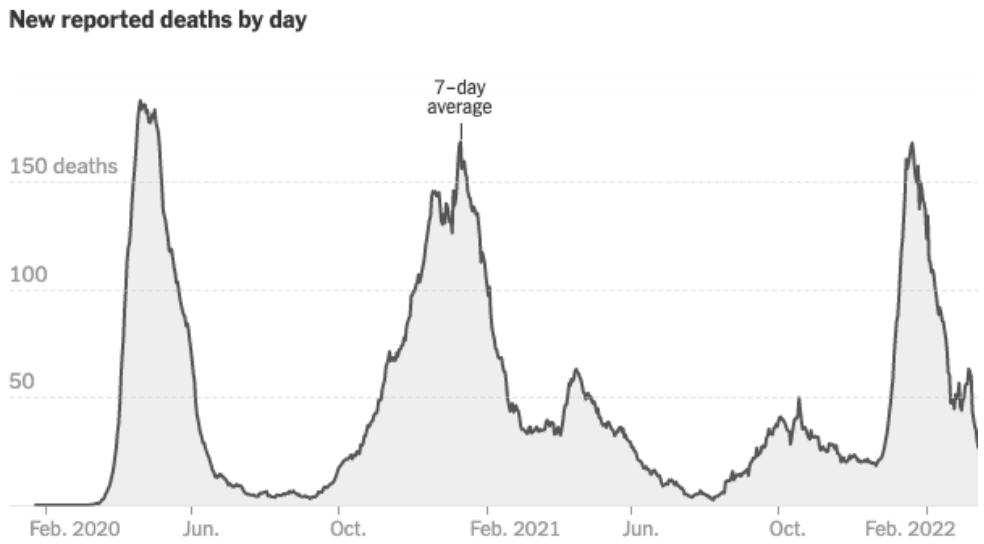
Both studies are collecting dried blood spots using kits mailed to participants.



Canada Coronavirus Epidemic Curve and Latest Trends

- An average of 5,103 cases per day were reported in Canada in the last week.
- Cases have decreased by 8 percent from the average two weeks ago. Deaths have decreased by 39 percent.
- At least 1 in 11 residents have been infected, a total of 3,392,164 reported cases.
- At least 1 in 1,014 residents have died from the coronavirus, a total of 37,080 deaths.
- January 2022 was the month with the highest average cases
- April 2020 was the month with the highest average deaths in Canada.





Source: New York Times. Population data from Statistics Canada.

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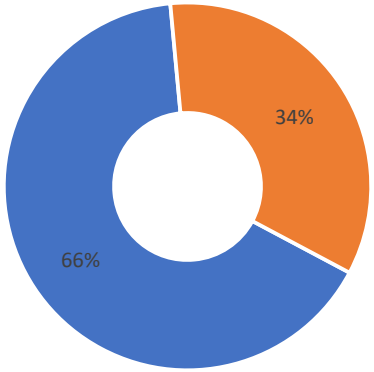
Objectives of the antibody study

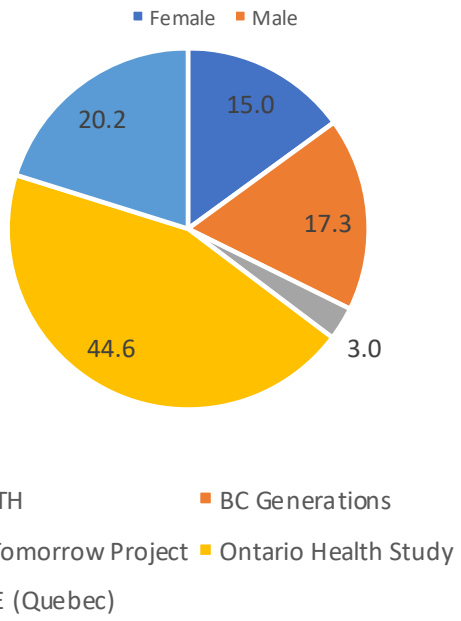
- Analyzing **serologic data**:
  - What is the antibody response following vaccination? Following infection?
  - Are there sub-groups in whom antibody response is suboptimal, such as those with cancer?
  - Does the immune response vary according the number of vaccine doses and the vaccine product received?
  - Are antibody levels waning over time?

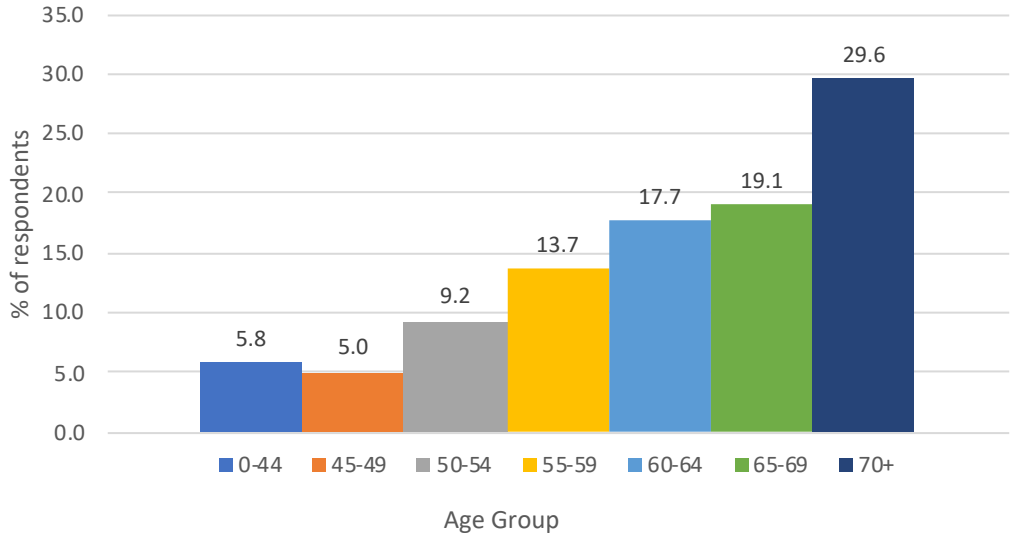
- Determining **risk factors of infection**

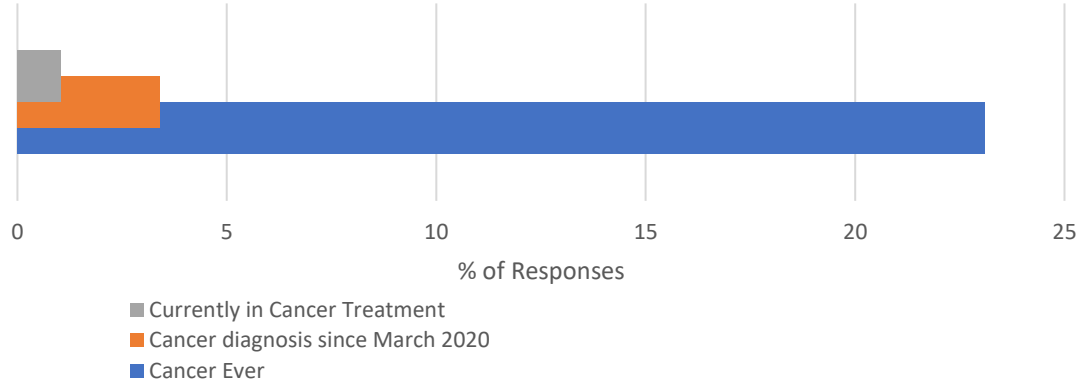
- **Boosters**:
  - How have booster shots affected antibody levels?
  - How have booster shots affected risk of infection?

Study Population









*Alberta's data were not available at the time of analysis

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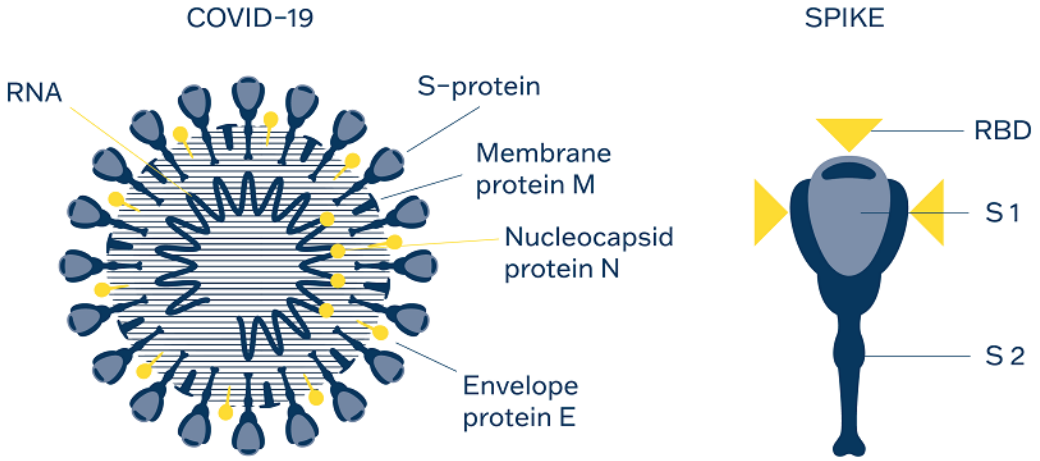
Methods: laboratory testing

- SARS-CoV-2 antibody levels were measured from dried blood spots
- Measured three antibody levels:
  - anti-spike (S) IgG
  - anti-receptor binding domain (RBD) IgG
  - anti-nucleocapsid (N) IgG
- Spike protein is the main antigenic target of antibodies generated by infections and of most vaccines
- Anti-RBD and anti-S antibodies are markers of vaccination
- Anti-N antibodies indicate natural infection (along with anti-RBD and anti-S)

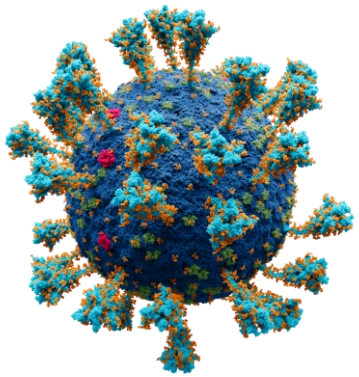


Methods: SARS-CoV-2 variants

- Multiple SARS-CoV-2 variants have circulated globally, most notably:
  - Alpha (B.1.1.7) variant: detected in UK
  - Delta (B.1.617.2) variant: emerged in India
  - Omicron (B.1.1.529): detected in South Africa
    - multiples 70x faster than Delta in the bronchi, but less severe than previous strains
    - 60 mutations, 32 affect the spike protein, and many of those mutations not seen previously

- In estimating incidence of infection, we considered risk for SARS-CoV-2 during 4 periods:
  - Mixed Wild type (Wuhan) strain and Alpha period (11 Jan to 4 Apr)
  - Alpha period (5 Apr to 27 Jun): ~77% Alpha
  - Delta period (28 Jun to 1 Dec): ~97% Delta
  - Omicron period (2 Dec to now): ~100% Omicron

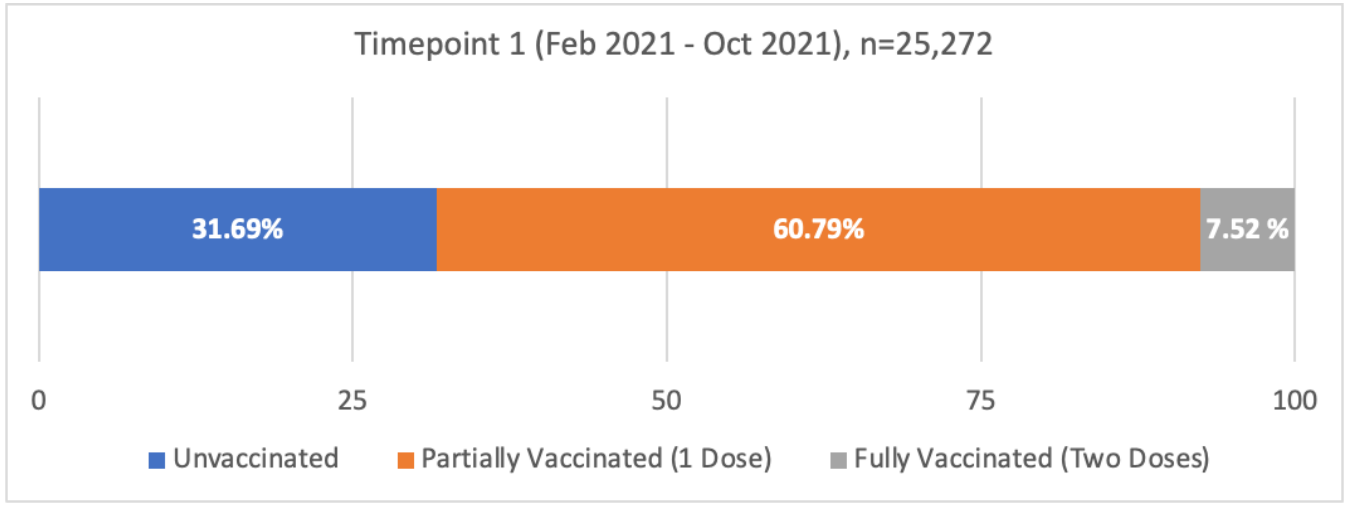
  and assume infections during these timeframes were based on the predominant variant

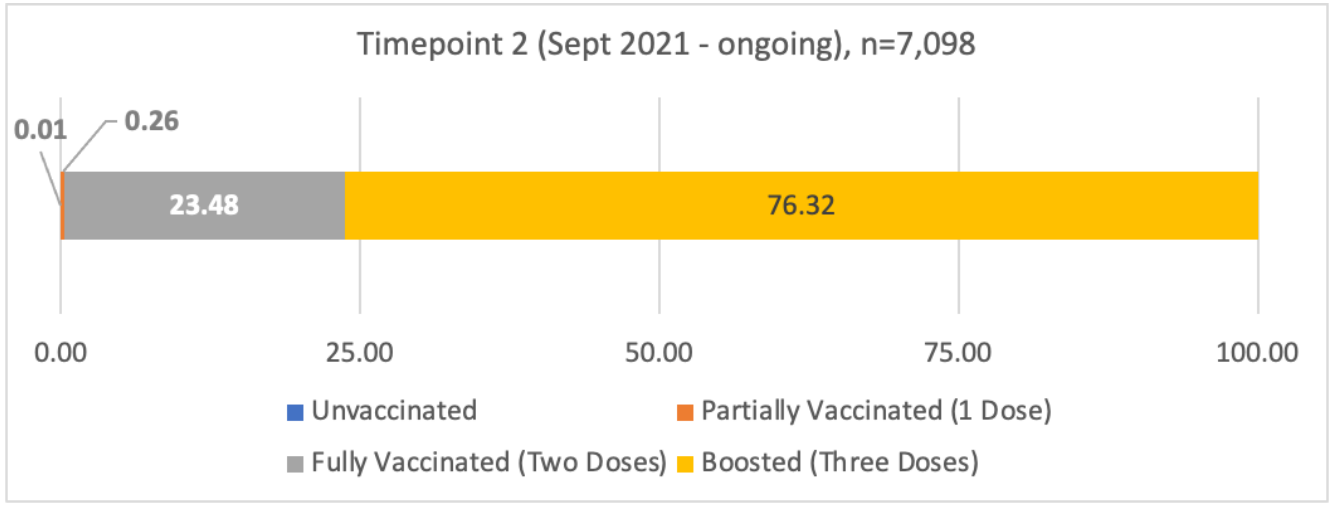


Methods: exposures, covariates, and outcomes

- Exposure
  - vaccination status, number of doses, time since last dose, product received
- Covariates
  - age, sex, geographic region
  - calendar time
  - influenza vaccination (proxy for health behaviours)
  - comorbidities
  - area-level measures: income, essential workers, household size, visible minorities
- Outcomes
  - Positive COVID-19 test: PCR, rapid antigen, antibody
  - Hospitalizations

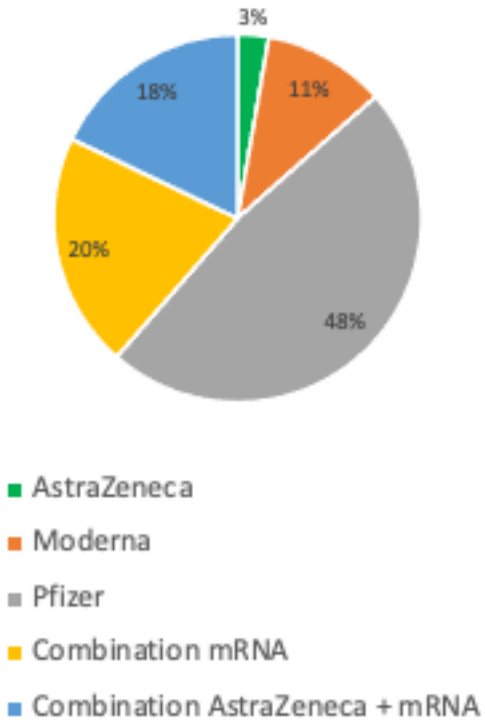
Dried blood spot collection at two timepoints

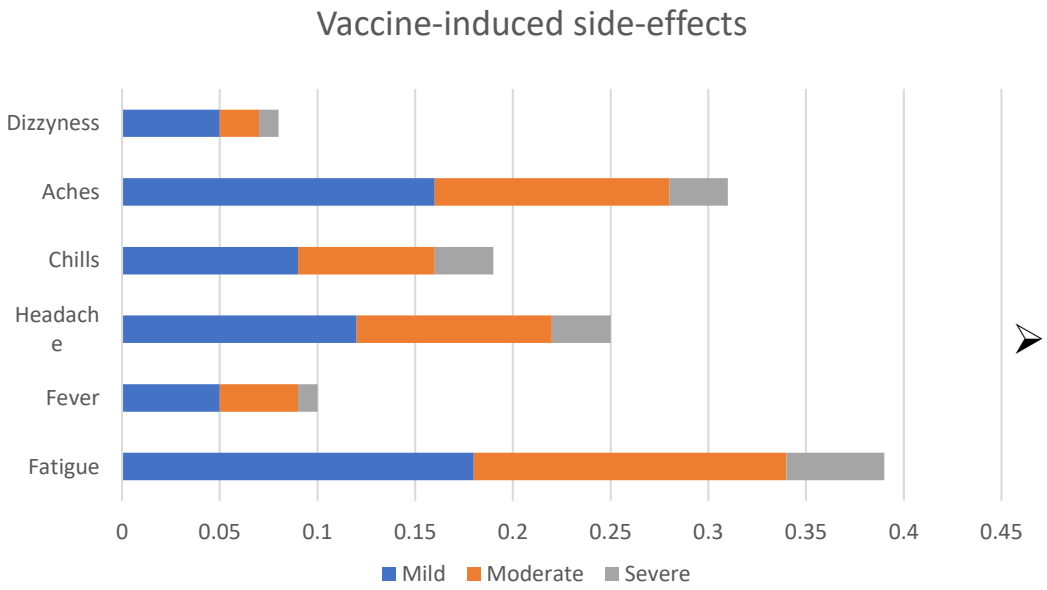




- Anticipate ~25,000 biospecimens collected at each timepoint
- Supporting questionnaires at both timepoints
- At timepoint 1, 61% and 8% of the study population had received one and two doses, respectively
- At timepoint 2, 23% and 76% the study population had received two and three doses, respectively
- At timepoint 2, only 0.3% had received one dose, and only 0.01% were unvaccinated

Vaccine distribution and safety





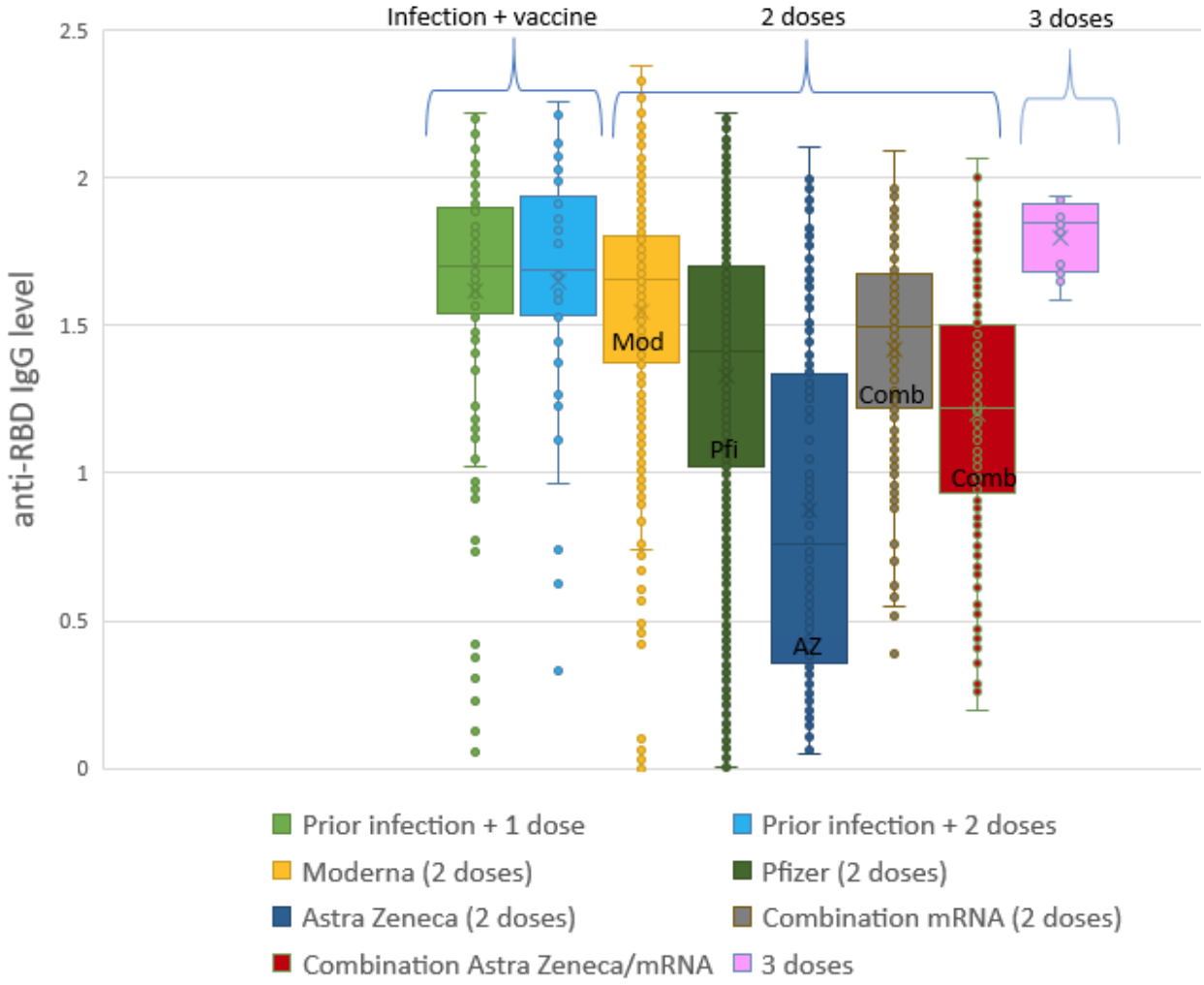
- Among those fully vaccinated (with or without a booster),
  79% received mRNA vaccines only:
  - Pfizer (48%), Moderna (11%) or a combination of the two (20%)

  21% received a regimen that included Astra Zeneca:
  - AstraZeneca, two doses (3%) or a combination of AstraZeneca and an mRNA vaccine (18%)

- Vaccine safety:
  - Vaccine recipients reported local reactions (e.g., pain, erythema, swelling) and systemic reactions (e.g., headache, fatigue, muscle aches)
  - Most reactions were mild to moderate
  - **0.18%** (n=13/7098) required **hospitalization for their symptoms**
  - **2.6%** (n=186/7098) **contacted a healthcare provider** about these symptoms

Vaccine-induced anti-RBD antibody levels

- Dots depict antibody levels; boxes represent the first quartile and third quartile; the line represents the mean.
- Those with **prior infection** have more antibodies
- Heterologous dosing (**AstraZeneca/mRNA vaccine**) induced a response comparable to **mRNA regimens**.
- A **third dose** boosted mean antibody-levels to just above initial post-second dose levels.



Vaccine-induced anti-spike antibody levels

- Findings are generally similar to those for the anti-RBD antibody levels:

- Dots depict antibody levels; boxes represent the first quartile and third quartile; the line represents the mean.
- Heterologous dosing (**AstraZeneca/mRNA vaccine**) induced a response comparable to **mRNA regimens**.
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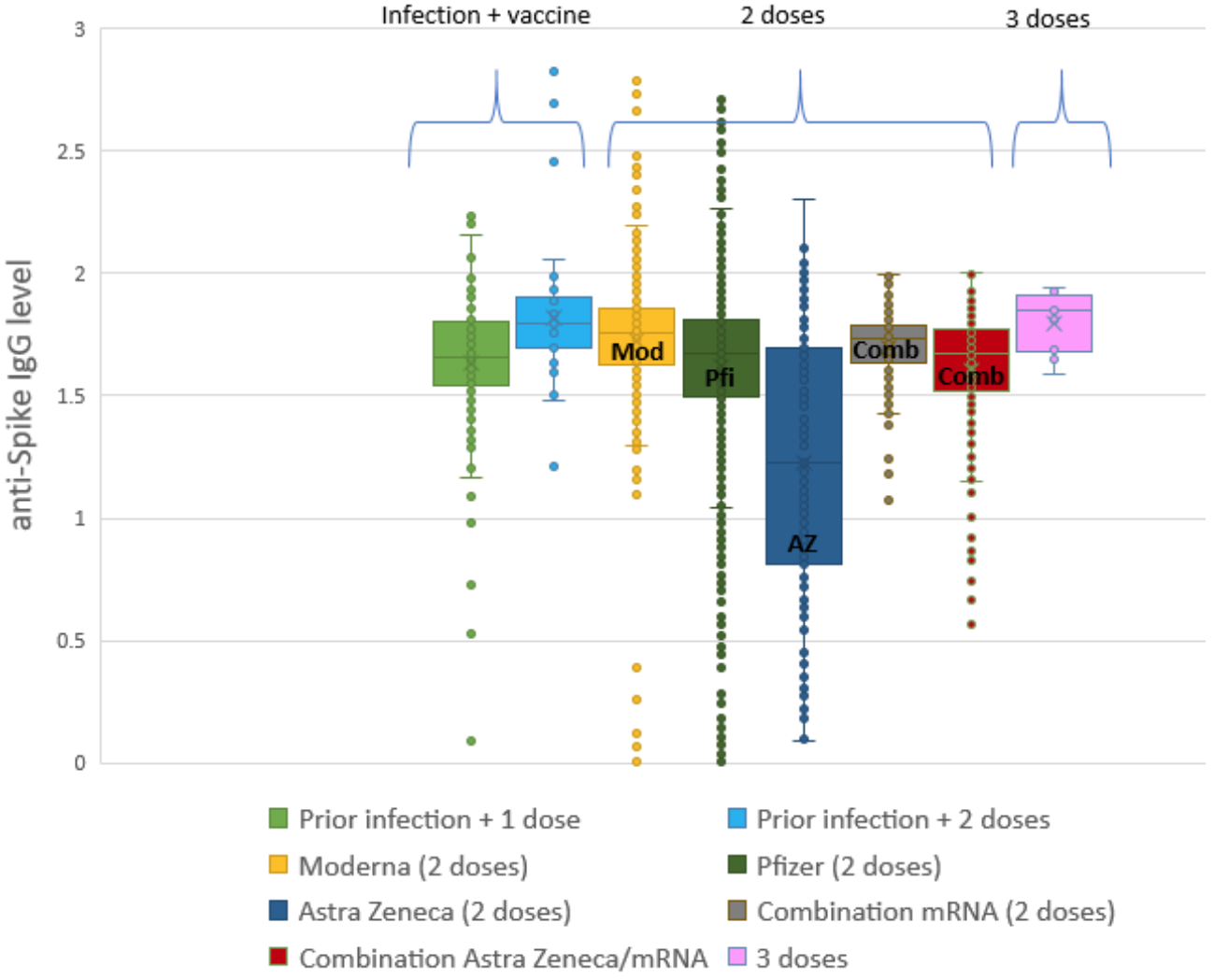

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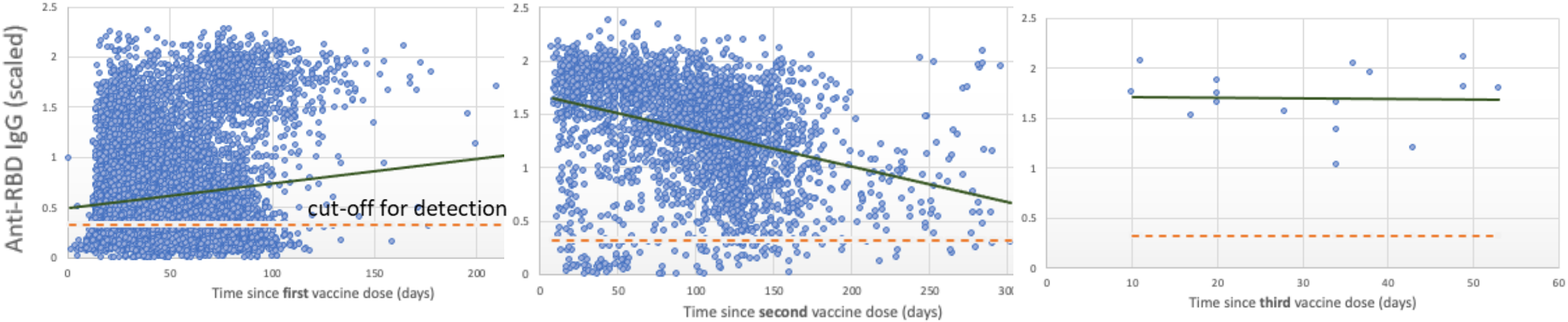
Evolution of anti-RBD antibody levels after 1st, 2nd, and 3rd vaccine doses

- The **dots** depict antibody levels; the **green** line shows the linear trend; the **orange** line shows the cut-off for seropositivity.
- Substantial interindividual variability
- Increasing time since second vaccine dose is associated with decreasing anti-RBD IgG levels ($p<0.01$) (adjusting for age, sex, product type, time since dose, interval between doses)
- Rate of decline is much more pronounced for anti-RBD than for anti-spike antibodies



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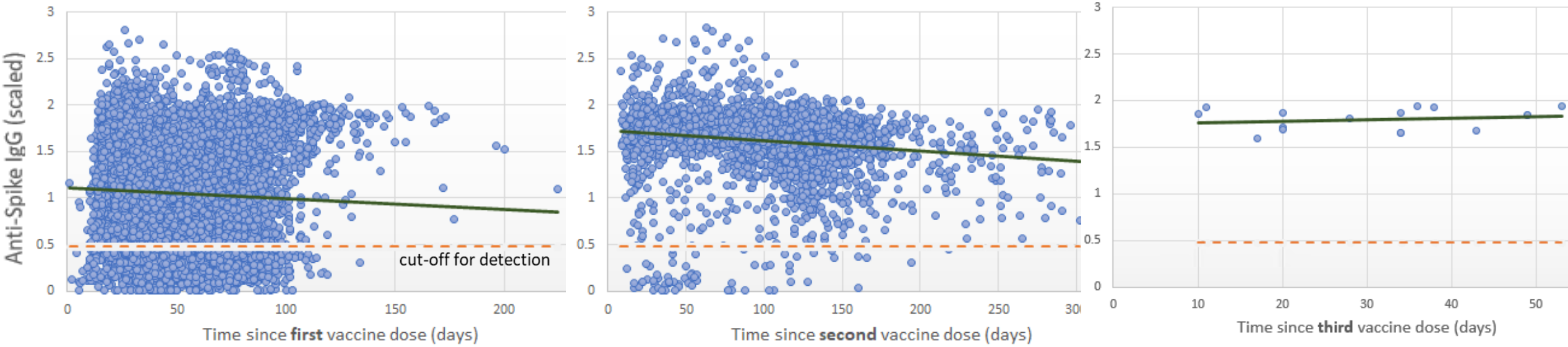

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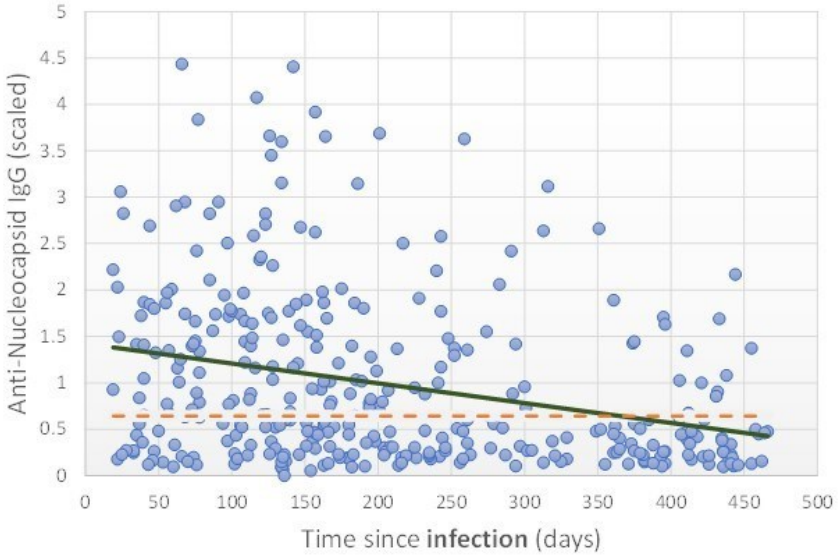
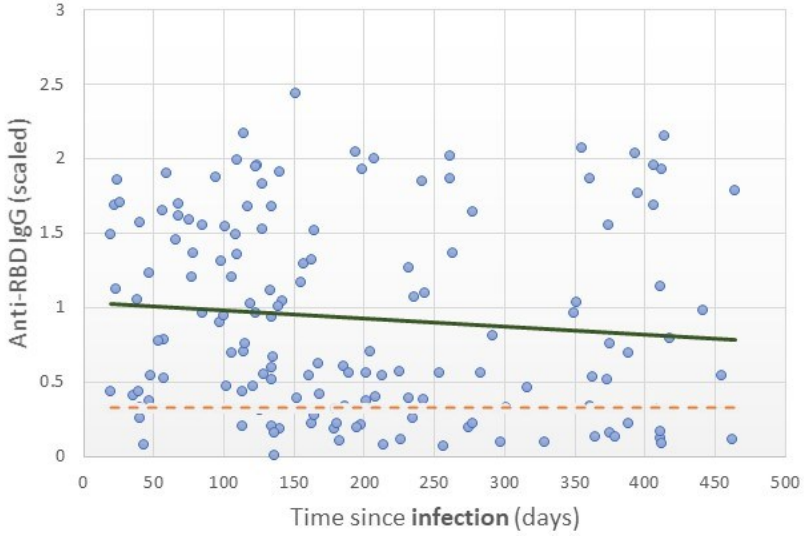
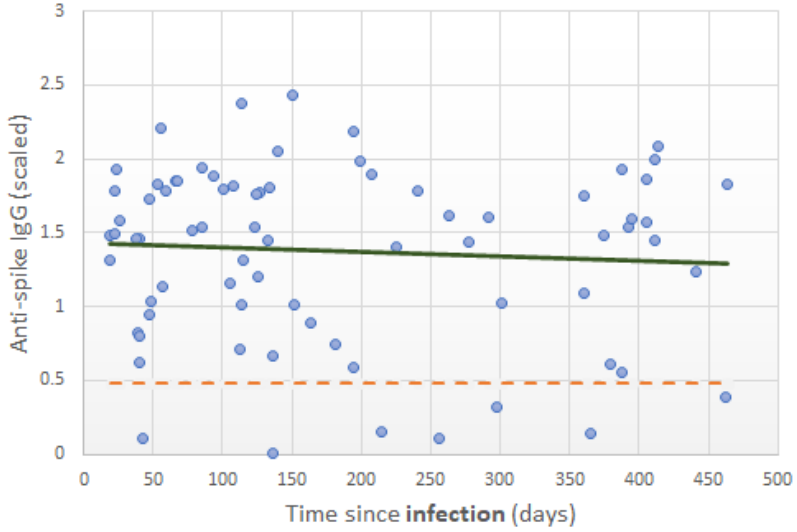
Infection-induced antibody levels: anti- nucleocapsid (N), receptor binding domain (RBD,) and spike (S) IgG

- The **dots** depict antibody levels; the **green** line shows the linear trend; the **orange** line shows the cut-off for seropositivity.
- Sensitivity in discerning previous infections varied: **49% for anti-N IgG**, **78% for anti-RBG IgG**, and **91% for anti-S IgG**
- Anti-N IgG levels degraded quickly, with 35% of individuals seropositive for anti-N IgG at six months and 22% at 12 months.
- Anti-RBD and anti-S remain detectable for significant periods
- Reliance on anti-N IgG to measure infection-induced seroprevalence in a vaccinated population is challenging





among unvaccinated



among unvaccinated

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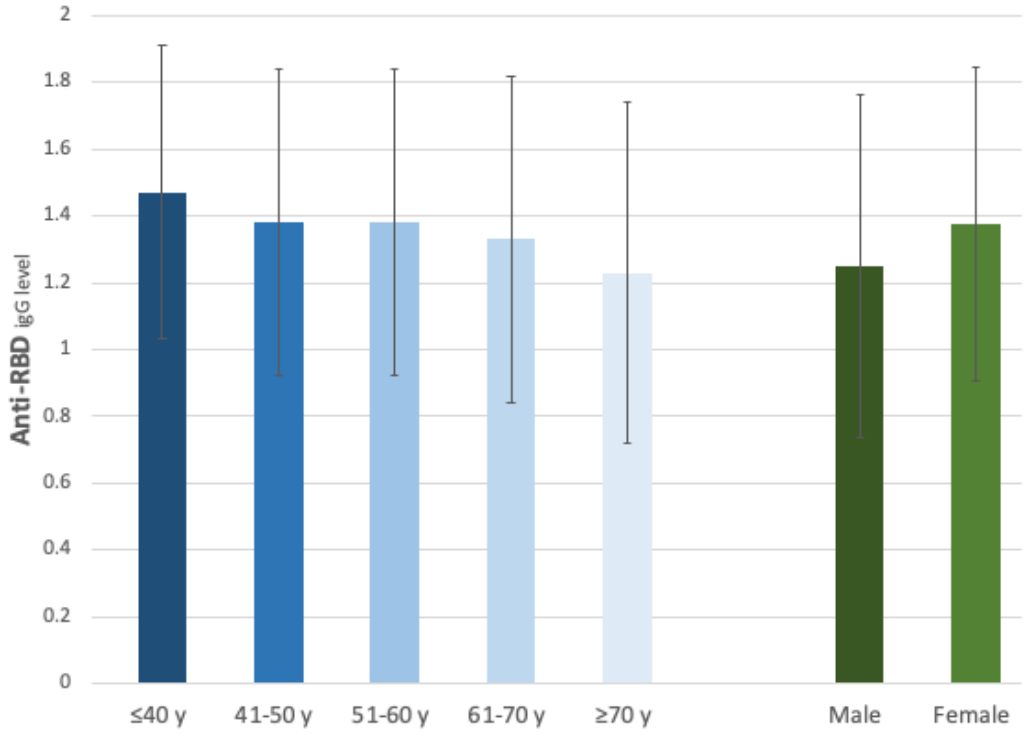
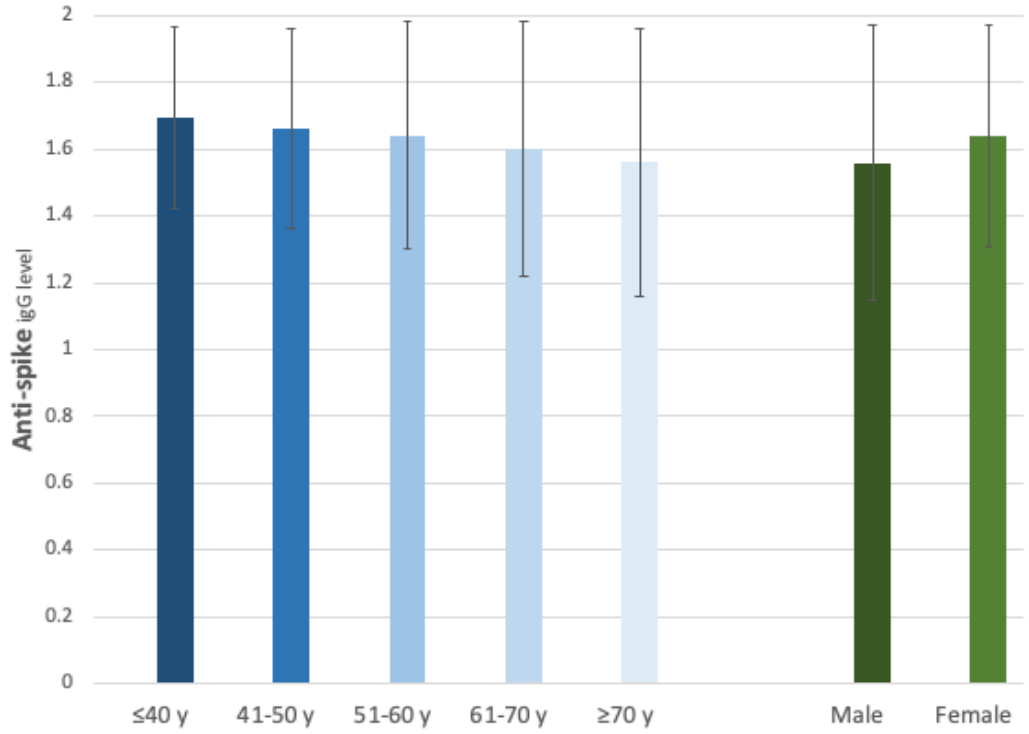
Variation in immune response by age and sex (among fully vaccinated)

- Antibody levels decrease with increasing age, consistent with systematic reviews
- Females had a higher IgG levels, consistent with widely reported enhanced immune responses in females
- Sex differences might be hormone related: testosterone, which is higher in men, naturally suppresses the immune system, whereas estrogen, which is higher in women, is known to amplify immune responses.
- Also, some genes that code for certain immune proteins are on the X chromosome, and since women have two X chromosomes, this might help increase immune activity.





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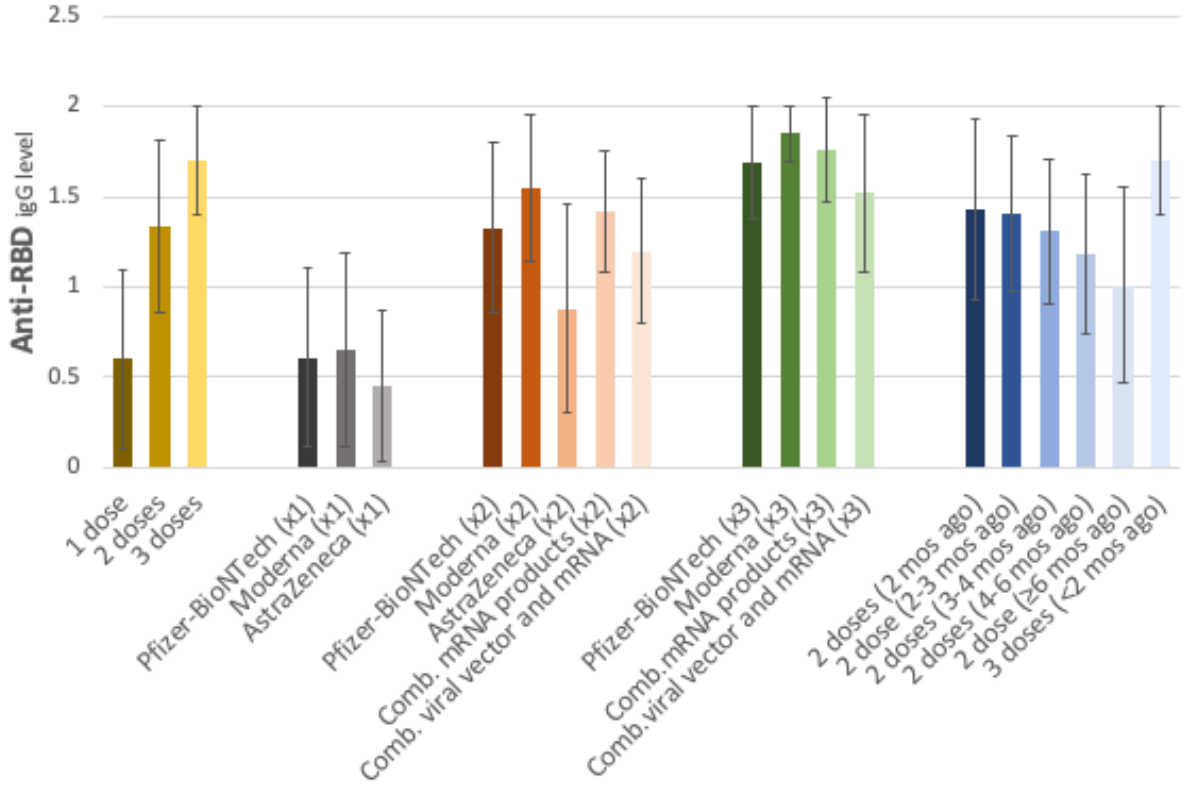
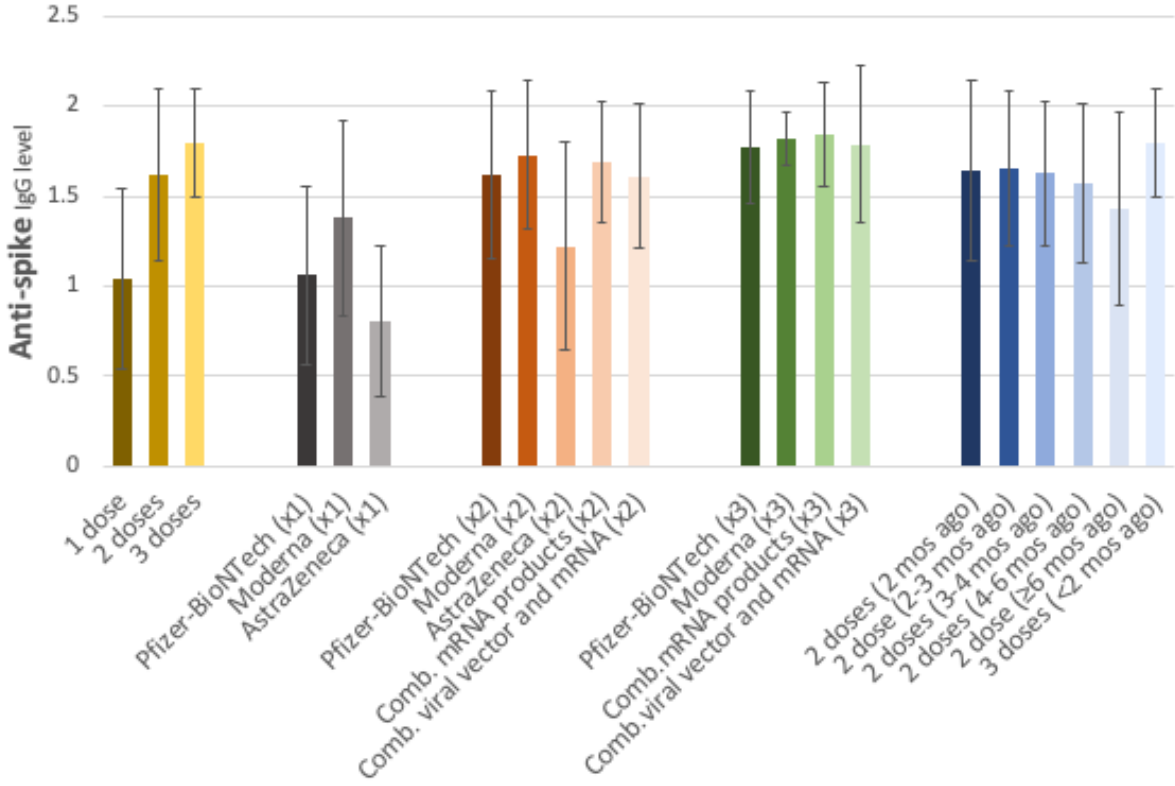
Variation in anti-RBD and anti-spike antibody levels: vaccine factors

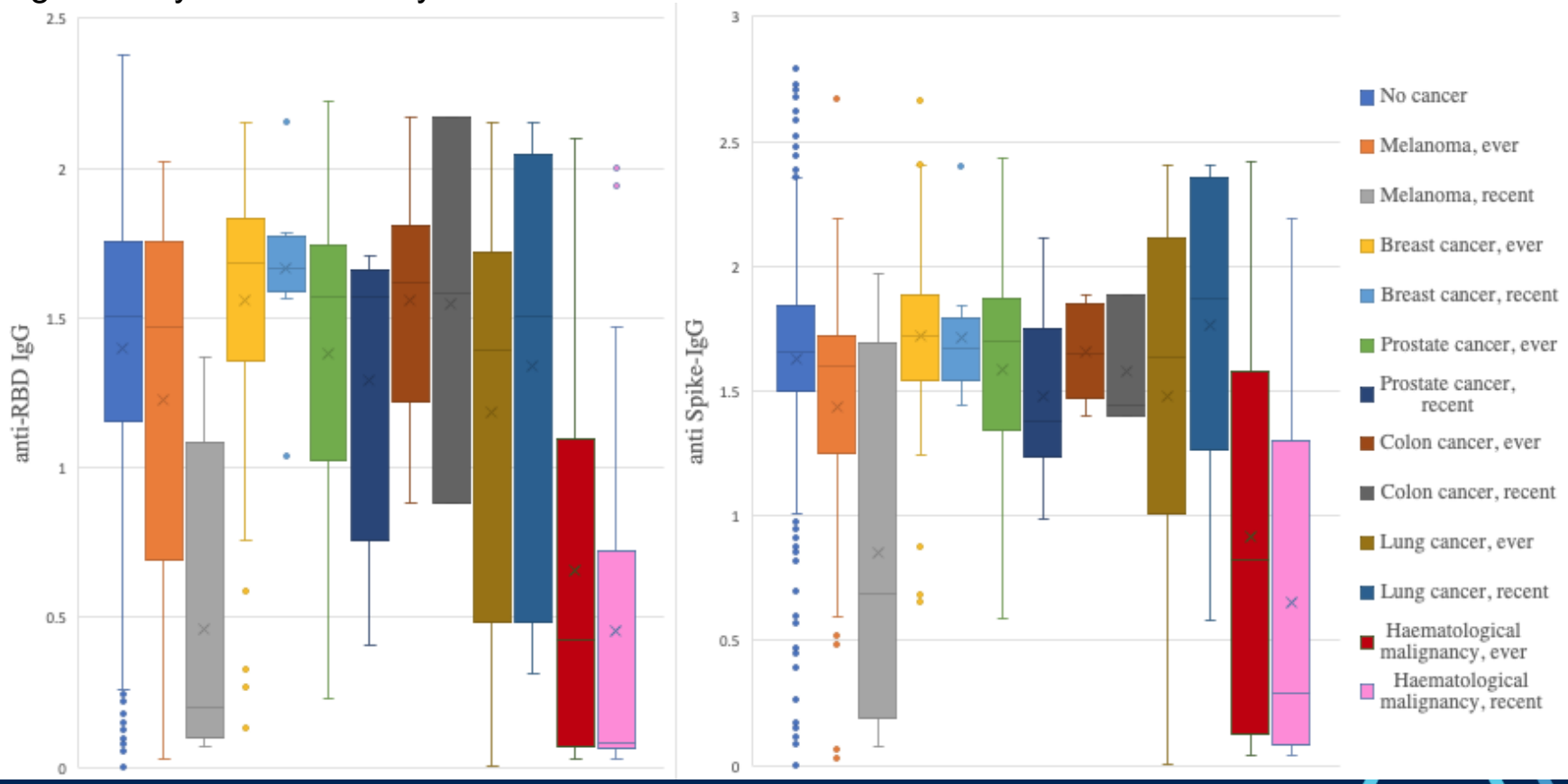
- Antibody levels increase with increasing number of vaccine doses received.
- The strongest antibody responses were elicited by full vaccination with Moderna, followed by a combination of mRNA vaccines.
- Dosing regimens that included the AstraZeneca vaccine induced a lower response, but the decrease was not significant among those who received three doses.
- Antibody levels decrease with increasing time since vaccination.





Variation in antibody levels by cancer status

- Seropositivity after full vaccination was particularly low among those with:
  - a haematological malignancy (50% if ever diagnosed; 29% if recently diagnosed)
  - melanoma (82% if ever diagnosed; 25% if recently diagnosed)
- In multivariable models of antibody levels after the second dose of a COVID-19 vaccine, those with haematological malignancies had statistically significantly lower antibody levels.



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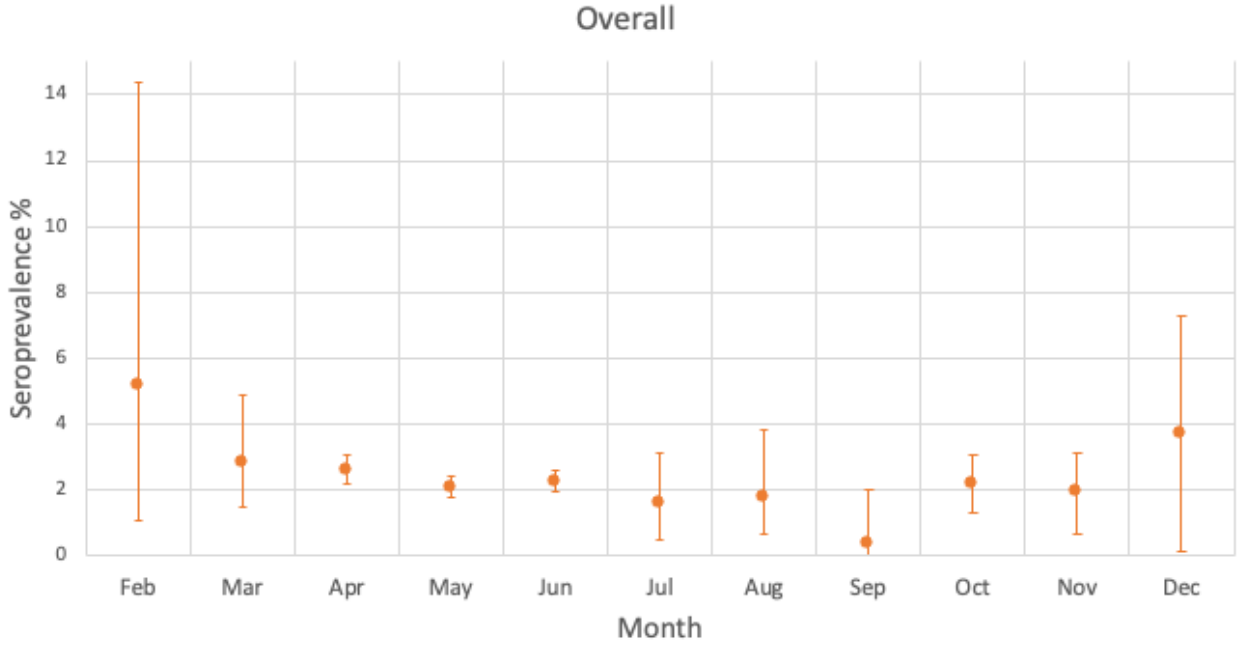
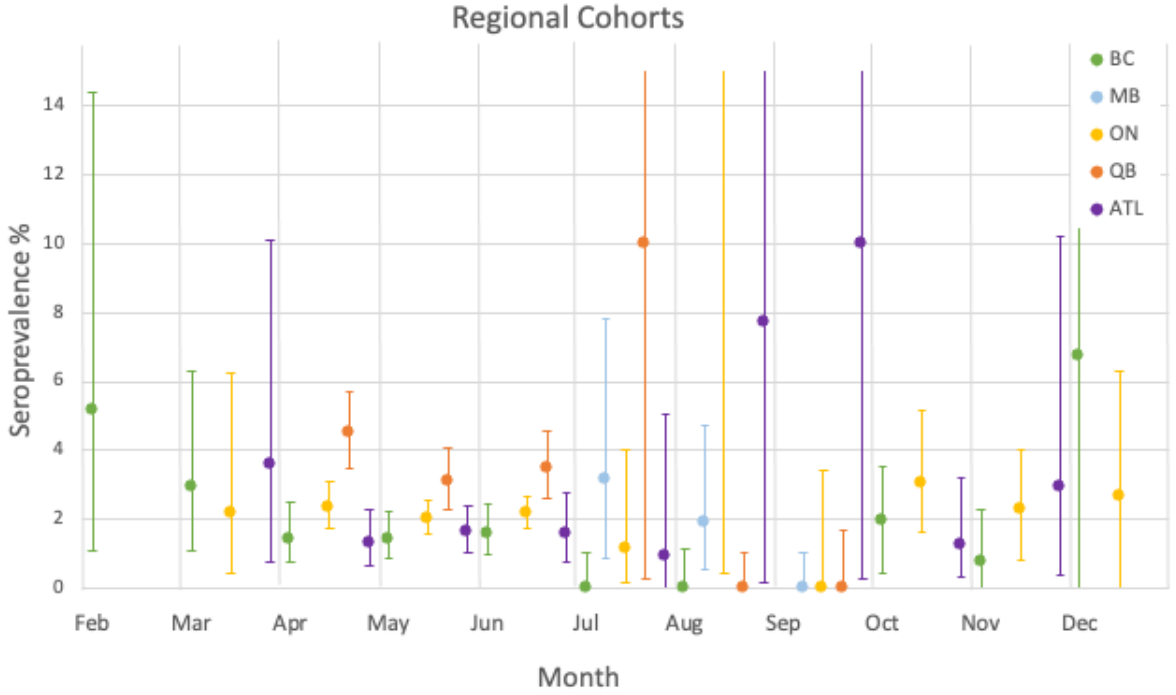
Infection-induced SARS-COV-2 seroprevalence, Feb 2021-Dec 2021

- Specimens were tested for antibodies against the nucleocapsid (N) antibodies to differentiate infection- and vaccination-induced seropositivity
  - The study-wide infection-induced seroprevalence varied from 0.4% to 5.2%, and overall was **2.4%** (95% CI, 2.2%-2.6%)
- We expect the 23-fold increased risk of infection with the Omicron variant to be reflected in upcoming seroprevalence estimates





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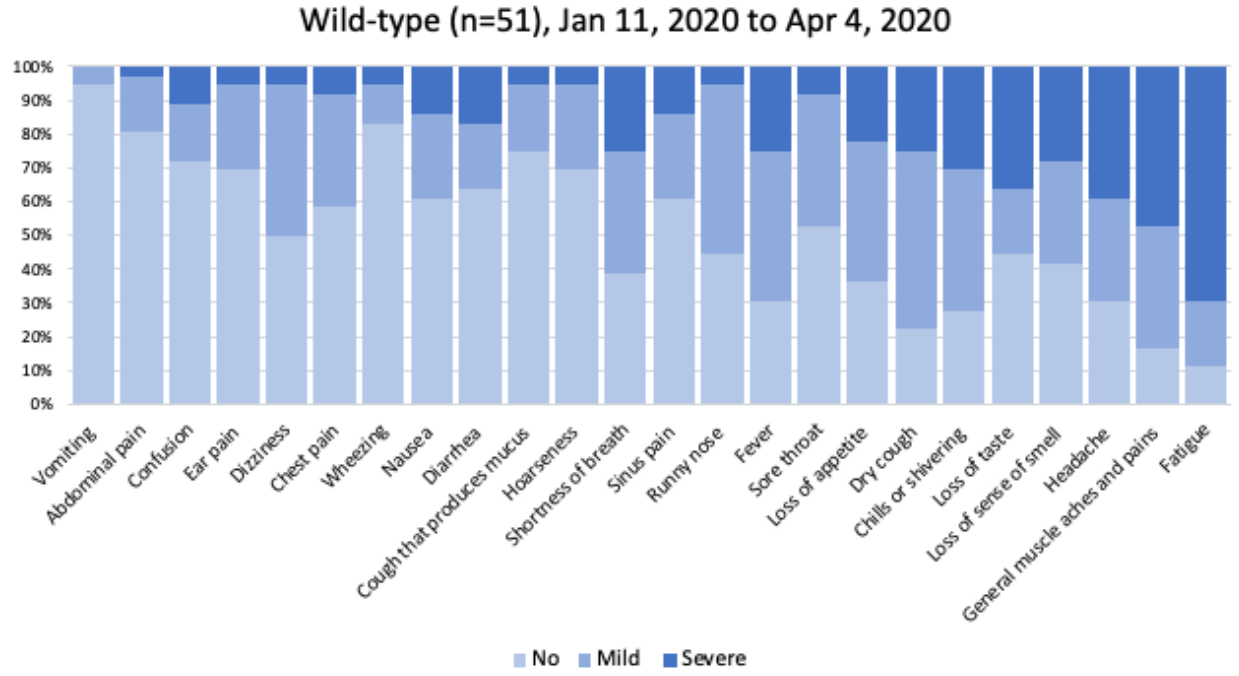
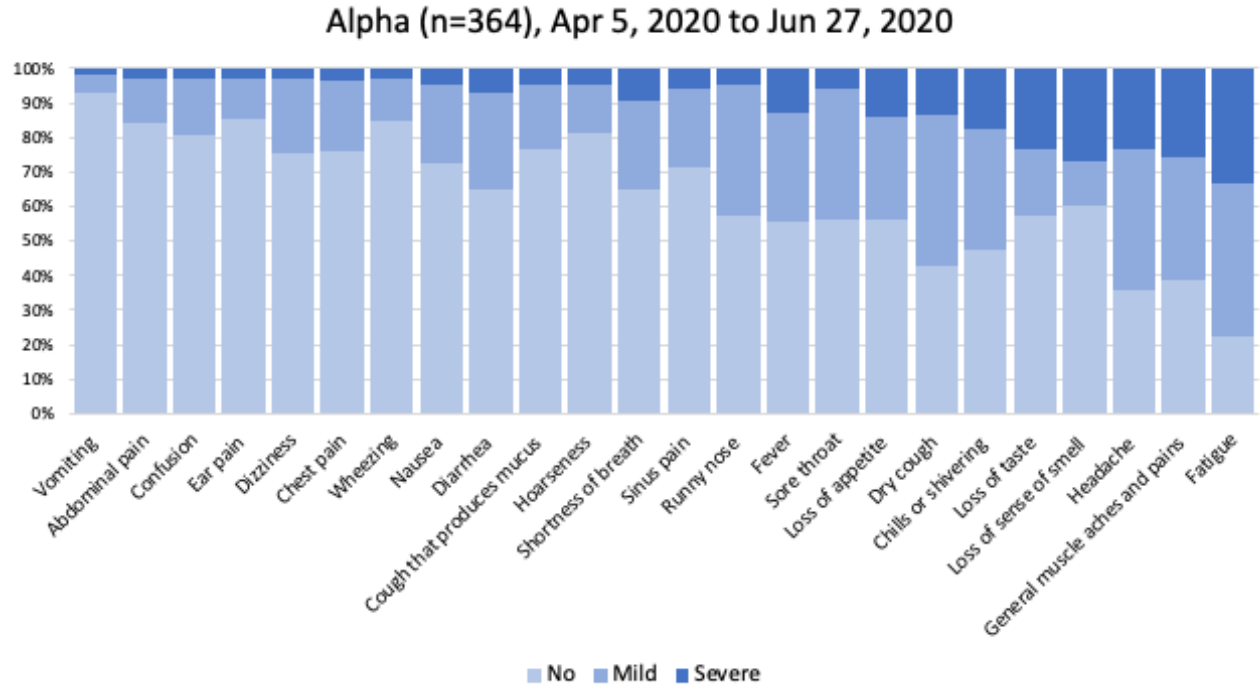
Symptoms by viral variant: Wild-type and Alpha

- 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





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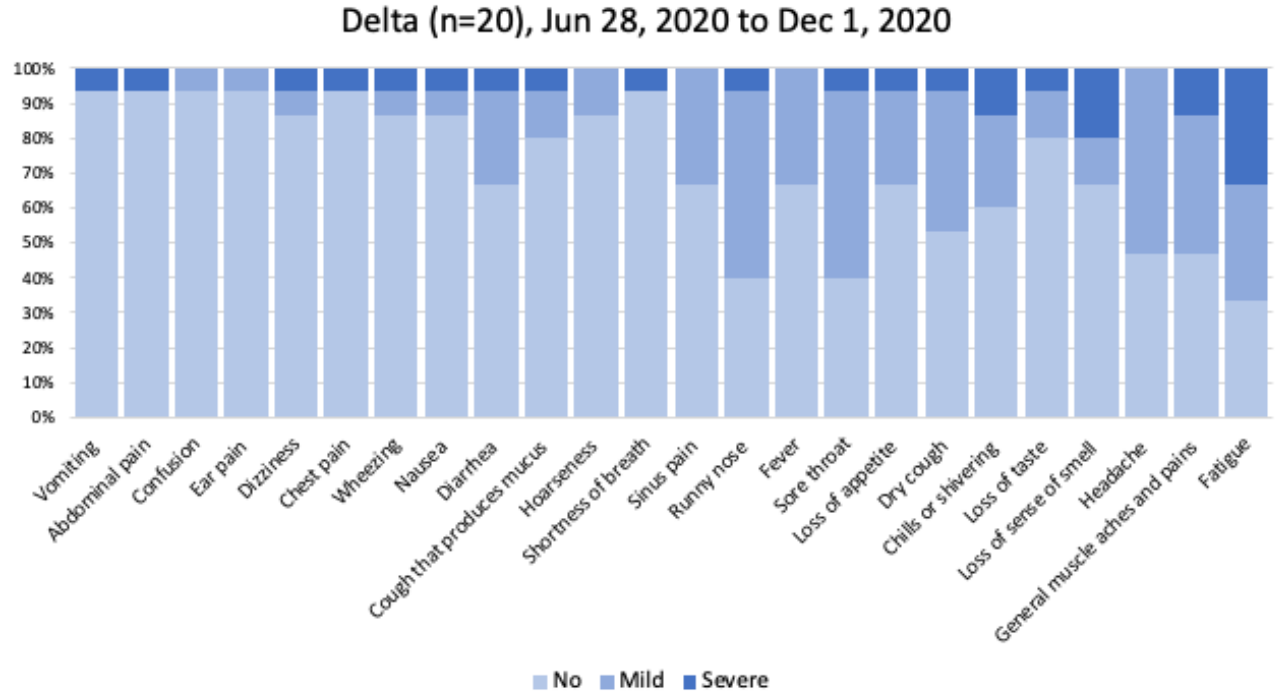
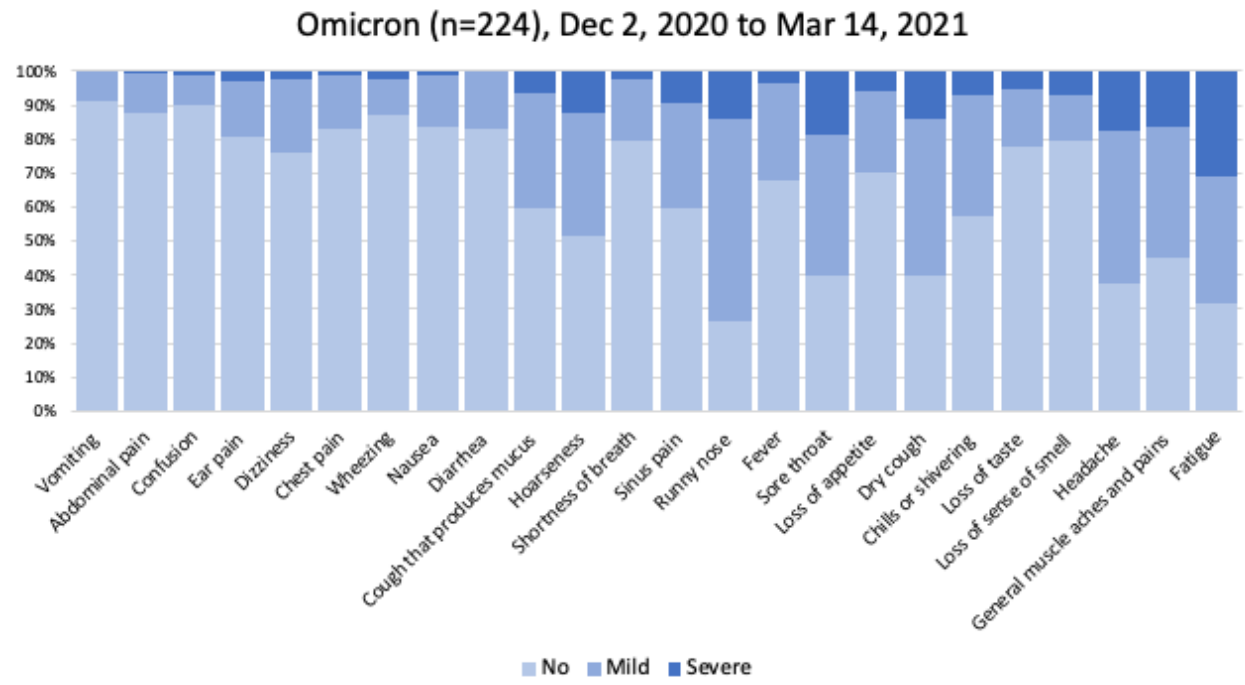
Symptoms by viral variant: Delta and Omicron

- 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





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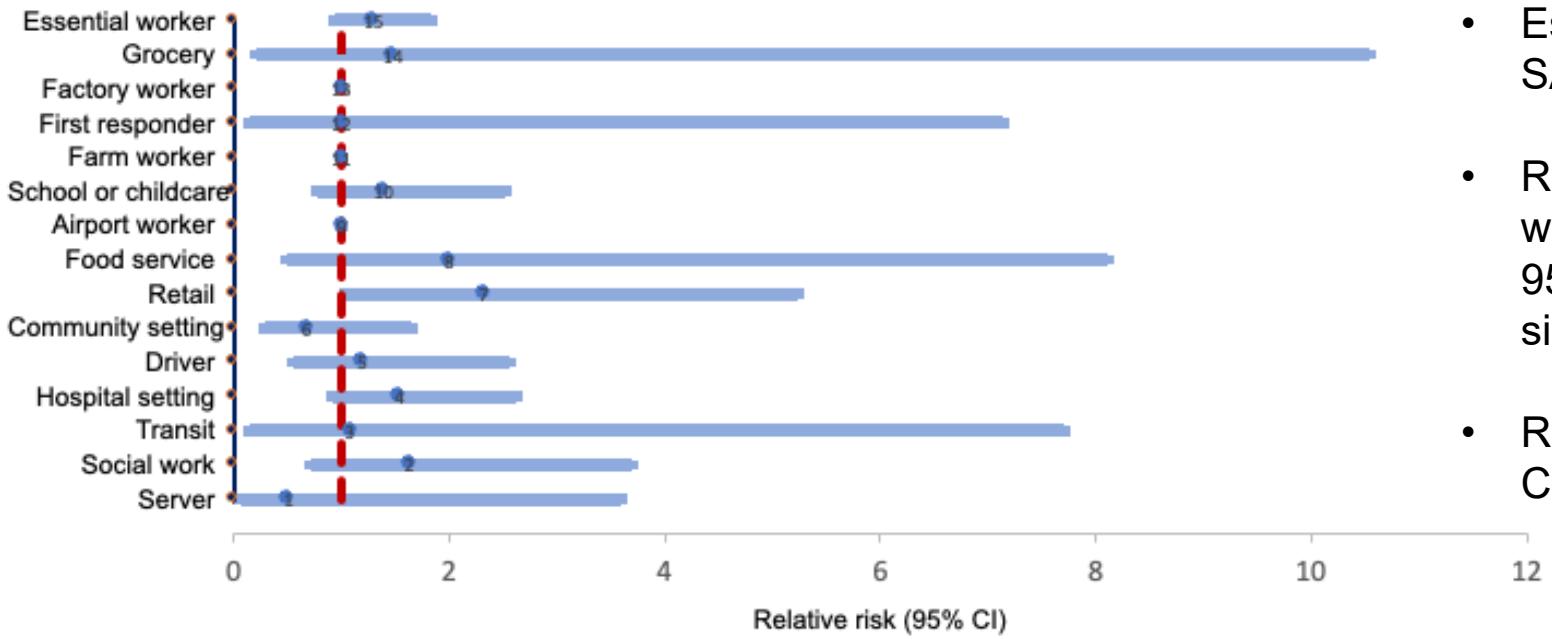
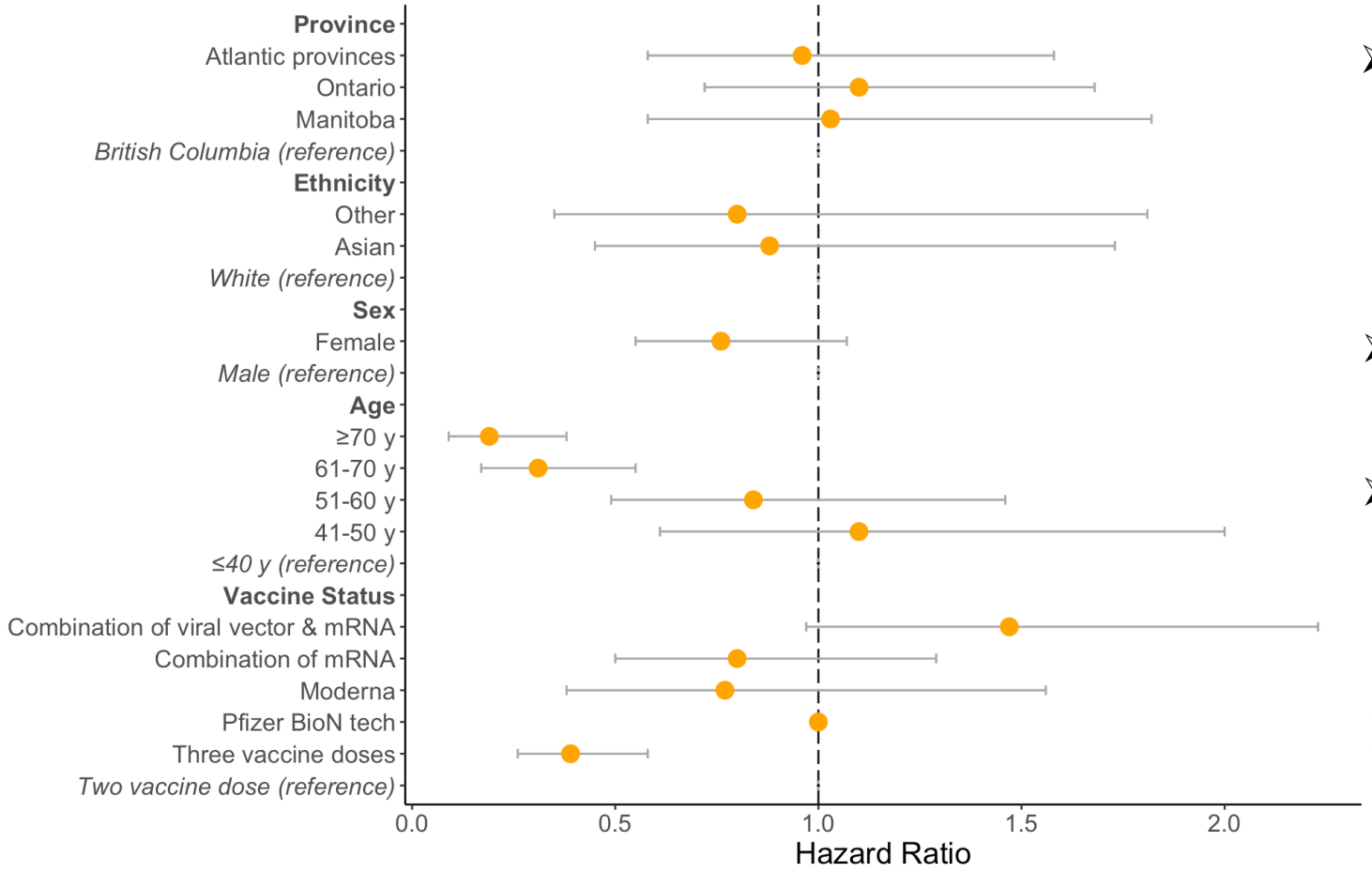
Risk of SARS-CoV-2 infection during the Omicron wave, by occupation



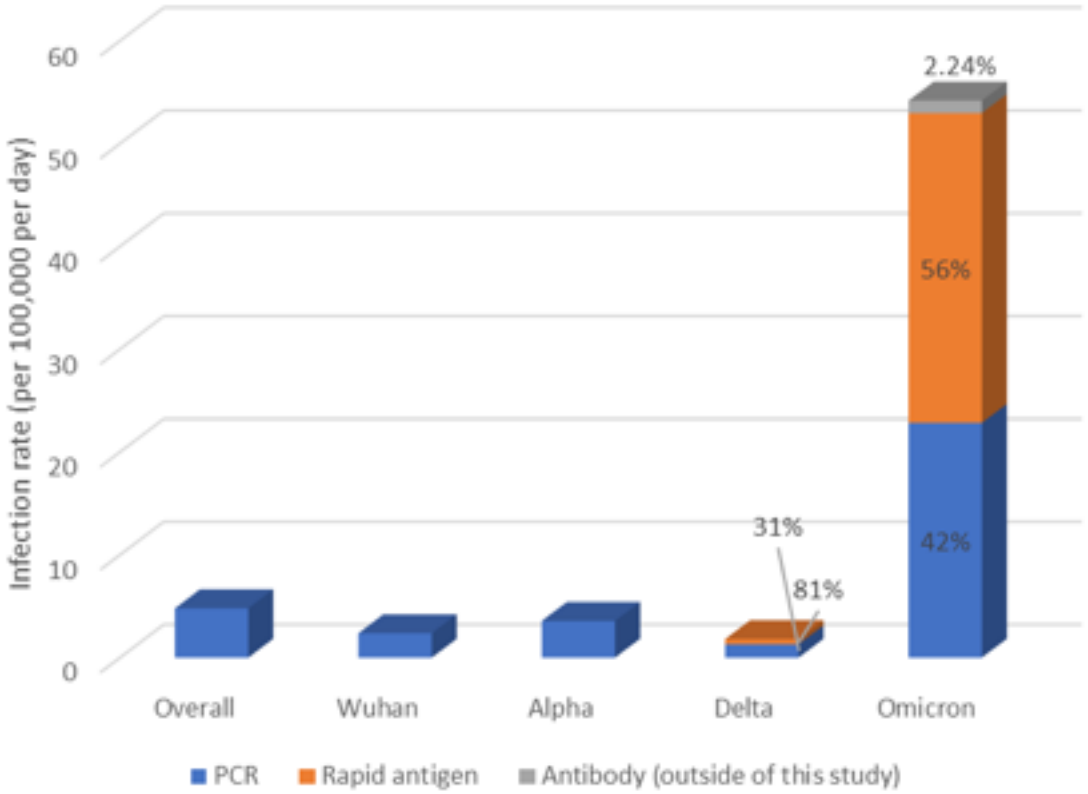
- Essential workers have a higher exposure to the SARS-CoV-2 virus due to the nature of their work.
- Relative to non-essential workers, essential workers had a higher risk of COVID-19 (RR=1.3, 95% CI 0.93 to 1.83), although not statistically significantly higher
- Retail workers specifically had a higher risk of COVID-19 (RR 2.23, 95% CI 1.03 to 5.23)

Risk of SARS-CoV-2 infection during the Omicron wave



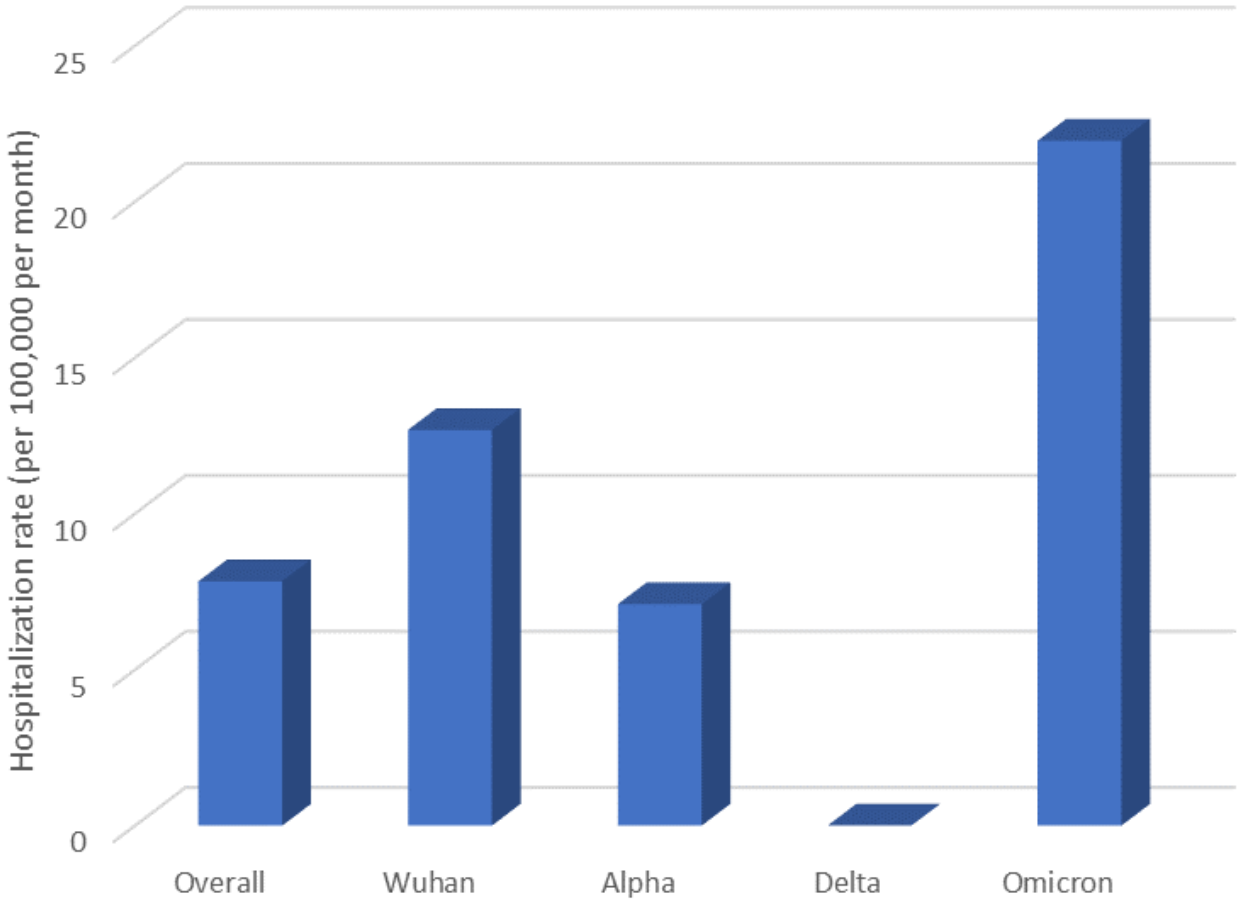
- Compared to those ≤40 y:
  - Those ≥70 y were 80% less likely to be infected (RR=0.20, 95% CI 0.09 to 0.38)
  - Those 61-70 y were 69% less likely to be infected (RR=0.31, 95% CI, 0.17 to 0.55)
- Vaccine effectiveness is the percentage reduction in the hazard ratio.
- Compared to those who received 2 vaccine doses:
  - 3 dose vaccine effectiveness = 61% (RR=0.39, 95% CI, 0.26 to 0.58)
- Future analyses: vaccine efficacy by time since third dose

Risk of infection caused by Omicron vs. other variants, including PCR, and rapid antigen test results



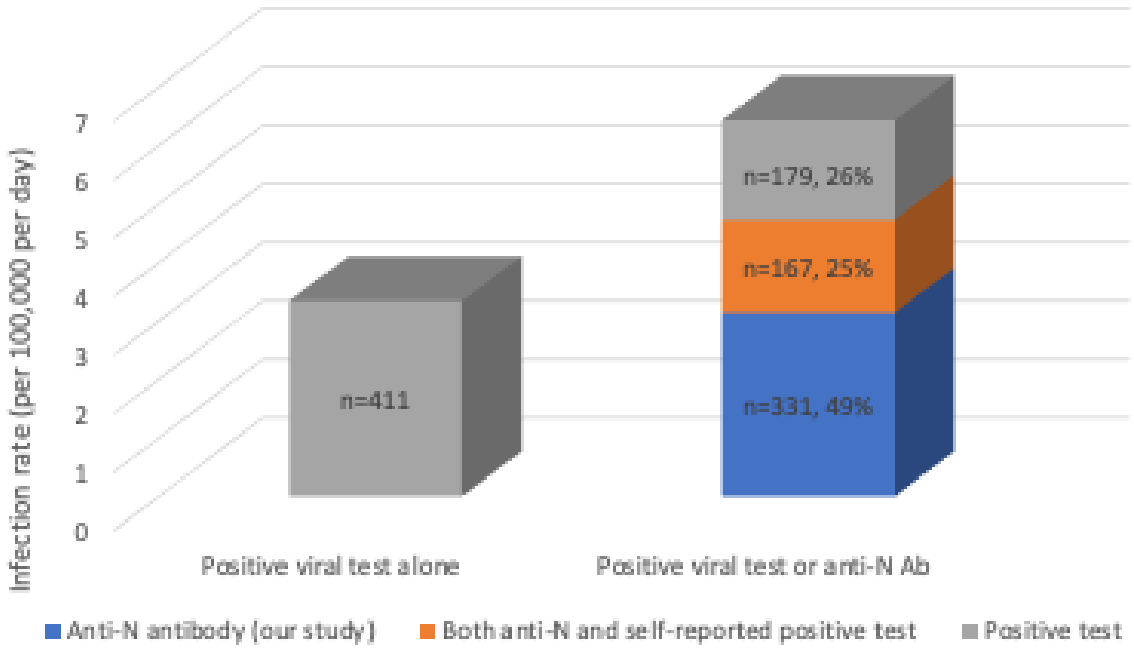
- Risk of infection caused by Omicron
  - **23 X higher** than risk caused by Wuhan strain
  - Incidence rate= 54/100,000 persons per day
- Source of positive test during Omicron period
  - 42% PCR
  - 56% rapid antigen
  - 2% antibody test (outside of this study)
- **Plus** those **positive for anti-nucleocapsid IgG** (to be determined through CanPath serology testing)

Risk of hospitalization caused by Omicron vs. other viral variants



- Absolute number of hospitalizations was low (n=36 total)
- Risk of hospitalization caused by Omicron
  - **1.7 X higher** than risk caused by Wuhan strain
  - Hospitalization rate= 22/100,000 persons **per month**
- Although the risk of hospitalization among those infected is lower during the Omicron period (RR=0.20 Omicron period vs. pre-Omicron period), due to increased transmissibility of Omicron, the absolute number of cases poses an increased risk of hospitalization

Risk of SARS-CoV-2 infection (Jan 2020 to Sep 2021), ascertained by a combination of self-reported test results and CanPath serology results



- When serology results are incorporated, risk of infection is
  - **2 X higher** than rates ascertained through positive Covid-19 test results alone
- Source of positive test during pre-Omicron period
  - 26% PCR
  - 25% both PCR and anti-N IgG positive
  - 49% anti-N IgG positive
- Among the 49% detected through antibody testing alone, only 12% suspected they had an undiagnosed infection
- 12% of those with a positive test reported having no symptoms
- **49% of infections are asymptomatic**

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Conclusions

- Our findings:

- emphasized critical age-dependent immune responses following vaccination, with weaker immune responses in older individuals
- influenced changing guidelines on following the AstraZeneca vaccine by a second dose of an mRNA vaccine
- showed that stronger antibody responses were elicited by full vaccination with an mRNA vaccine compared to AstraZeneca
- showed that antibody levels decrease with increasing time since second vaccine dose and booster shots increase antibody levels
- confirmed that individuals with previous SARS-CoV-2 infection elicited stronger antibody responses, and
- showed that individuals with hematological malignancies had weaker vaccine-induced immune responses

- showed that the risk of infection with Omicron is 23 X higher than the Wild type
- 56% of current SARS-CoV-2 infections are diagnosed using rapid antigen tests
- ~ 49% of infections are asymptomatic
- 3 vaccine doses reduce the risk of infection with Omicron by 61%

Future Directions

- Identify correlates of protection
  - Correlate antibody levels with vaccine efficacy
  - Moving target requiring a constantly evolving understanding
- Identify factors that influence the rate of antibody decline
- Quantify vaccine effectiveness by time since third vaccine dose

Accessing CanPath Data

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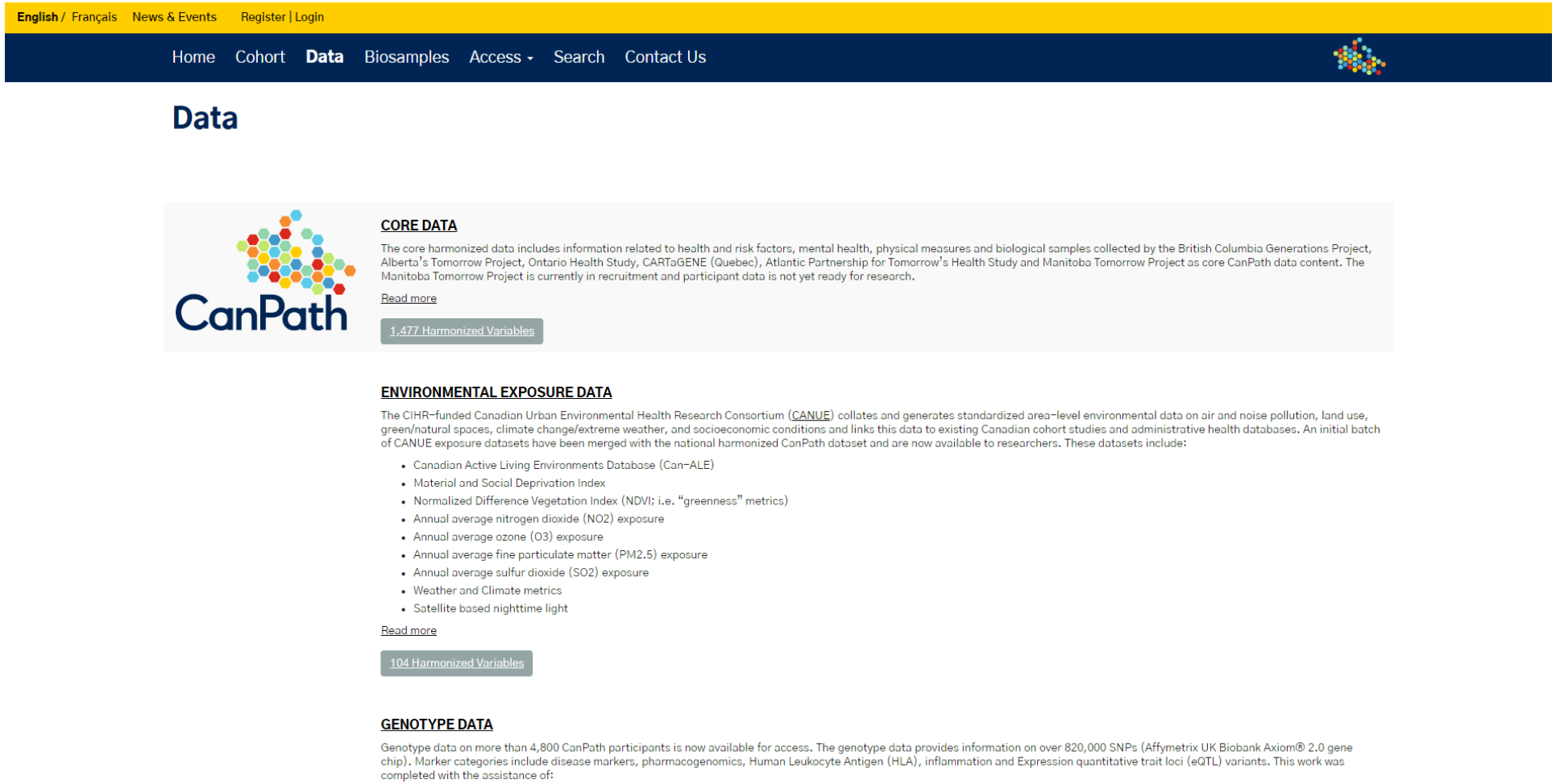

Accessing CanPath Data

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CanPath Data and Biosamples Access Application Form

This Access Application Form is to be used by all researchers seeking access to Research Data and/or Biosamples, referred to as Material in the Data and Material Sharing Agreement. Please refer to the CanPath Access Policy for the meaning of all capitalized terms used in this form, which is available on the CanPath portal.

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

Institution

Institutional Mailing Address

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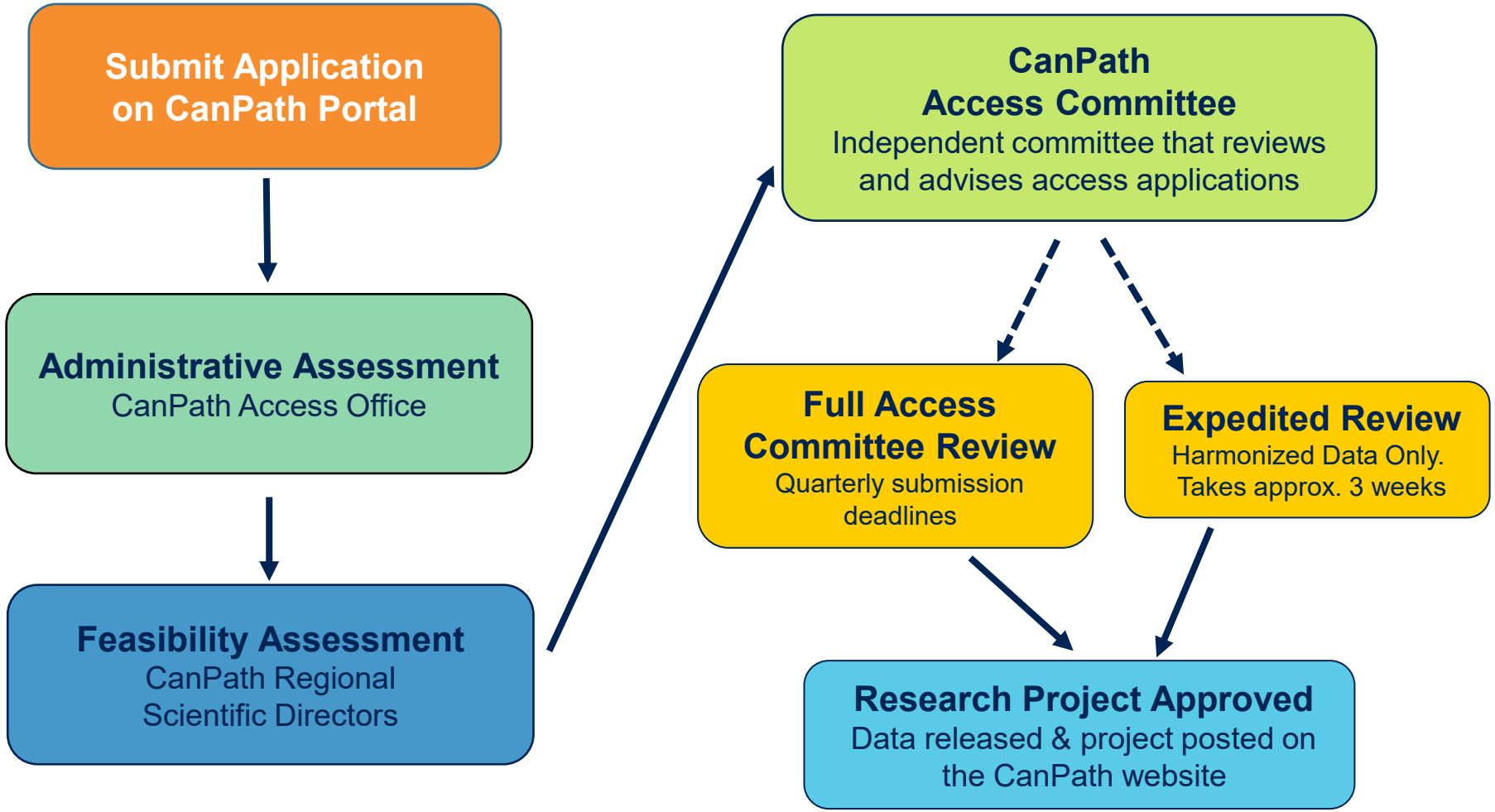
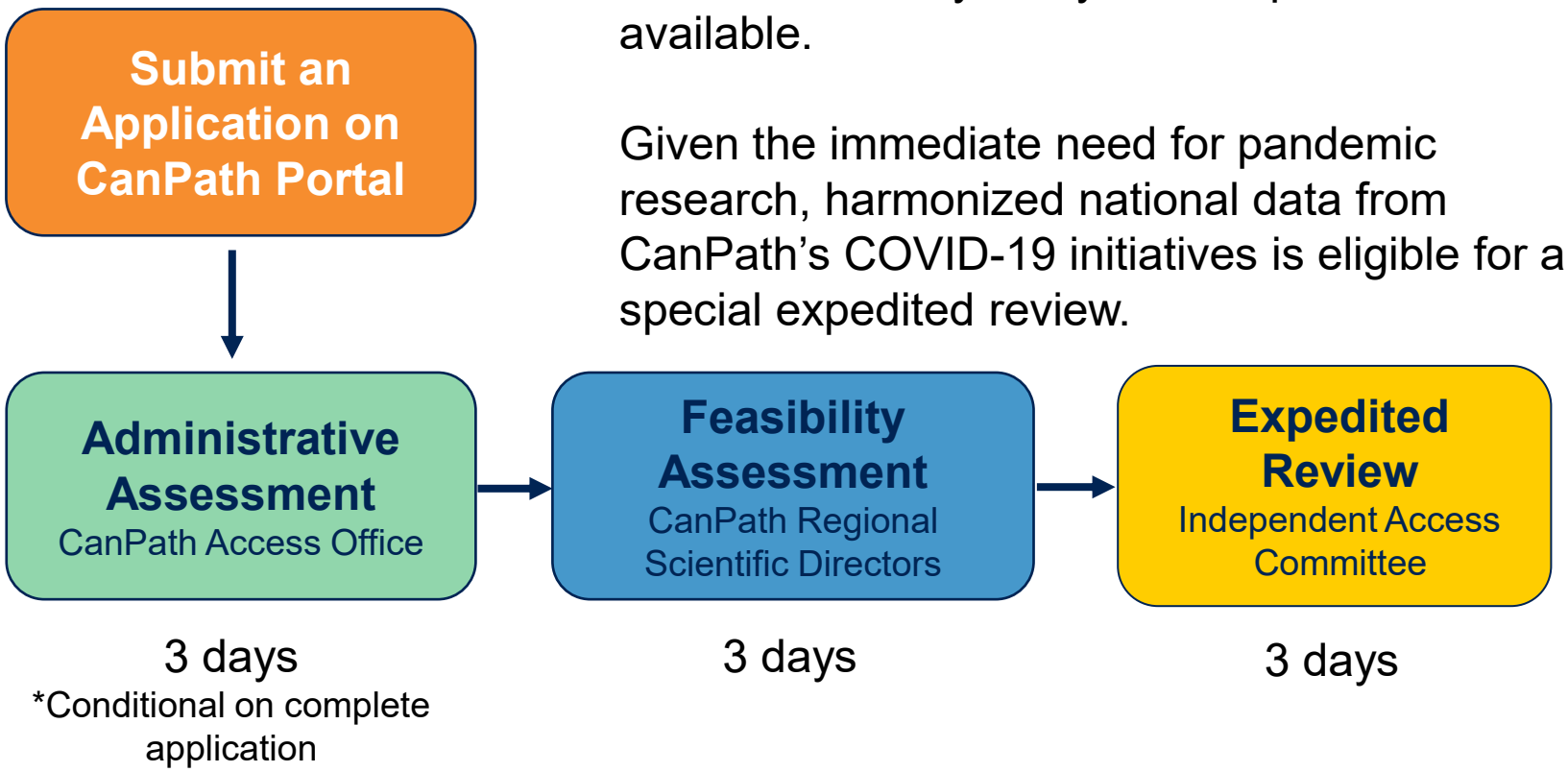
Access Process Overview



Expedited COVID-19 Data Access Process



Data from the first COVID-19 Questionnaire and from the antibody study, 1st timepoint are now available.

Given the immediate need for pandemic research, harmonized national data from CanPath's COVID-19 initiatives is eligible for a special expedited review.

National Coordinating Centre

Based at the Dalla Lana School of Public Health, University of Toronto

CanPath

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Thank you to CanPath participants across the regional cohorts who generously donate their time, information and biological samples.
CanPath is a success because of the participants' ongoing commitment.

Thank you to CanPath's sponsors and hosts!

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