COVID-19 IMMUNITY TASK FORCE | GROUPE DE TRAVAIL SUR L'IMMUNITÉ FACE À LA COVID-19

Seminar Series | Research Results & Implications

People at higher risk due to other health conditions & COVID-19

November 24, 2022 | 11:30 a.m. to 1 p.m. EDT

Moderator

Catherine Hankins, MD, PhD, FRCPC, CM

Co-Chair, COVID-19 Immunity Task Force

Professor and Interim Chair, Department of Global and Public Health at McGill's School of Population and Global Health

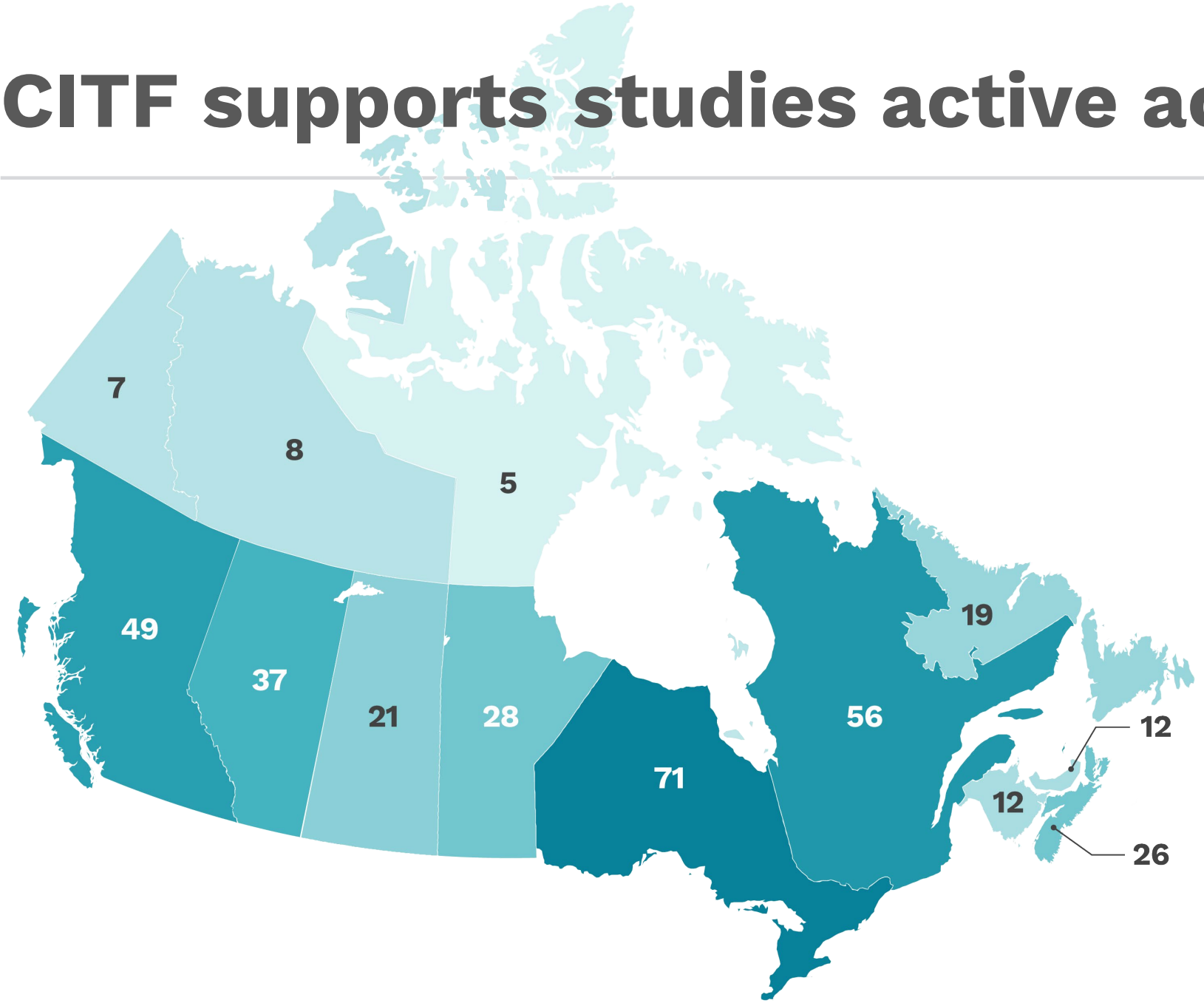
COVID-19 Immunity Task Force mandate

Established by the Government of Canada in April 2020

Mandate:

Catalyze, support, fund, and harmonize knowledge on SARS-CoV-2 immunity for federal, provincial, and territorial decision-makers to inform their efforts to protect Canadians and minimize the impact of the COVID-19 pandemic.

CITF supports studies active across Canada



119 studies

9 of which focus on people at higher risk of severe COVID-19 due to other health conditions

Speakers

(SOTR) **Deepali Kumar** MD, MSc, FRCPC, FAST, Professor of Medicine, University of Toronto; Transplant Infectious Diseases Consultant, University Health Network; Director of Transplant Infectious Diseases, University Health Network

(IMID) **Vinod Chandran**, MBBS, MD, DM, PhD, FRCPC, Associate Professor, University of Toronto; Staff Rheumatologist, University Health Network and Sinai Health

(IBD) **Gilaad Kaplan**, MD, MPH, FRCPC, CAGF, AGAF, FCAHS, Killam Laureate, Professor of Medicine, Division of Gastroenterology and Hepatology, Cumming School of Medicine, University of Calgary

(CKD) **Sara Wing**, MDCM, FRCPC, Clinical Associate, Division of Nephrology, St Michael's Hospital, Toronto

Speakers

(HIV) **Ann N. Burchell**, PhD, Scientist, MAP Centre for Urban Health Solutions, St. Michael's Hospital, Unity Health Toronto; Associate Professor, Department of Family and Community Medicine, University of Toronto

(HIV) **Cecilia T. Costiniuk**, MD, MSc, FRCPC, Associate Professor, Faculty of Medicine and Health Sciences, McGill University; Department of Medicine, Division of Infectious Diseases, McGill University Health Centre; Scientist, Research Institute, MUHC

Joining for Q&A

(IMID) **Sasha Bernatsky**, MD, PhD, Professor of Medicine, McGill University; Senior Clinical Investigator, Research Institute of the McGill University Health Centre

(CKD) **Matthew Oliver**, MD, MHS, FRCPC, Associate Professor, University of Toronto; Staff Nephrologist & Division Head of Nephrology, Sunnybrook Health Sciences Centre; Regional Medical Lead – Toronto Central – Ontario Renal Network, Ontario Health

Land Acknowledgement

on behalf of Drs. Hankins, Costeniuk and Bernatsky

We are speaking to you from our place of work at McGill University, which is on land which has long served as a site of meeting and exchange amongst Indigenous Peoples, including the Haudenosaunee and Anishinabeg nations. We would like to acknowledge and thank the diverse Indigenous Peoples whose presence marks this territory on which peoples of the world now gather.

Land Acknowledgement

on behalf of Drs. Kumar, Chandran, Wing, Burchell and Oliver

We appreciate the opportunity to present from Toronto which is on the traditional territory of many nations including the Mississaugas of the Credit, the Anishnabeg, the Chippewa, the Haudenosaunee and the Wendat peoples and is now home to many diverse First Nations, Inuit and Métis peoples.

Why understanding the impact of COVID-19 is important in these disease conditions?

Health condition	Total number of people affected in Canada	Impact of COVID-19
SOLID organ transplant Recipients (SOTR)	40 000 people are living with a transplant	4% higher hospitalization rate (vs. healthy people)
Immune-mediated inflammatory Diseases (Overall) – this includes people with Rheumatoid arthritis, Ankylosis spondylitis, Psoriasis, and psoriatic arthritis, Inflammatory Bowel Disease (IBD)	Over 7 million Canadians	8.27 COVID-19 related deaths per 1000 person-years (vs. 4.88 in the general population) 14.31 COVID-19-related hospital admissions per 1000 person-years (vs. 8.77 in the general population)
Chronic Kidney Disease (CKD)	Between 1.3 and 2.9 million Canadians	Study found 44.6% mortality rate in CKD patients with COVID-19 (vs. 4.7% in CKD patients without COVID-19) 63% higher risk of hospitalization in CKD patients with SARS-CoV-2 infection (vs. healthy people)
People living with HIV	Over 62,000 people	24% higher risk of infection and 78% higher risk of death when compared to people without HIV

Primary series and boosters in **solid organ transplant recipients**

Ontario, Canada

Deepali Kumar, MD, MSc, FRCPC

Professor Of Medicine, University Of Toronto

Director, Transplant Infectious Diseases, Ajmera Transplant Centre

UHN Ajmera Transplant Centre

Disclaimer

I would like to acknowledge that I have received clinical trials grants from Roche and GSK. I also receive honoraria from Roche, GSK, Astellas, Merck, and Exevir. I will be discussing off-label use of vaccines.

Rationale for further study of COVID-19 vaccine in immunocompromised (two doses is not enough)

- Many patients with no antibody or T-cell response after 2 doses
- Patients had more breakthrough infections with severe disease (pre-Omicron) than the general population
- Potential evolution of variants in immunocompromised
- Immunocompromised patients need higher doses or additional doses (e.g. influenza vaccine)
- Patient demand

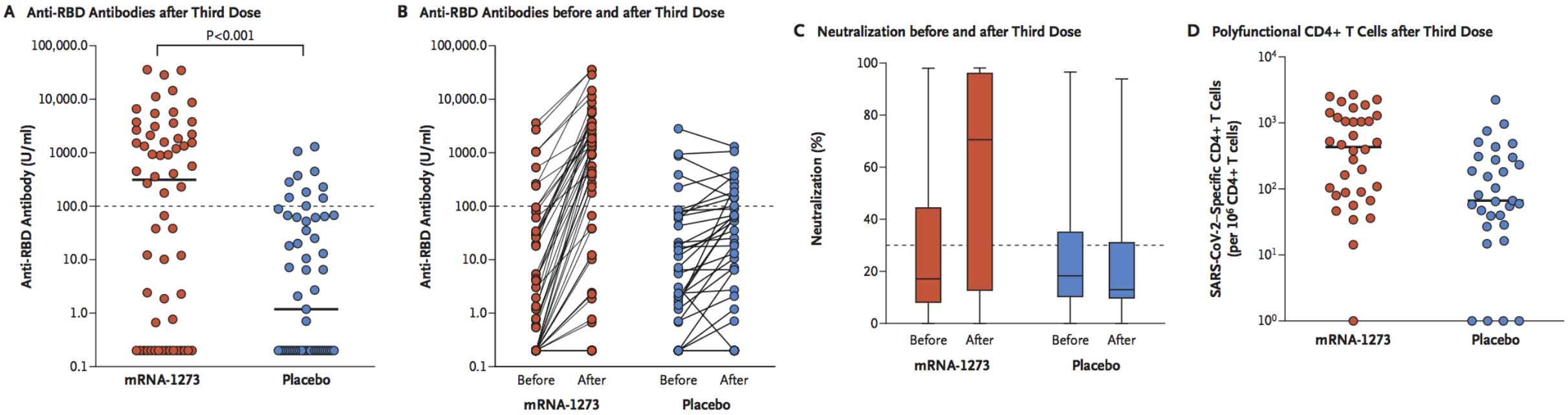
Transplant patients who received two doses Moderna (mRNA-1273)

3rd dose Moderna (n=60)

3rd dose placebo (n=60)

Randomized; Double-blinded; Doses at 0, 1 and 3 months

3rd vaccine dose increases antibody and T-cell responses in transplant patients



Hall & Ferreira et al., **Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients**. *New England Journal of Medicine*, 2021

FDA NEWS RELEASE

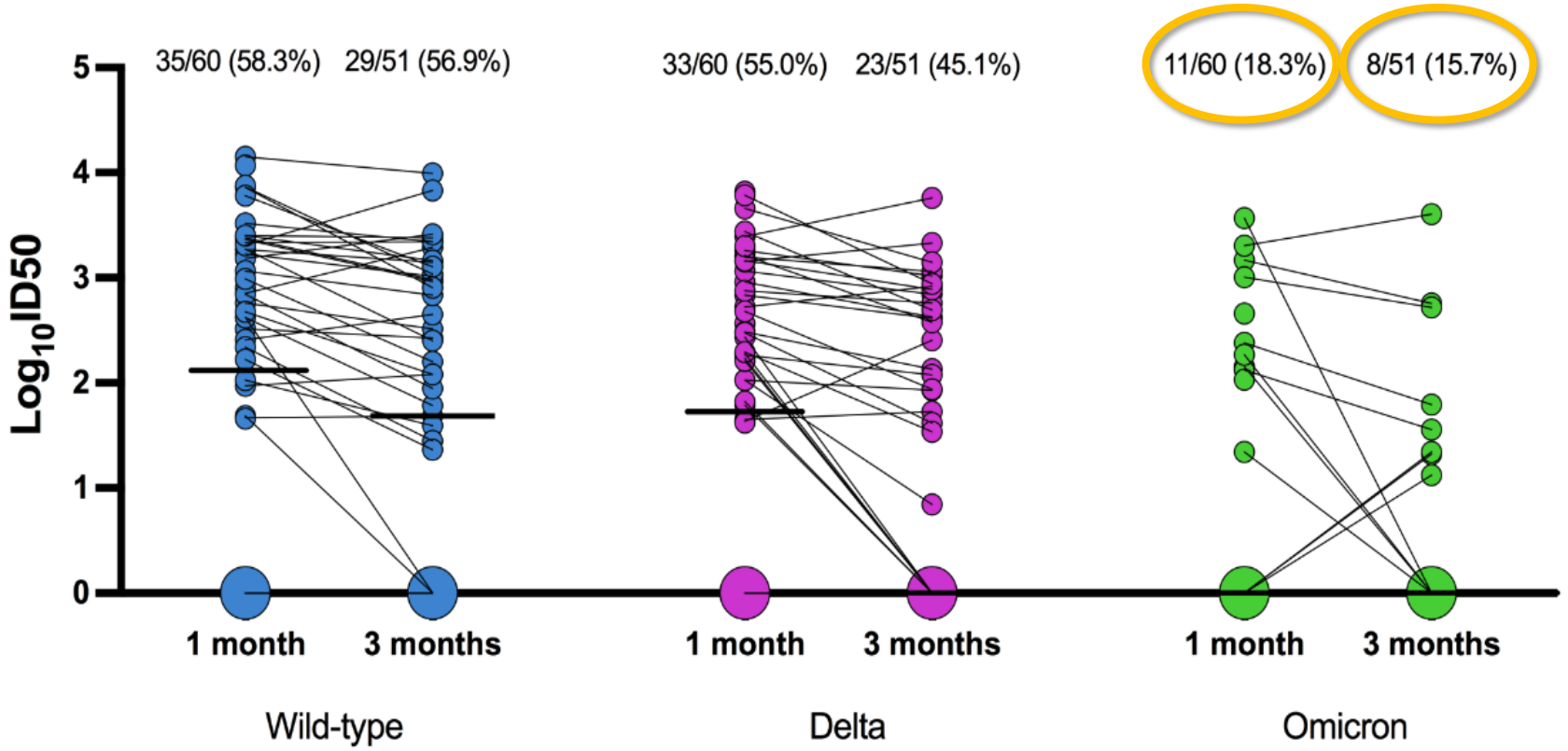
Coronavirus (COVID-19) Update: FDA Authorizes Additional Vaccine Dose for Certain Immunocompromised Individuals

Other fully vaccinated individuals do not need an additional vaccine dose right now

For Immediate Release: August 12, 2021


OMICRON

1 and 3 months after the 3rd vaccine, there was reduced neutralization against Omicron BA.1

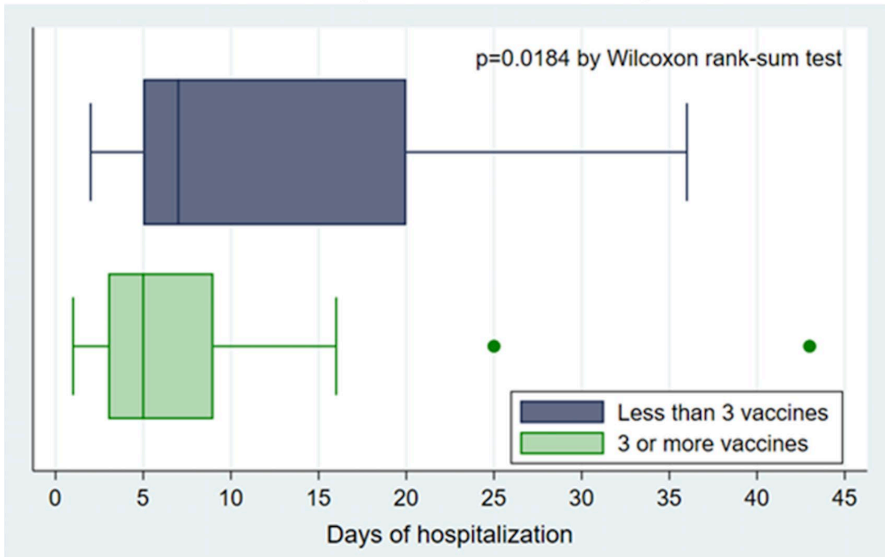


15-200 fold reduction in neutralizing activity against Omicron compared to original virus

Kumar et al., *AM J Transplant*, 2022

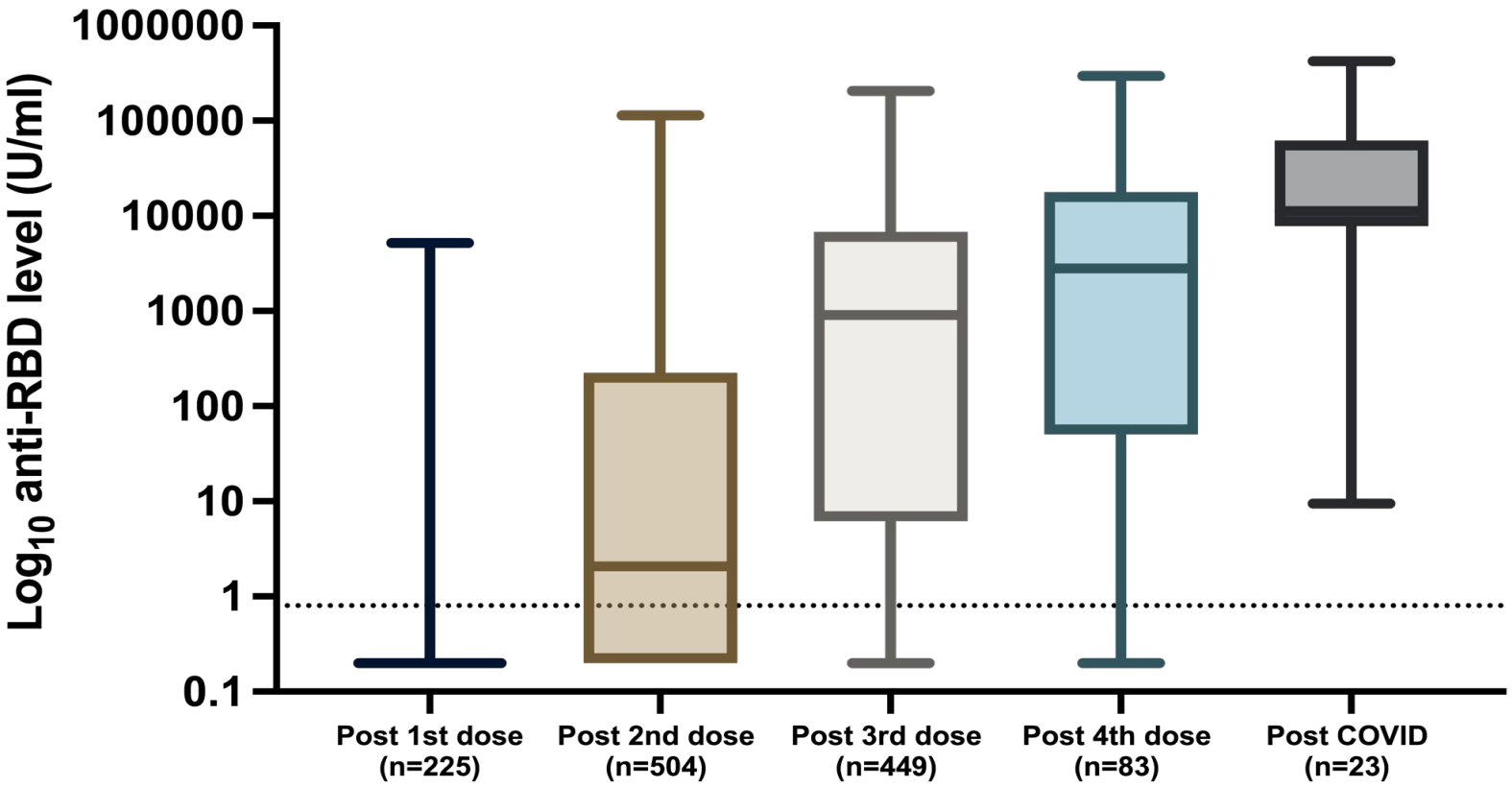
3 doses protect against severe Omicron BA.1 & reduce hospital stays

By vaccination status					
End points	≥3 vaccines (n=190)	<3 vaccines (n=103)	Risk ratio (95% CI)	Risk diff. (95% CI) ‡	Adjusted p value †
Primary end point					
Oxygen requirement by day 30 n (%)	15 (7.9%)	27 (26.2%)	0.30 (0.17 to 0.54)	-18.3 (-28 to -9.4)	<0.001
Secondary end points					
COVID-19-related hospitalization >24h n (%)	31 (16.3%)	38 (36.9%)	0.44 (0.29 to 0.67)	-20.5 (-31.2 to -10.1)	<0.001



Solera et al., *Clin Infect Dis*, 2022

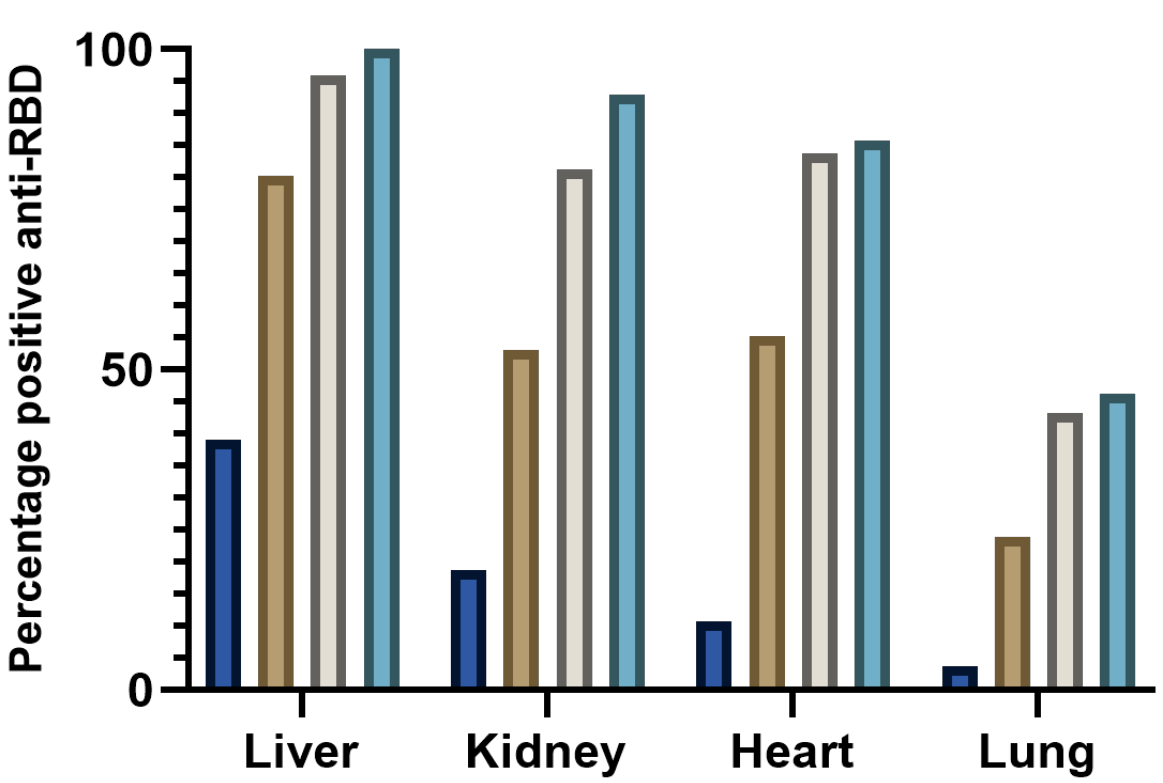
Fourth (booster) dose increases antibody levels



Data from a pan-Canadian cohort of >500 organ transplant recipients

Kabbani et al., submitted

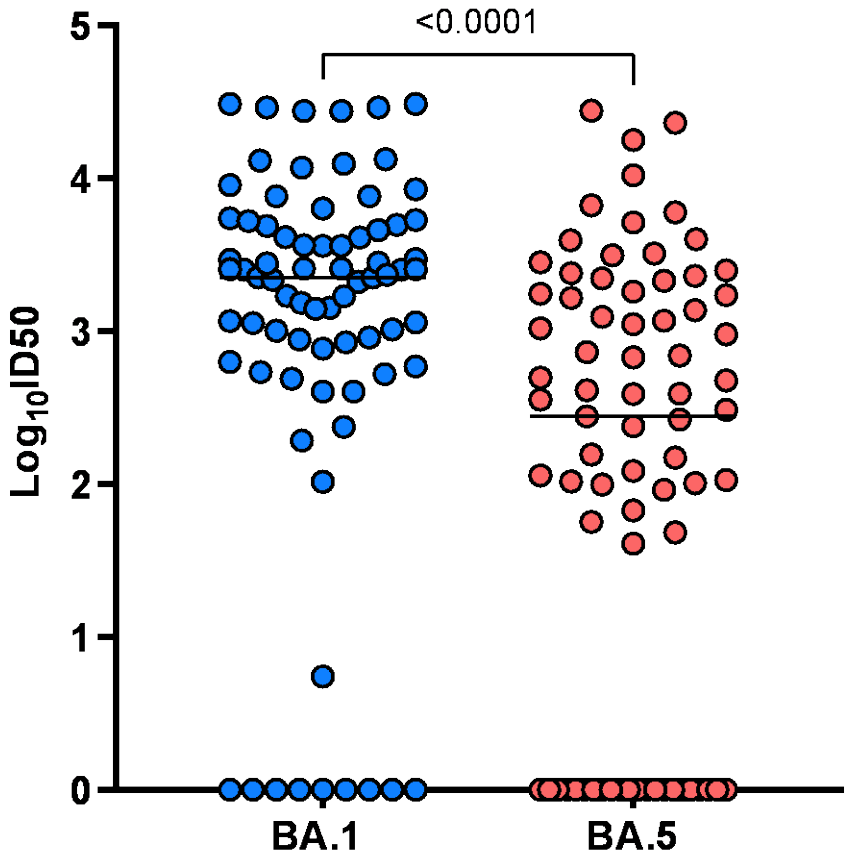
Liver transplant recipients have the best antibody responses followed by kidney, heart, lung



Lung transplant recipients may have fared worse because they are the **most immunosuppressed** of the groups

Kabbani et al., submitted

Hybrid immunity (vaccination + infection) offers cross-protection



N=75 transplant patients infected with BA.1 after 2 or 3 doses of vaccine

- **90%** develop BA.1 neutralizing antibody
- **69%** develop BA.5 cross-protection

Ferreira et al., *AJT*, 2022

Take-home messages

- Three doses of mRNA vaccine should be considered the primary series in transplant recipients
- Having at least three doses prevents severe COVID-19
- Booster doses are important since protection wanes over time
- Ensuring vaccination of caregivers, friends, family

UHN Ajmera Transplant Centre

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COVID-19 IMMUNITY TASK FORCE | GROUPE DE TRAVAIL SUR L'IMMUNITÉ FACE À LA COVID-19

Immunity to SARS-CoV-2 mRNA vaccines in patients with **immune mediated inflammatory diseases (IMIDs)**

Toronto, Ontario

Vinod Chandran MBBS, MD, DM, PhD, FRCPC

Scientist, Schroeder Arthritis Institute & Krembil Research Institute, University Health Network

Associate Professor, Department of Medicine & Department of Laboratory Medicine and Pathobiology, University of Toronto

UHN Schroeder Arthritis Institute

TEMERTY FACULTY OF MEDICINE UNIVERSITY OF TORONTO

Disclaimer

I wish to acknowledge that I sit on the following advisory boards/get honoraria from: Abbvie, Amgen, BMS, Eli Lilly, Janssen, Novartis, Pfizer, UCB. I receive salary support from the Pfizer Chair Rheumatology Research Award at the University of Toronto. I also acknowledge that my spouse is employed by AstraZeneca.

IMPACT study:

Immune response after COVID-19 vaccination during maintenance therapy in immune-mediated inflammatory diseases (IMID)

150 participants:

- Adults (>18) with inflammatory bowel disease, rheumatoid arthritis, ankylosing spondylitis, or psoriatic disease and healthy subjects
- With or without maintenance immunosuppressive therapies (IMID patients)
- Having been vaccinated with Pfizer-BioNTech and/or Moderna SARS-CoV-2 vaccines

Exclusions:

- Prior COVID-19 infection, steroids, other vaccines

We recruited:

- 26 healthy controls
- 9 patients not requiring immunomodulatory treatment for their IMID
- 44 on antiTNF agents
- 16 on antiTNF with azathioprine or methotrexate (AZA/MTX)
- 10 on anti-IL23
- 28 on anti-12/23
- 9 on Anti-IL17
- 8 on AZA/MTX

There were 80 patients with IBD, 18 with psoriasis, 22 with psoriatic arthritis, 12 with ankylosing spondylitis, and 4 with rheumatoid arthritis.

Antibody responses increased from T1 to T2 to T3, then decreased by T4; Lower antibody responses in people with IMID on anti-TNF treatment

Dose 1

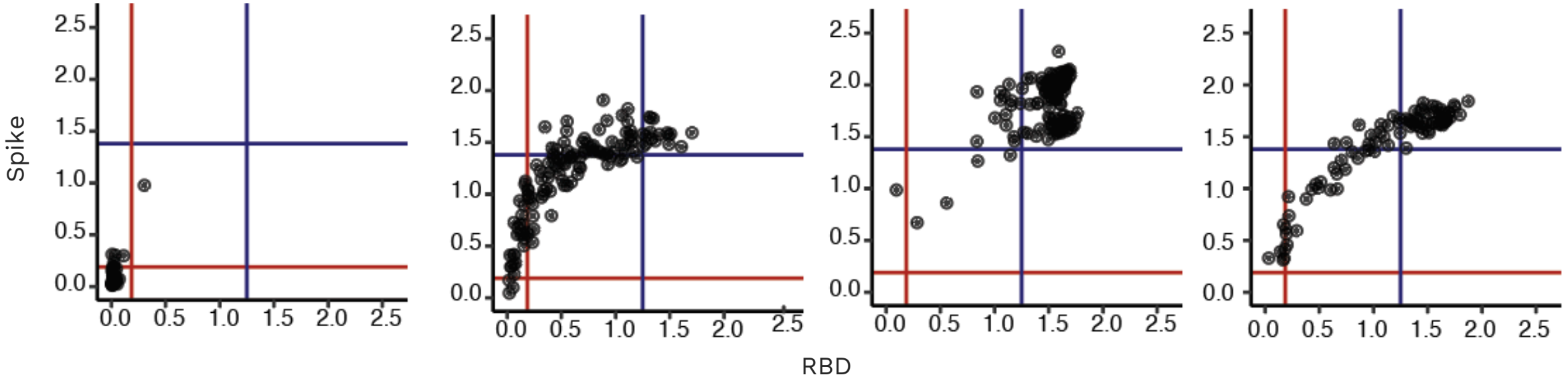
Dose 2

T1
Pre-vaccination

T2
2-4 weeks post dose 1
(median 26 days)

T3
2-4 weeks post dose 2
(median 16 days)

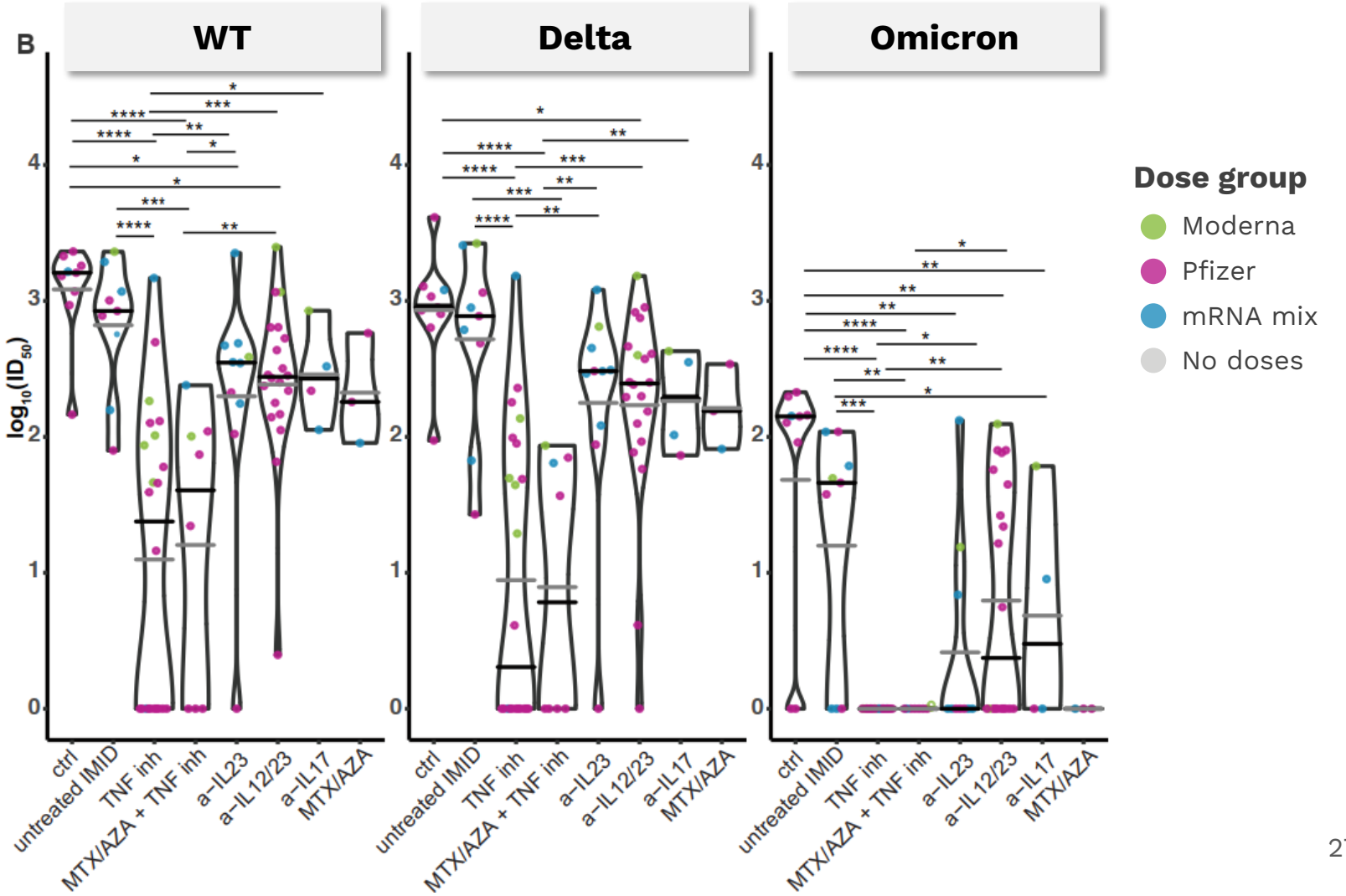
T4
3 months post dose 2
(median 106 days)



IMID patients undergoing anti-TNF therapy show significantly lower neutralization responses

T4
3 months post dose 2
(median 106 days)

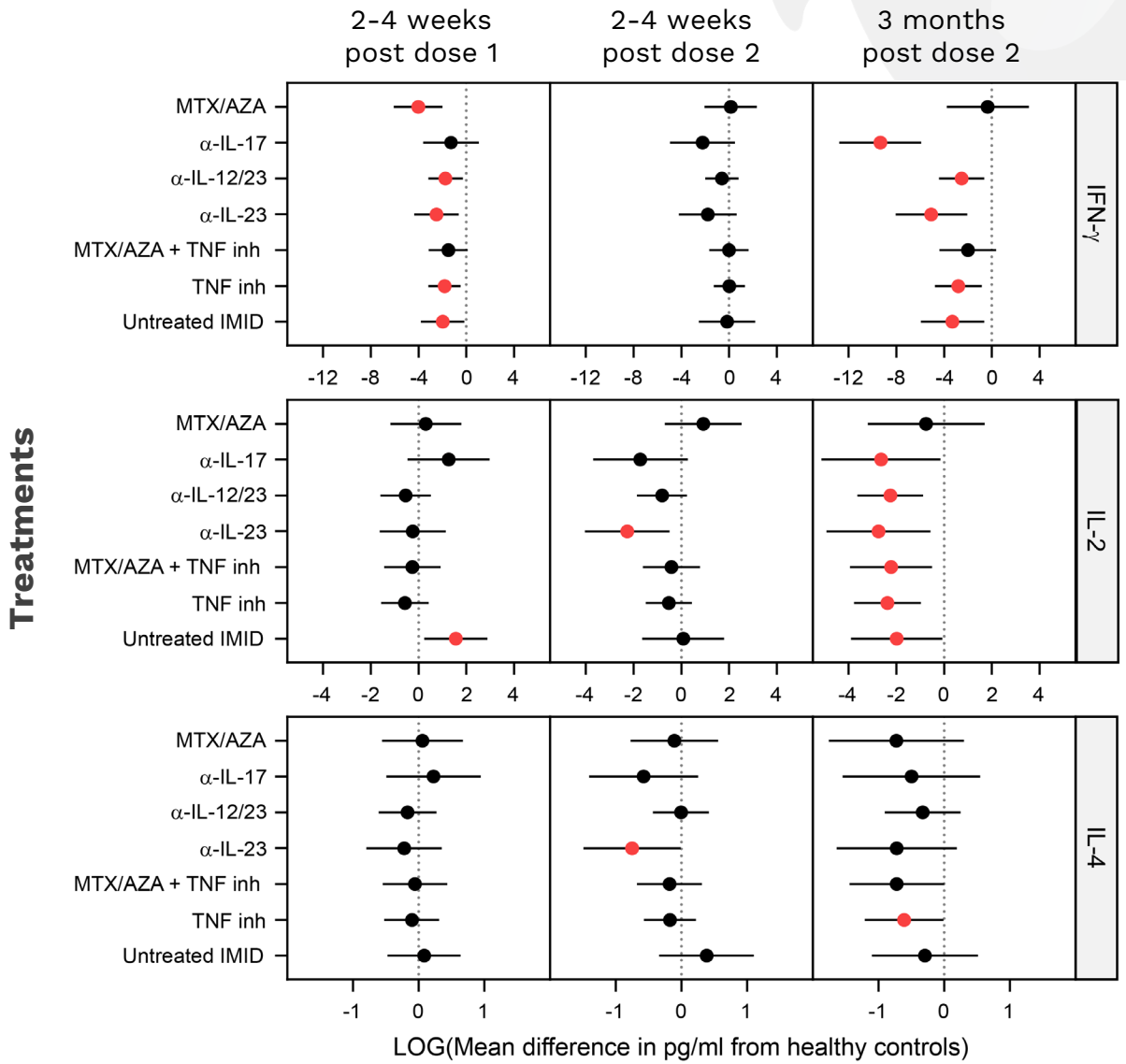
A spike-pseudotyped lentivirus assay for the detection of neutralizing antibodies



T-cell responses after dose 1 and dose 2

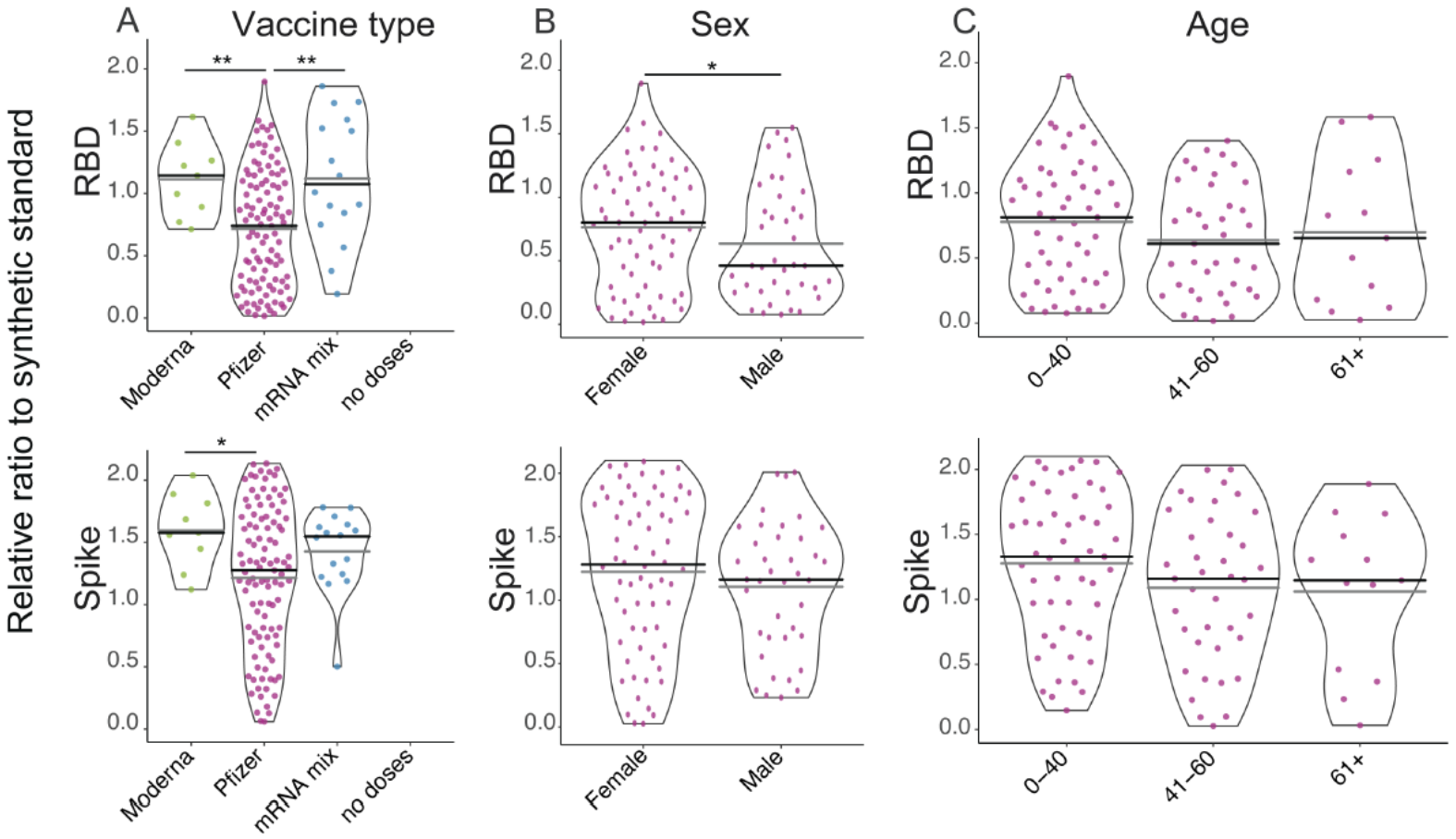
T-cell cytokine responses (as determined by measuring the release of cytokines in cell culture supernatants following stimulation with peptide) demonstrated that:

- The deficits in T-cell response after dose 1 were largely corrected after dose 2
- However, by 3 months , post-dose 2, T- cell responses (specifically IFN-γ and IL-2 responses) were lower in most treatment groups as well as in untreated people with IMID relative to controls



Red indicates statistically significant difference | Pfizer only

Stronger responses to 2 doses of Moderna vs. 2 doses of Pfizer



2 doses of vaccine not enough for people with IMIDs, continued monitoring after each dose required

Data based on antibody response

- 100% seroconversion, with increased antibody responses from T1 to T3
- Antibody levels and neutralization efficacy were lower in those on anti-TNF treatments than in controls
- Responses wane substantially by 3 months after dose 2, especially in people with IMID & may need more boosting

Data based on T cell response

- All patient groups showed T cell responses after 1st dose of mRNA vaccine
- Some improvement with 2nd dose
- **IL-2 and IL-4 responses waned within 3 months after 2nd dose, compared to healthy controls**
- IL-2 and IL-4 responses were more pronounced after the 2nd doses (vs. 1st dose)

- **Impact of vaccine type:** Stronger responses to 2 doses of Moderna vs. 2 doses of Pfizer (Ab, IL-4)
- Positive correlation between T cell and antibody responses

Limitations: Limited number of subjects in each study group, heterogeneity of drugs and disease within each group

Antibody responses after 3 doses of mRNA vaccine

Dose 1

Dose 2

Dose 3

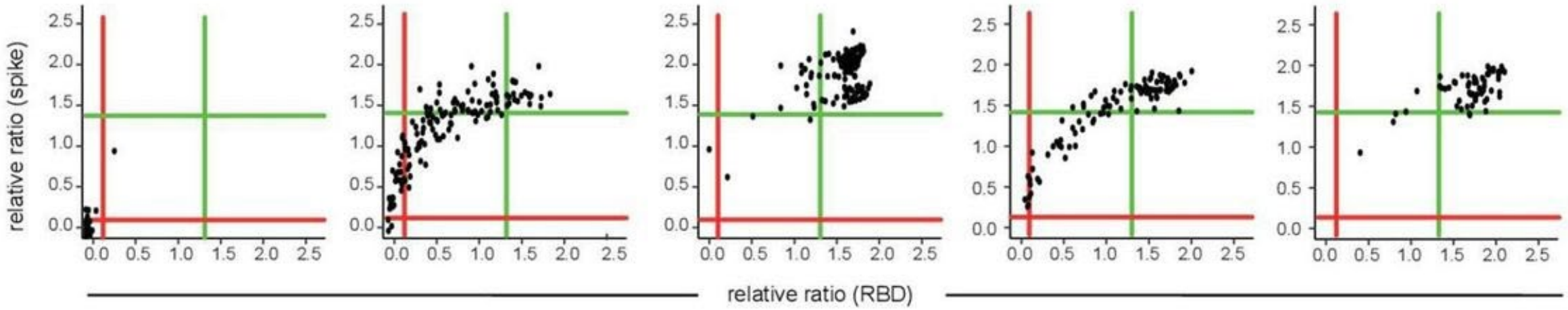
T1
Pre-vaccination

T2
2-4 weeks
post dose 1
(median 26 days)

T3
2-4 weeks
post dose 2
(median 16 days)

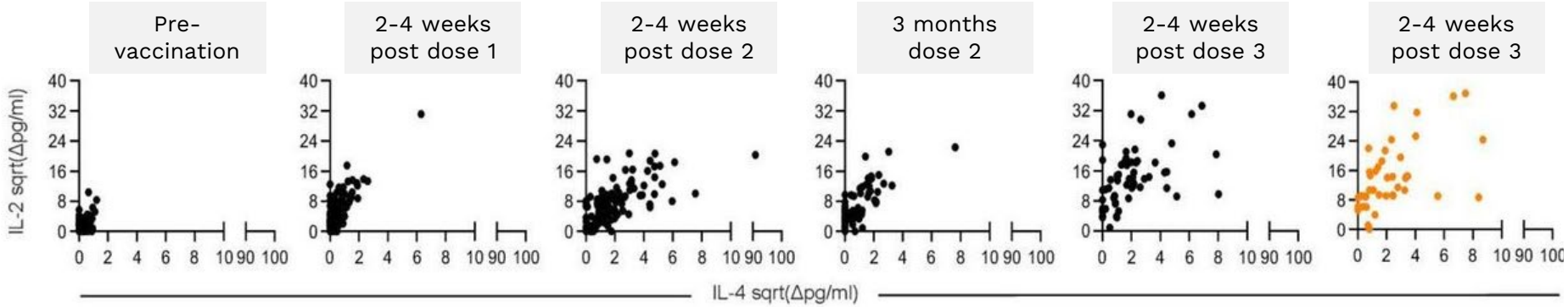
T4
3 months
post dose 2
(median 106 days)

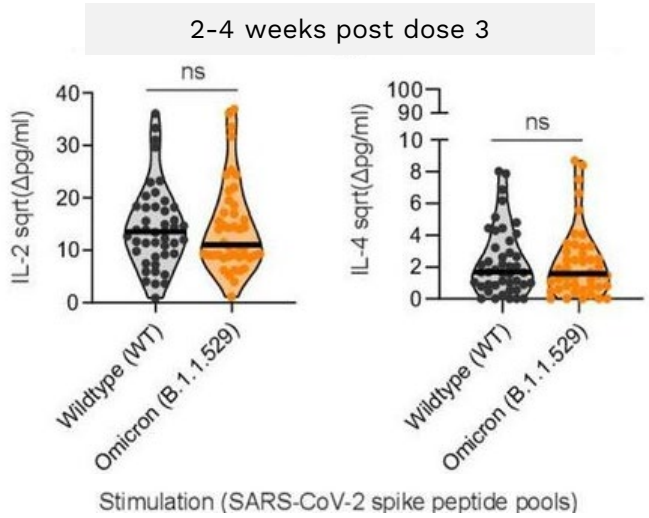
T5
2-4 weeks
post dose 3
(median 24 days)



Pfizer (BNT162b2) or Moderna (mRNA-1273)

T cell responses after 3 doses of mRNA vaccine





Stimulation (SARS-CoV-2 spike peptide pools)

- Wildtype (WT)
- Omicron (B.1.1.529)

Conclusions

- We observed robust serological and cellular responses in people with IMID following the 3rd of SARS-CoV-2 mRNA vaccine
- 3rd dose restores waned T cell-mediated and antibody-mediated immunity in people with IMID by 3 months after the second dose
- People with IMID retain T cell immunity to Omicron B.1.1.529.

- We are now conducting:
  - Additional cellular and humoral readouts
  - Durability of the responses
  - Effect of additional doses in this cohort

Acknowledgements | Study Team

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All patients & study participants who made this work possible

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CoVaRR-Net

Sinai Health | Lunenfeld-Tanenbaum Research Institute

Krembil Relentless.

RBC Royal Bank

Canada Research Chairs / Chaires de recherche du Canada

Canada

Generous donation from
Juan and Stefania Speck

Antibody response after the first, second, third, and fourth dose COVID-19 vaccines in **inflammatory bowel disease**

Gil Kaplan, MD, MPH, FCAHS

Professor, Department of Medicine

Gastroenterologist & Epidemiologist

Co-Chair, Crohn's and Colitis Canada COVID-IBD Task Force

University of Calgary

Serological Testing to Outline Protocols for COVID-19 in Inflammatory Bowel Disease (STOP COVID-19 in IBD) Research Group

Safety and immUnogenicity of COVID-19 vaCcines in systEmic immunE mediated inflammatory Diseases (SUCCEED)

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CUMMING SCHOOL OF MEDICINE

Crohn's and Colitis Canada
Crohn et Colite Canada

Land acknowledgement

I acknowledge the traditional territories of the people of the Treaty 7 region in Southern Alberta, which includes the Blackfoot Confederacy, comprising the Siksika, Piikani, and Kainai First Nations, as well as the Tsuut'ina First Nation, and the Stoney Nakoda, including the Chiniki, Bearspaw, and Wesley First Nations. The City of Calgary is also home to Métis Nation of Alberta, Region 3.

Disclaimer

I would like to acknowledge that I have been a speaker for Pfizer, AbbVie, Janssen, Takeda. I have acted as a consultant for Gilead and have received a grant from Ferring. I also have a patent for the treatment of inflammatory disorders, autoimmune disease and PBC.

From the first to the fourth dose of a SARS-CoV-2 vaccine, antibody titers increase, decay, and robustly recover

First dose of the vaccine:
81.8% seroconvert; average antibody levels are 276 AU/ml

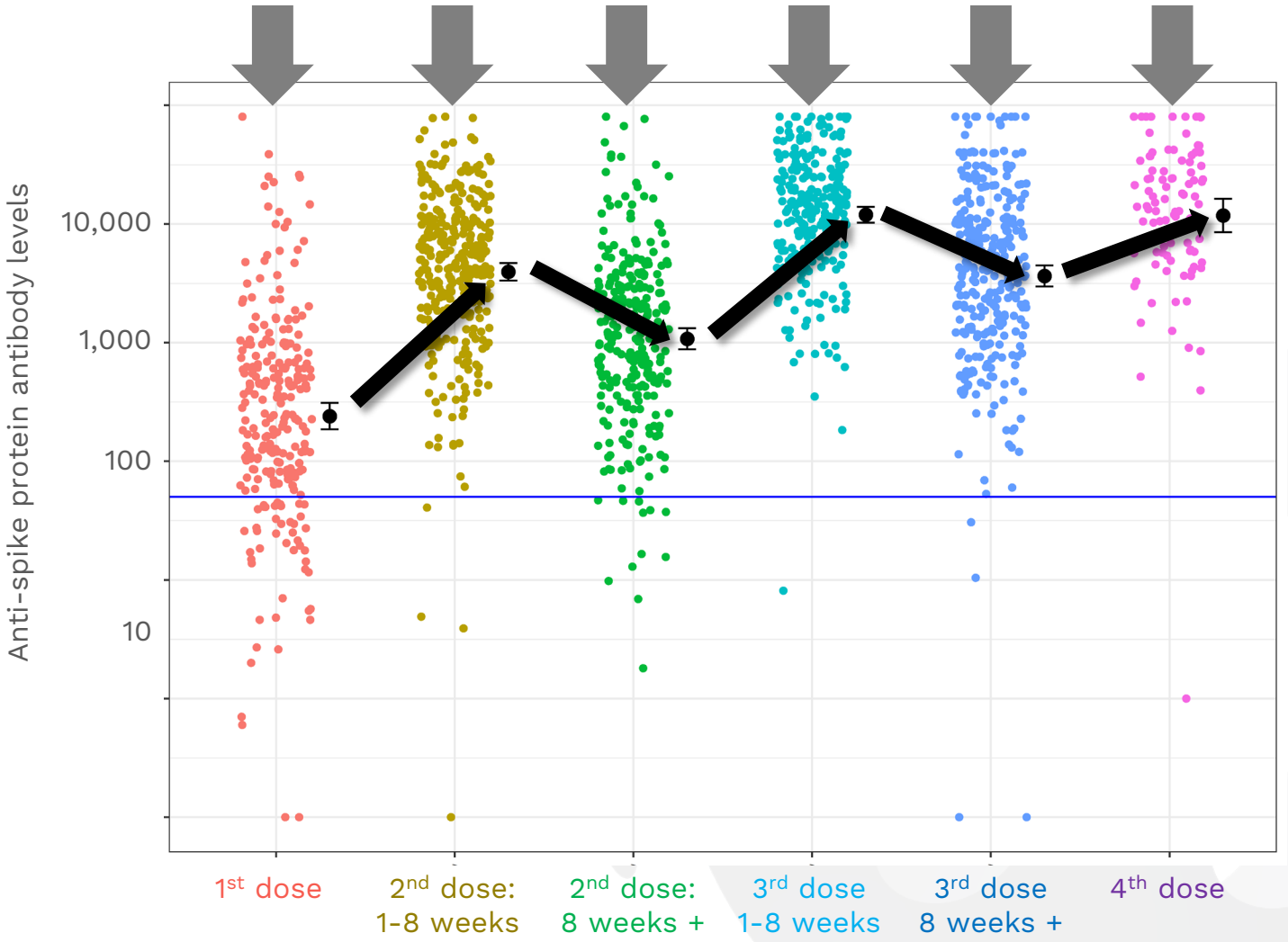
1 to 8 weeks after 2nd dose:
98.8% seroconvert; average antibody levels are 4,053 AU/ml

8+ weeks after 2nd dose:
95.6% seroconvert; average antibody levels are 1,127 AU/ml

1 to 8 weeks after 3rd dose:
99.6% seroconvert; average antibody levels are 12,016 AU/ml

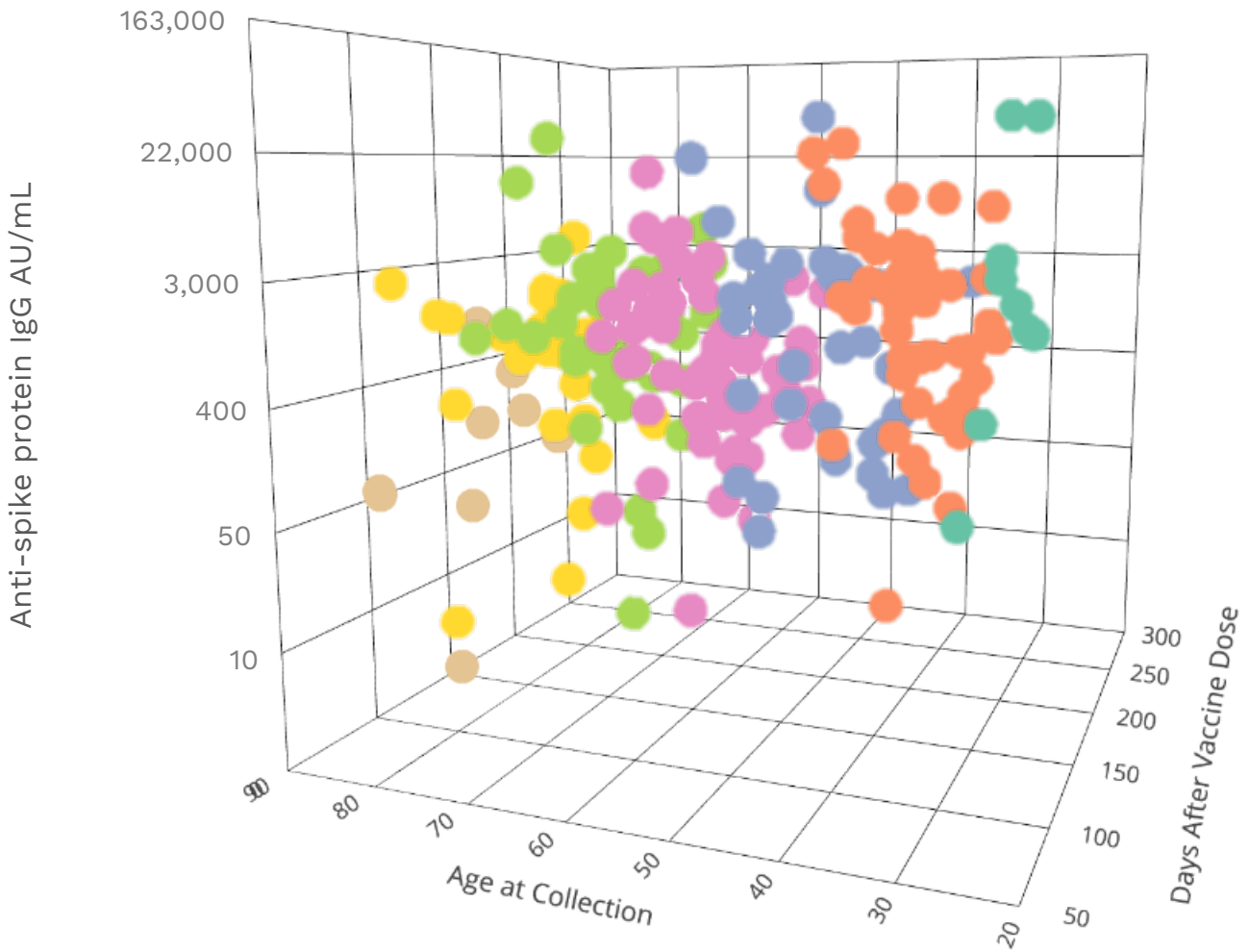
8+ weeks after 3rd dose:
98.8% seroconvert; average antibody levels are 4,247 AU/ml

After 4th dose:
97.4% seroconvert; average antibody levels are 10,405 AU/ml



Quan et al. *Lancet Gastroenterol Hepatol*. 2022 Oct 25:S2468-1253.

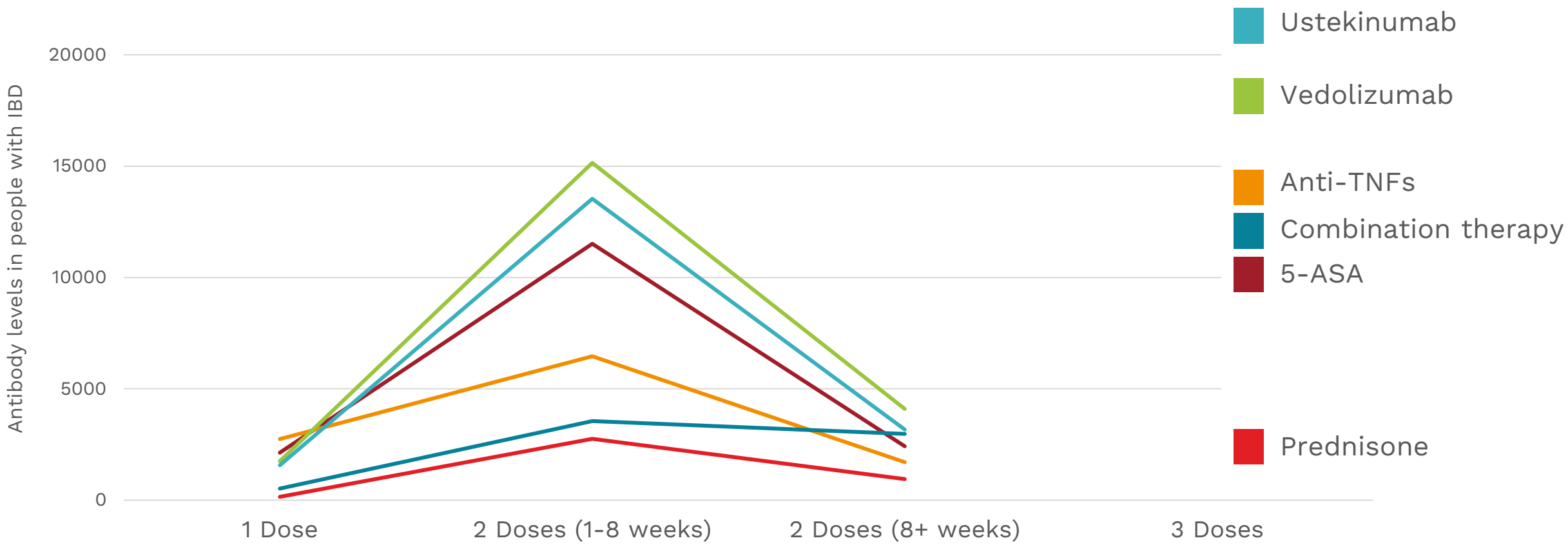
Antibody levels are higher in younger individuals with IBD



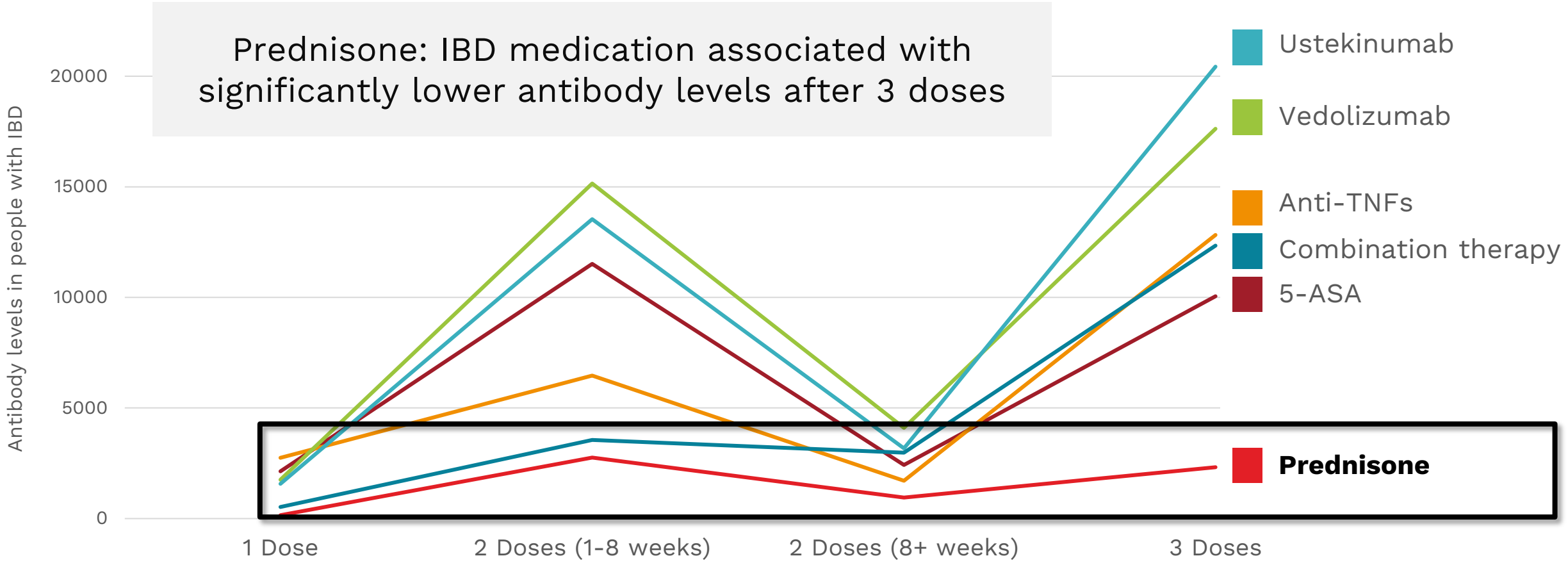
For example, after the third dose of a SARS-CoV-2 vaccine, for each decade of increased age antibody levels fell by 12%.

Quan...Kaplan; STOP COVID-19 in IBD Research Group. Serological responses to the first four doses of SARS-CoV-2 vaccine in patients with inflammatory bowel disease. *Lancet Gastroenterol Hepatol*. 2022 Oct 25:S2468-1253(22)00340-5.

Antibody levels were lower for those with IBD taking anti-TNF therapy (e.g. infliximab, adalimumab), combination therapies, and oral prednisone, which had the lowest antibody response



Antibody levels recovered after 3rd vaccine dose for all IBD medications, except oral prednisone



Vaccine adverse events in those with IBD similar to those in general population: very low risk of triggering a flare

Symptoms post vaccine:

Similar frequency and duration to general population

Adverse events:

Injection site pain, fatigue, & malaise most common
(GI symptoms <12%)

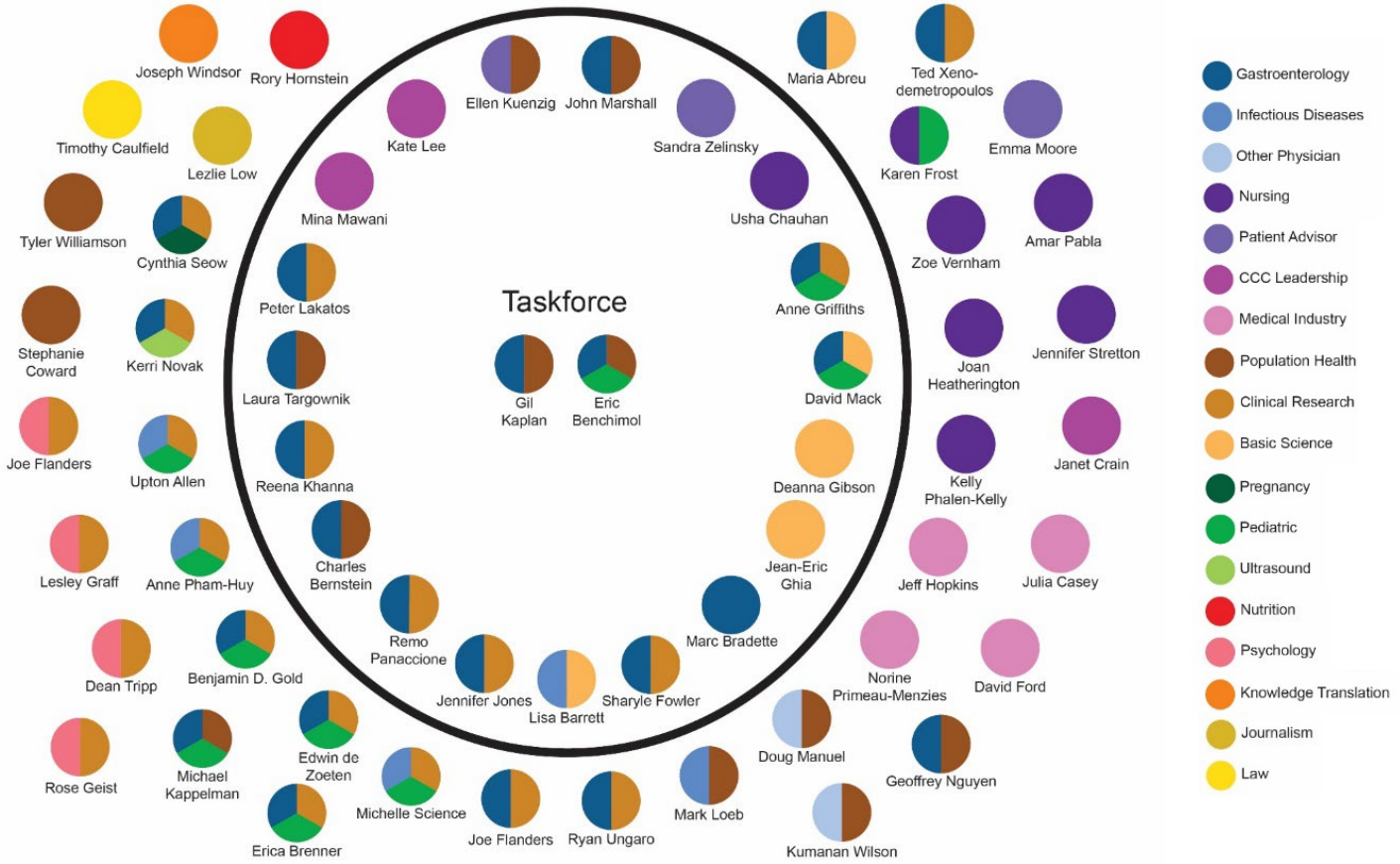
Risk of flare:

No objective flare within 30 days of vaccine across 3 doses

Injection site reactions associated with **higher levels of antibodies** after 4th dose.

Data from Canadian research on those with IBD inform Crohn's and Colitis Canada's COVID-19 & IBD Taskforce

CCC COVID-IBD Taskforce Recommendations:
https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD



Key messages

- Antibody levels increase and decay from 1st to 4th vaccine dose.
- Older individuals with IBD mount a lower antibody response to vaccine.
- Those on anti-TNF monotherapy, combination therapy, and oral prednisone mounted a lower antibody response to vaccine.
- People with IBD robustly recover antibody levels after 3rd and 4th doses across medications, except oral prednisone.
- SARS-CoV-2 vaccines appeared safe in this IBD sample which did not report disease flares within 30 days across 3 doses.

Stop COVID-19 in IBD | Team Members

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Serological Testing to Outline Protocols for COVID-19 in Inflammatory Bowel Disease (STOP COVID-19 in IBD) Research Group

is part of

Safety and immUnogenicity of COVID-19 vaCcines in systEmic immunE mediated inflammatory Diseases (SUCCEED)

Open access interactive data can be found on our online **ShinyApp**

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Partners & Funders

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Crohn's and Colitis Canada
Crohn et Colite Canada

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

Effectiveness of 3 doses of COVID-19 vaccine among **people on dialysis** during Omicron

Ontario, Canada

Sara Wing, MDCM, FRCPC

Clinical Associate

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Sunnybrook HEALTH SCIENCES CENTRE

Medicine UNIVERSITY OF TORONTO

UNITY HEALTH TORONTO

Disclaimer

I have no COIs to declare related to this study

Is a 3rd dose enough?

People on dialysis are considered at **high risk** of COVID-19 as they often suffer from additional chronic conditions

- 2 doses of COVID-19 vaccine were effective in reducing COVID-19 in the dialysis population when Alpha and Delta variants were predominant

Questions:

- Was a 3rd dose effective in reducing infection during Omicron in the dialysis population?
- Was a 3rd dose effective in reducing severe outcomes (severe infection, mortality) during Omicron?
- Does prior infection play a role in reducing future infection?

Our objective: determine vaccine effectiveness of 2 vs. 3 doses in the dialysis population

STUDY START
December 1, 2021

989
individuals received a third dose (28%)

+

STUDY COMPLETION
February 28, 2022

7,468
individuals received a third dose (88%)

=

TOTAL PATIENT PARTICIPATION

8,457
hemodialysis patients (in centre, no home dialysis patients) across Ontario

THREE DOSES

86% were all Pfizer or Moderna

PRIOR INFECTION

627 individuals with history of prior COVID-19 infection (7%)

→ Individuals with a prior COVID-19 infection were **less likely** to receive third dose

3 doses significantly increased vaccine effectiveness, even during Omicron

Three doses (vs two doses) =

42% reduction in infection

60% reduction in severe outcomes

*Between December 1, 2021 and February 28, 2022 (Omicron)

Hybrid immunity offers most robust protection, regardless of vaccine type

Lowest risk → individuals with prior infection AND a third dose

- Vaccine effectiveness (VE) = 83%, compared to those with two doses and no prior infection

No significant difference by vaccine type

- Higher point estimates for Moderna (VE 66%) in comparison to Pfizer (VE 50%), the difference was **not** statistically significant

Conclusions

1. Hemodialysis patients should be informed of the benefits of vaccination
2. COVID-19 vaccination was prioritized for the dialysis population due to high rates of mortality and hospitalization in the first wave of the pandemic
3. Prior infection is likely protective but does not remove the need for further vaccination: lowest risk was found with prior infection AND a third dose

Further studies needed:

- Impact of COVID-19 on long-term morbidity and mortality in the dialysis population
- Waning of vaccine effectiveness in the dialysis population

Study Team

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Ontario Health

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COVID-19 Vaccination among **People Living with HIV**: Immunogenicity, Effectiveness, and Safety

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the CTN
CIHR Canadian
HIV Trials Network

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Réseau canadien
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Research Institute
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UNIVERSITY OF TORONTO

Disclaimer

Neither Dr. Cecilia Costiniuk nor Dr. Ann Burchell have COIs to declare related to this study

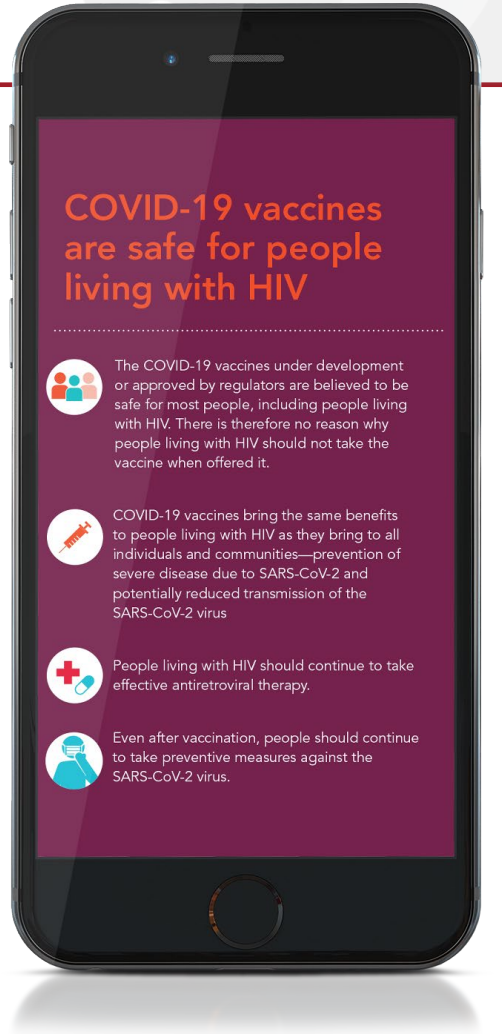
Why is it important to study COVID-19 vaccination among people living with HIV?

People living with HIV display **poor immunogenicity to common vaccines**, such as influenza, pneumococcal, meningococcal and Hepatitis A and B vaccines, especially with low CD 4 T cell counts (<200 cells/mm^3)/viremia

Other intersecting vulnerabilities increase risk of COVID-19 and severe outcomes

Those included in clinical trials did not represent the broader spectrum of PLWH:

- Only people with normal CD4 T cell counts (>500 cells/mm3)/ few comorbidities were included
- Data were excluded from primary publications

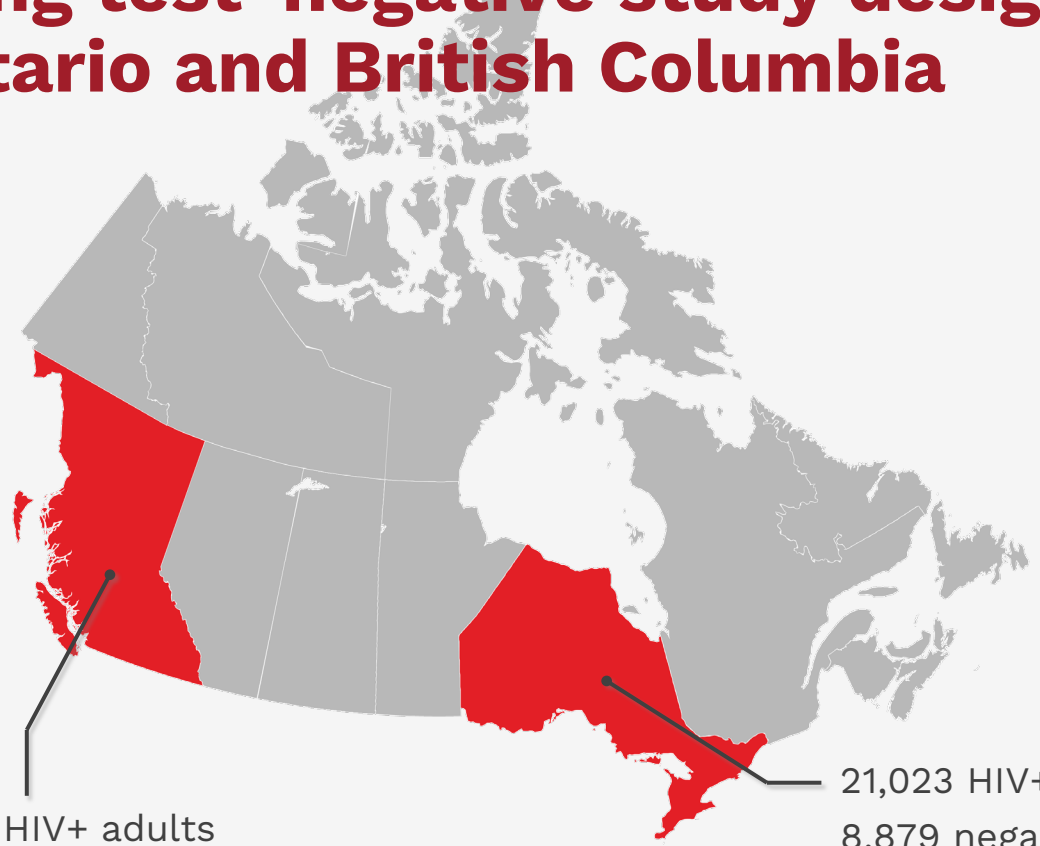


COVID-19 vaccines and HIV, 01 June 2021, *UNAIDS*

Aim 1

Do COVID-19 vaccines effectively prevent infection with SARS-CoV-2 and COVID-19 disease among people living with HIV?

Vaccine effectiveness estimated using test-negative study design in Ontario and British Columbia

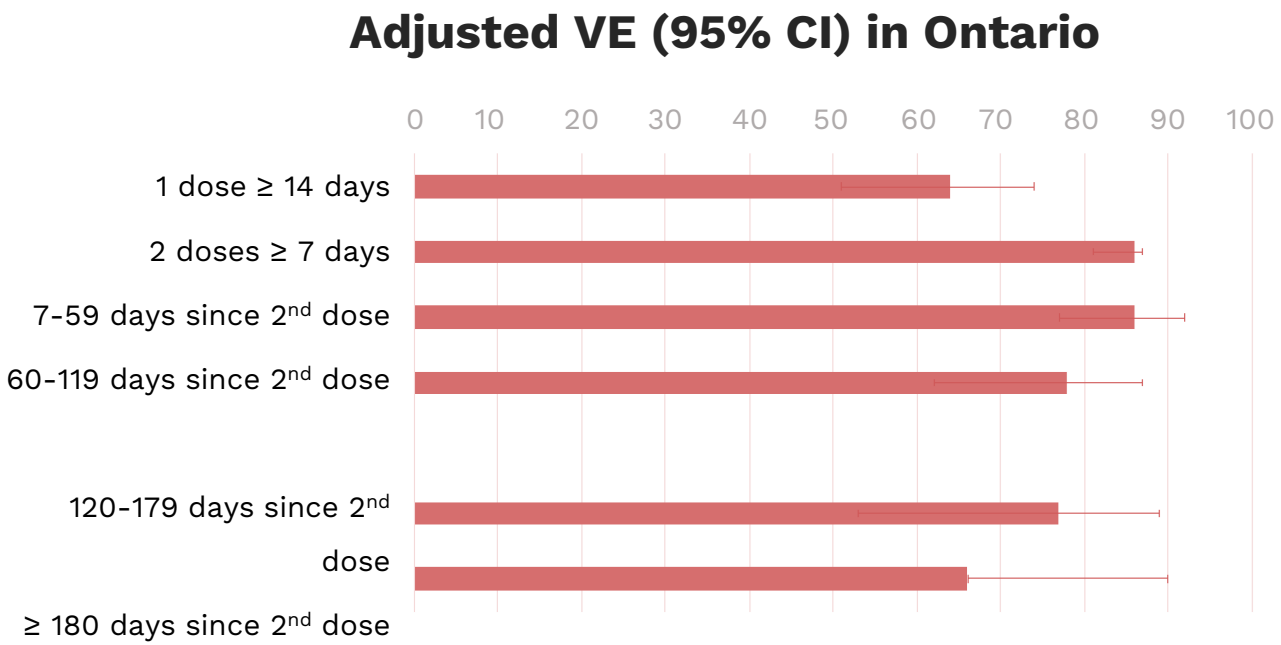


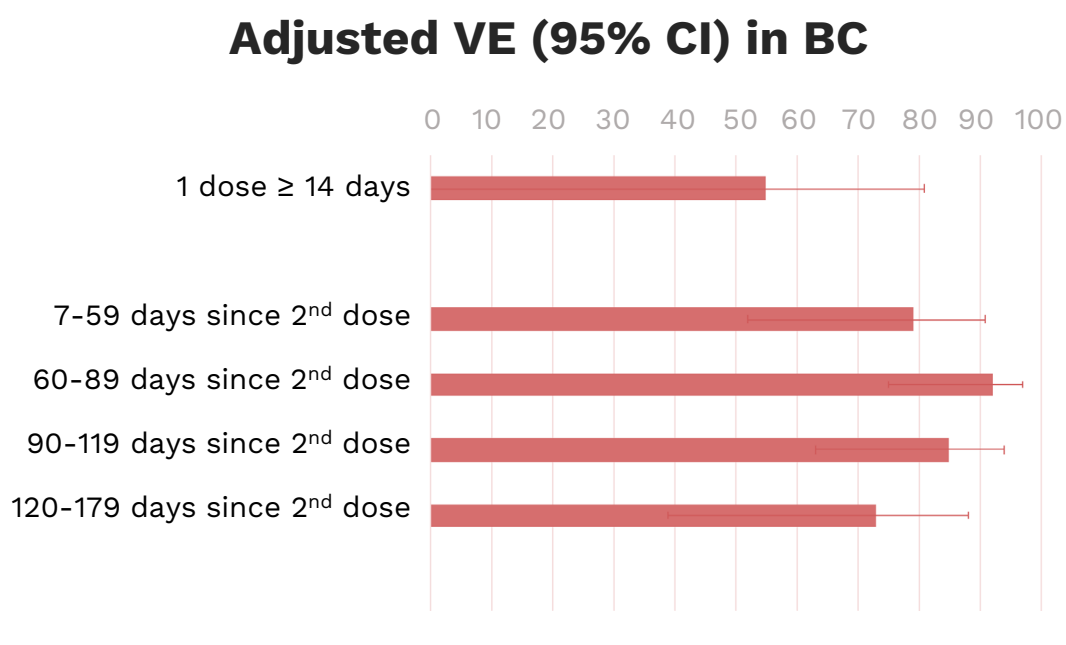
8,200 HIV+ adults
2,349 negative tests
351 positive tests

21,023 HIV+ adults
8,879 negative tests
801 positive tests
- 99 hospitalizations
- 18 deaths

- Linked administrative health data
- Restricted to adults living with HIV with 1+ SARS-CoV-2 PCR test
- Dec 14, 2020 to Nov 21, 2021 (pre-Omicron period)
- Vaccine effectiveness (VE) estimated by comparing vaccine status between SARS-CoV-2 test positives and test-negative controls

Vaccine effectiveness (VE) against SARS-CoV-2 infection was similar for adults living with HIV in Ontario and BC, Dec 2020–Nov 2021



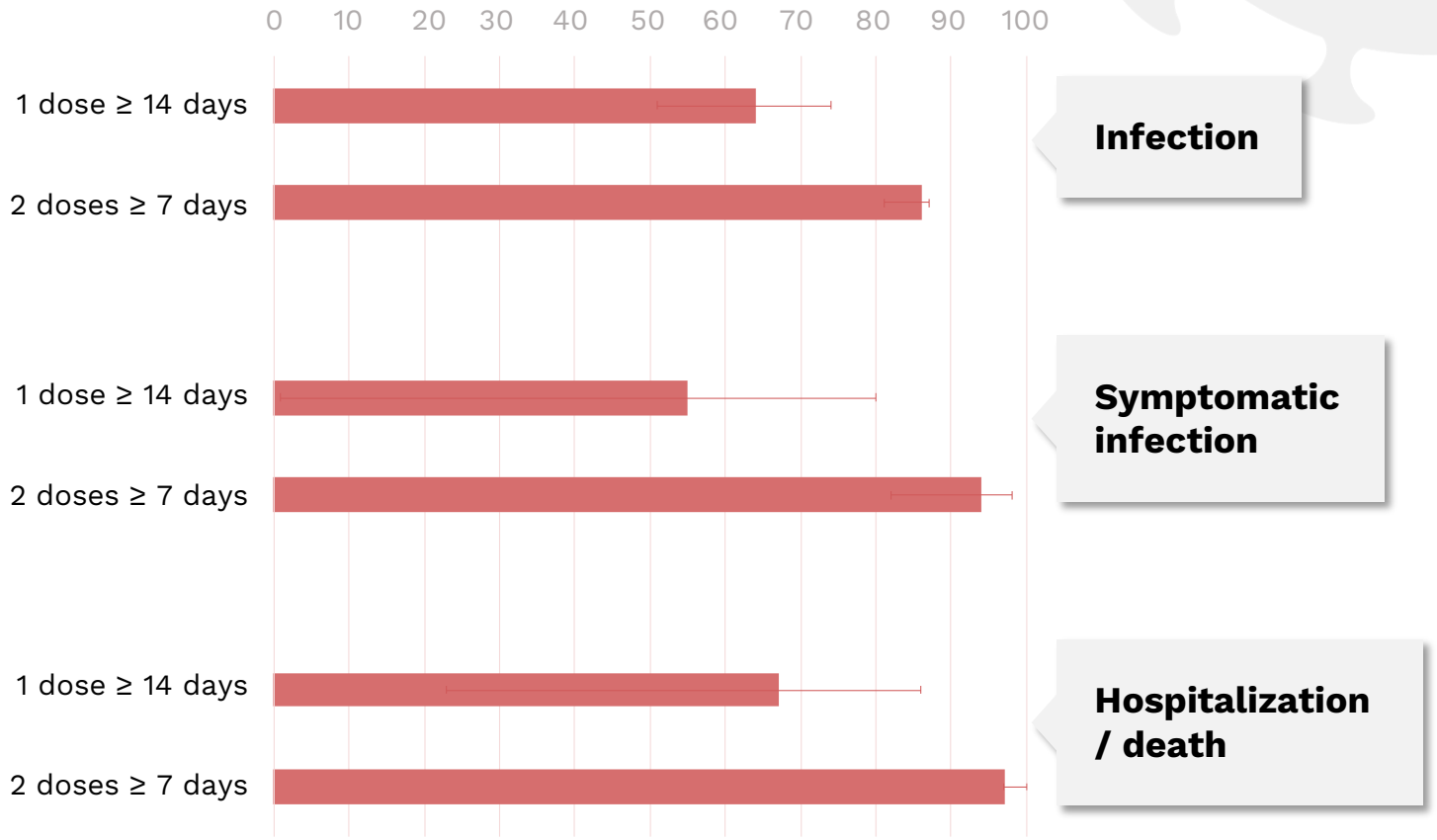


Adjusted for age, sex, region, time, SARS-CoV-2 test histories, influenza vaccination, comorbidities, and neighbourhood-level measures of social determinants of health

Two doses offered substantial protection against symptomatic illness and severe outcomes prior to the emergence of the Omicron variant

No evidence of variation in VE according to age, sex, region, number of comorbidities, or pandemic wave

Adjusted VE (95%CI) in Ontario



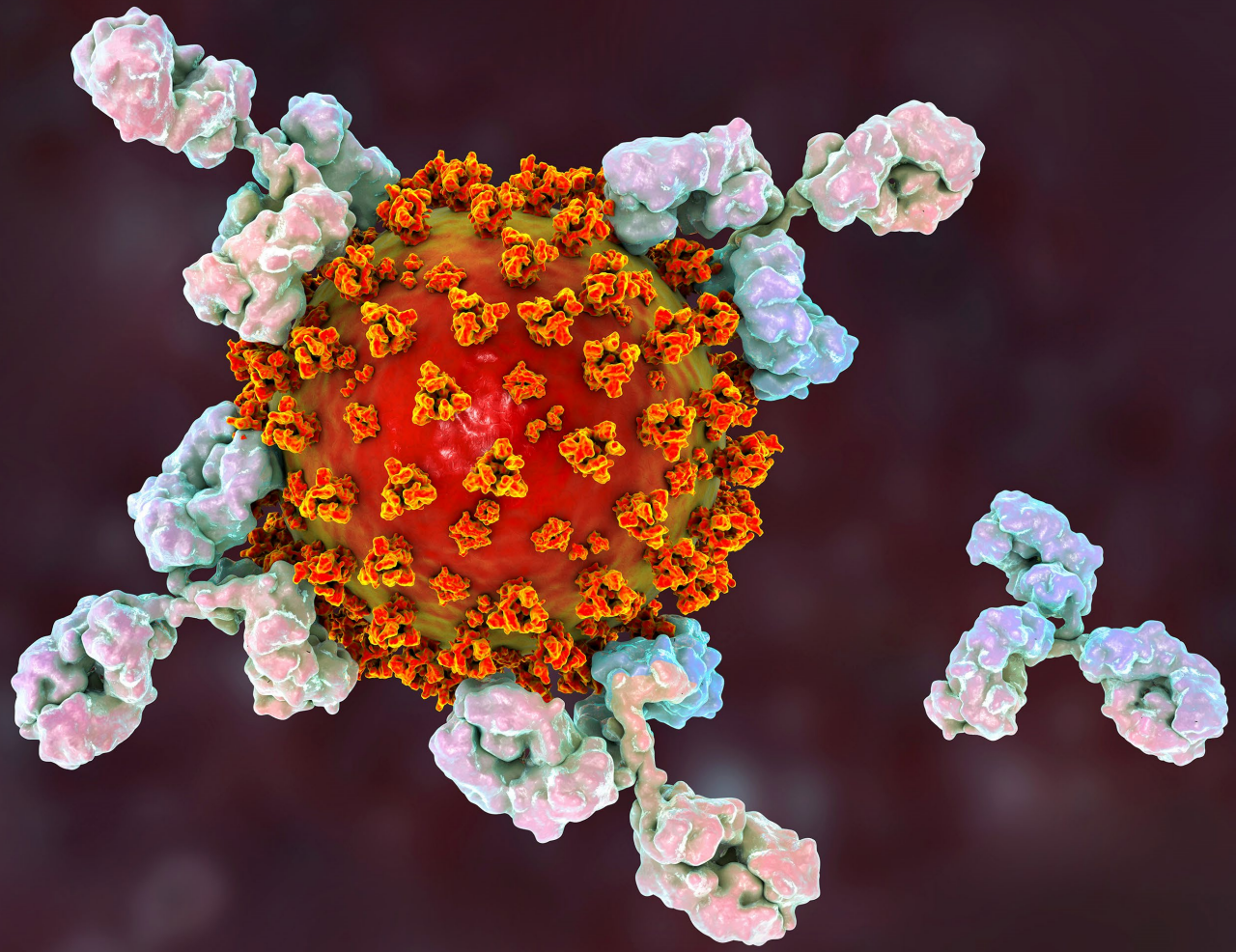
Adjusted for age, sex, region, time, SARS-CoV-2 test histories, influenza vaccination, comorbidities, and neighbourhood-level measures of social determinants of health

Aim 1 | Main findings

- Two-dose COVID-19 vaccine effectiveness broadly similar among people living with HIV (PLWH) compared to general population prior to emergence of Omicron variants
- Findings may provide reassurance for PLWH and their healthcare providers, particularly for those whose HIV is well controlled
- **More work needed:** VE likely lower against Omicron variants, with time since last dose, or if AIDS-defining illness, low CD4, unsuppressed viral load, or other immunocompromising conditions
- For PLWH, we recommend following 3rd dose and additional booster guidance as for the general population

Aim 2

What is the immune response to COVID-19 vaccines among people living with HIV?

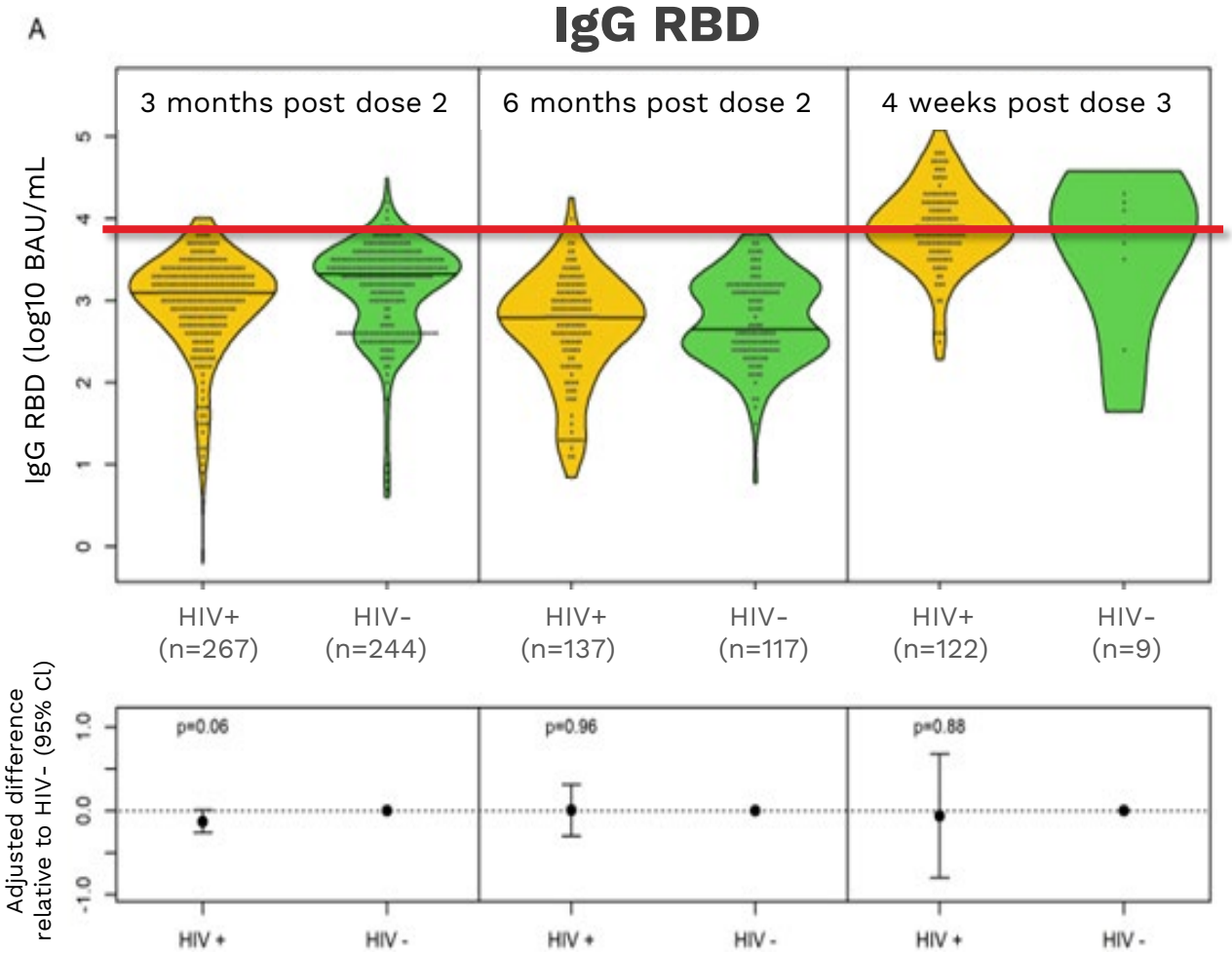


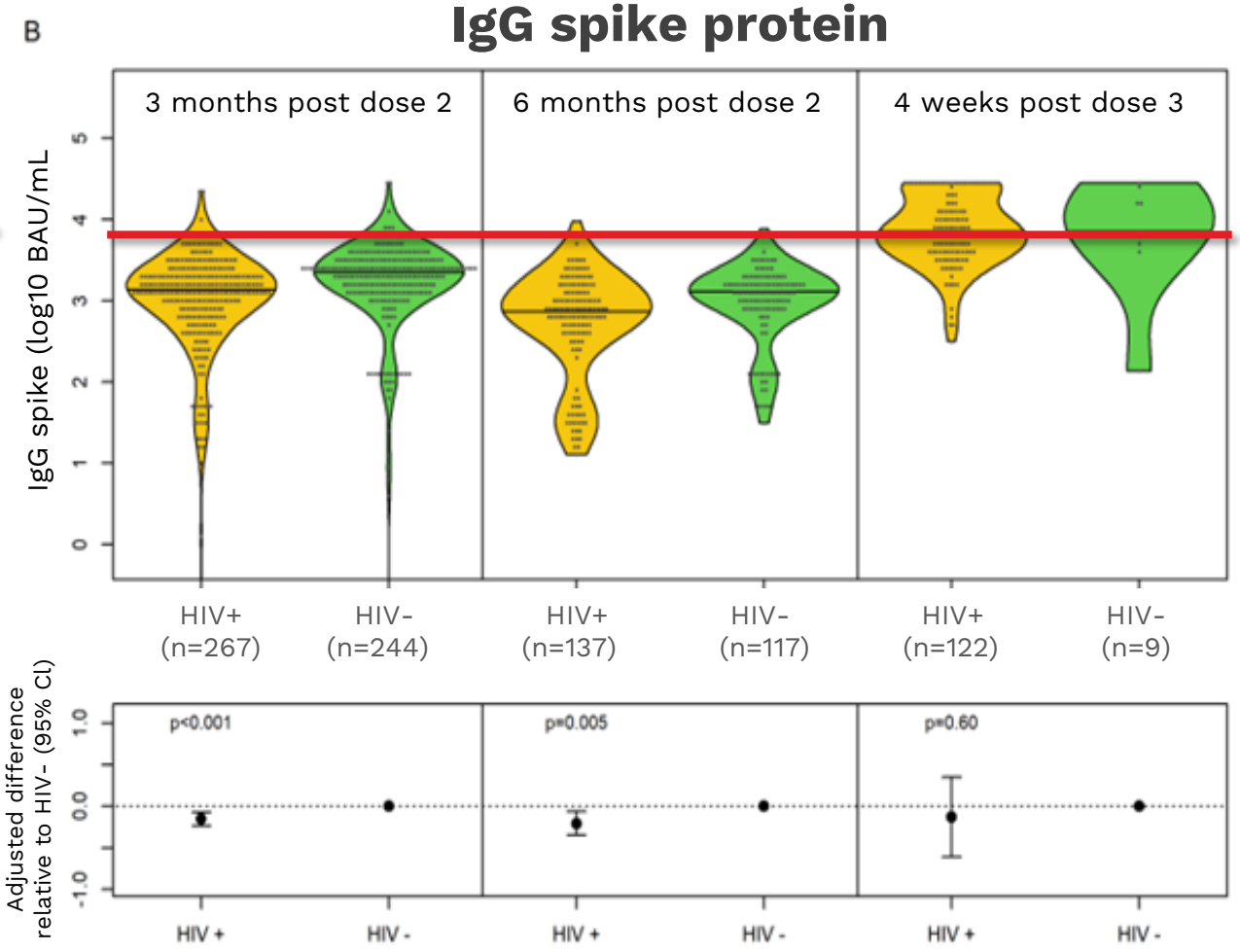
Main characteristics of participants prior to COVID infection n (%)

Variable	HIV+ (n=294)	HIV- (n=267)
AGE Median (IQR)/Range	54.4 (42.3, 62.8)/(19.7, 83.5)	42.0 (34.0, 54.0)/(20.0, 79.0)
AGE ≥55	139 (47.3)	61 (22.8)
Sex		
Male	227 (77.2)	70 (26.2)
Female	65 (22.1)	197 (73.8)
Prefer to self describe	2 (0.7)	0
Multimorbidity (≥2 comorbidities)	84/288 (29.2)	46/265 (17.4)
Duration of HIV infection, years (n=273), Median (IQR)/Range	17.0 (8.0, 25.0)/ (0.0, 39.0)	
CD4 nadir (cells/mm3), Median (IQR)/Range	256 (120, 444)	
CD4 nadir (cells/mm3)<100	36 (21.7)	
CD4 count (cells/mm3) (n = 273), Median (IQR)/ Range	650 (434, 855)/ (9,1800)	
CD4 <250	18 (6.6)	
CD4 = 250-349	17 (6.2)	
Detectable viral load for at least 6 months, n (%)	31/289 (10.7)	
Immune non-responder *	23/276 (8.3)	
HIV+ stable/reference (CD4 ≥350, suppressed VL and ≤ 1 comorbidity)	145/271 (53.5)	

AIDS, In Press

3rd dose elicits stronger immune response irrespective of HIV status





AIDS, In Press

No difference in vaccine-induced antibodies between HIV+ and HIV – individuals after the 3rd vaccine dose

Subgroup and time point	HIV+	HIV-	Odds ratio HIV+ vs HIV- (95% CI)	P
All participants				
3 months post dose 2 (±1 month)	257/267 (96.3)	238/244 (97.5)	0.67 (0.25, 1.81)	0.428
6 months post dose 2 (±2 months)	126/137 (92.0)	116/117 (99.1)	0.14 (0.03, 0.80)	**0.027**
4 weeks post dose 3 (±2 weeks)	122/122 (100.0)	9/9 (100.0)	-	
Among males				
3 months post dose 2 (±1 month)	200/208 (96.2)	62/64 (96.9)	0.94 (0.22, 4.01)	0.937
6 months post dose 2 (±2 months)	99/109 (90.8)	29/29 (100.0)	0.16 (0.01, 2.96)	0.219
4 weeks post dose 3 (±2 weeks)	107/107 (100.0)	3/3 (100.0)	-	
Among females				
3 months post dose 2 (±1 month)	55/57 (96.5)	176/180 (97.8)	0.57 (0.12, 2.76)	0.482
6 months post dose 2 (±2 months)	26/27 (96.3)	87/88 (98.9)	0.30 (0.03, 3.12)	0.316
4 weeks post dose 3 (±2 weeks)	14/14 (100.0)	6/6 (100.0)	-	

AIDS, In Press

Antibodies against SARS-CoV-2 were detected in both people with well-controlled HIV and people with less stable HIV after dose 3

	HIV+ stable/reference* participants			
Time point	No	Yes	Odds ratio (95% CI)	P
3 months post dose 2 (±1 month)	107/112 (95.5)	127/132 (96.2)	1.19 (0.35, 4.00)	0.783
6 months post dose 2 (±2 months)	56/63 (88.9)	60/63 (95.2)	2.29 (0.61, 8.68)	0.221
4 weeks post dose 3 (±2 weeks)	47/47 (100.0)	61/61 (100.0)	-	

*CD4 ≥350, suppressed VL and ≤ 1 comorbidity

AIDS, In Press

- Neither age >55 years, low CD4 count or multimorbidity was associated with reduced antibody levels following a 3rd dose
  - Low CD4 count defined as under 350 cells/mm3
  - Multimorbidity defined as 2 or more comorbidities

Following the 3rd vaccine dose, PLWH receiving both mRNA and non-mRNA vaccines mounted detectable antibodies towards COVID-19 vaccination

Spike

Time point:	3 months post dose 2 (±1 month)		6 months post dose 2 (±2 months)		4 weeks post dose 3 (±2 weeks)	
COVID-19 vaccine received, dose 1 & 2	Difference (95% CI)	P	Difference (95% CI)	P	Difference (95% CI)	P
mRNA – mRNA	0.69 (0.37, 1.00)	<0.001	1.32 (1.06, 1.58)	<0.001	**0.07 (-0.46, 0.59)**	**0.804**
ChAdOx1 - mRNA	0.65 (0.28, 1.03)	<0.001	1.32 (0.96, 1.67)	<0.001	**-0.14 (-0.88, 0.60)**	**0.713**
ChAdOx1- ChAdOx1	Referent		Referent		Referent	
Time between dose 1 & 2 (per 10 day increase)	-0.01 (-0.04, 0.02)	0.488	-0.05 (-0.13, 0.02)	0.174	-0.02 (-0.09, 0.06)	0.679

RBD

Time point:	3 months post dose 2 (±1 month)		6 months post dose 2 (±2 months)		4 weeks post dose 3 (±2 weeks)	
COVID-19 vaccine received, dose 1 & 2	Difference (95% CI)	P	Difference (95% CI)	P	Difference (95% CI)	P
mRNA – mRNA	0.65 (0.27, 1.02)	<0.001	0.87 (0.40, 1.33)	<0.001	**-0.19 (-0.76, 0.37)**	**0.497**
ChAdOx1 - mRNA	0.46 (-0.01, 0.94)	0.055	0.67 (-0.04, 1.39)	0.066	**-0.42 (-1.24, 0.41)**	**0.320**
ChAdOx1- ChAdOx1	Referent		Referent		Referent	
Time between dose 1 & 2 (per 10 day increase)	0.00 (-0.04, 0.04)	0.965	-0.05 (-0.15, 0.05)	0.310	-0.02 (-0.09, 0.05)	0.594

AIDS, In Press

Time interval between first and second COVID-19 vaccine doses did not impact antibody levels following third COVID-19 vaccine dose

Spike

Time point:	3 months post dose 2 (±1 month)		6 months post dose 2 (±2 months)		4 weeks post dose 3 (±2 weeks)	
COVID-19 vaccine received, dose 1 & 2	Difference (95% CI)	P	Difference (95% CI)	P	Difference (95% CI)	P
mRNA – mRNA	0.69 (0.37, 1.00)	<0.001	1.32 (1.06, 1.58)	<0.001	0.07 (-0.46, 0.59)	0.804
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Time point:	3 months post dose 2 (±1 month)		6 months post dose 2 (±2 months)		4 weeks post dose 3 (±2 weeks)	
COVID-19 vaccine received, dose 1 & 2	Difference (95% CI)	P	Difference (95% CI)	P	Difference (95% CI)	P
mRNA – mRNA	0.65 (0.27, 1.02)	<0.001	0.87 (0.40, 1.33)	<0.001	-0.19 (-0.76, 0.37)	0.497
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AIDS, In Press

Aim 2 | Main findings

- Adult PLWH with well-controlled HIV on anti-retroviral therapy (ART) build antibody responses similar to HIV-negative individuals following 2nd and 3rd COVID-19 vaccine doses.
- Fewer PLWH have detectable antibodies against SARS-CoV-2, so **timely boosters are required**.
- Additional information will help continue to inform COVID-19 vaccination guidelines for PLWH:
  - Durability of antibody response
  - Neutralization capacity
  - Contribution of cell-mediated immunity

Study Team

We thank all participants of the Immunogenicity Study and members of the Community Advisory Boards for COVAXHIV and the CHESS Study

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Funders

CIHR IRSC
Canadian Institutes of Health Research | Instituts de recherche en santé du Canada
the CTN CIHR Canadian HIV Trials Network
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Key takeaways

- COVID-19 vaccines have proven to be safe for people at higher risk of severe COVID-19 due to pre-existing health conditions
- Vaccines have worked well
  - At generating immune responses
  - Warding off severe disease and death in various high-risk populations
- Though in many cases 3 doses (not 2) should be considered the primary regimen.

Key takeaways

- Keeping up to date with the recommended vaccine booster schedule (i.e., a dose every 4-6 months) is important to sustain adequate levels of protection.
- New bivalent vaccines may offer greater protection, but it's too early to say for sure.
- People with other health conditions – like those we've discussed today – are more at risk of severe COVID-19 and therefore should continue to be cautious:
  - Wear masks, physical distancing, avoiding crowded settings, and getting regular boosters.

Questions?

You'll find our summary of this seminar at

covid19immunitytaskforce.ca

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