Serologic response and vaccine effectiveness of a third dose of a COVID-19 mRNA vaccine in the advanced chronic kidney disease (CKD) population.

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CITF Scientific Meeting

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Medicine
UNIVERSITY OF TORONTO

Sunnybrook
HEALTH SCIENCES CENTRE

Declarations

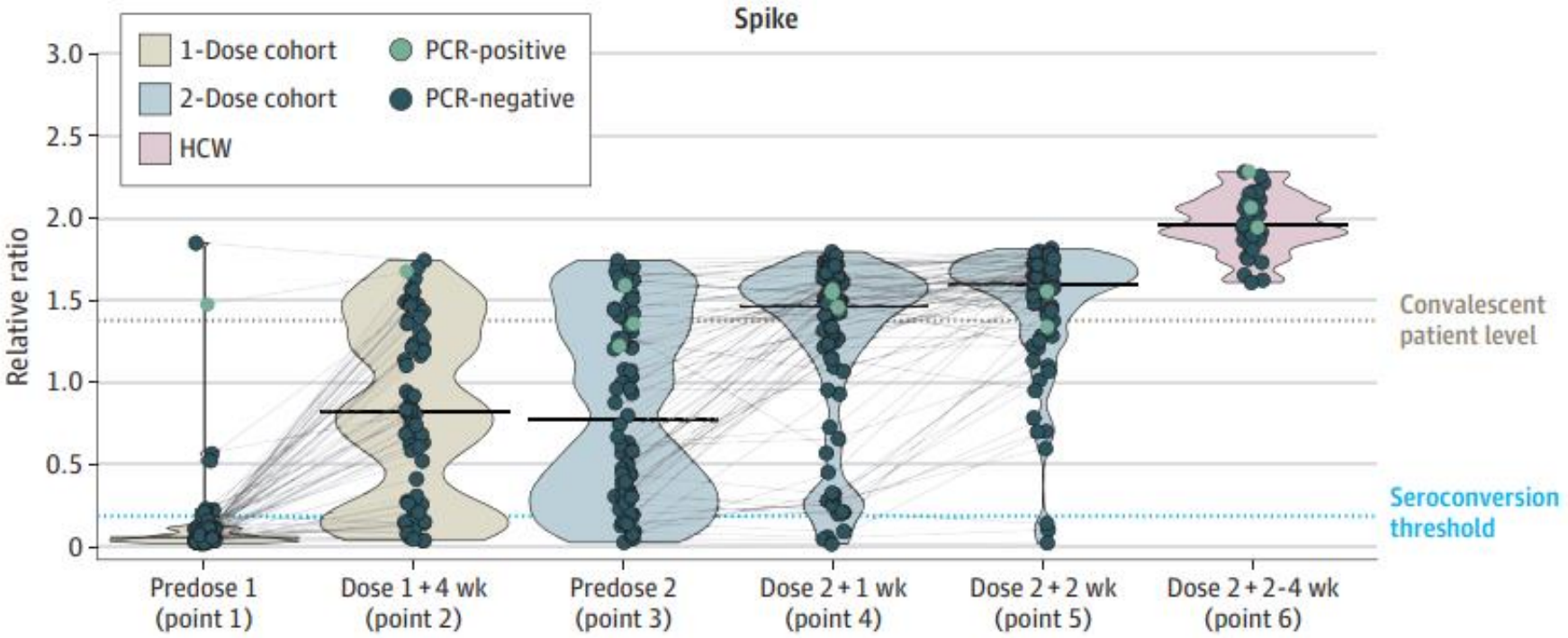
1. Speaking honorarium from Baxter Healthcare
2. Co-inventor of DMAR systems
3. Regional Medical Lead for the Ontario Renal Network, Ontario Health

Background

1. Early in the pandemic, SARS-CoV-2 infection in the maintenance dialysis population required hospitalization in 60% of cases and was associated with a 20 to 25% mortality rate (severe outcomes).
2. COVID-19 vaccines were prioritized in this population were prioritized in Canada.
3. Serology response to vaccines was variable and less than healthy controls.

Taji L et al. COVID-19 in patients undergoing long-term dialysis in Ontario. CMAJ. 2021 Feb 22;193(8):E278-E284. doi: 10.1503/cmaj.202601. Epub 2021 Feb 4

Suboptimal serology response



Yau et al. *JAMA Network Open.* 2021;4(9)

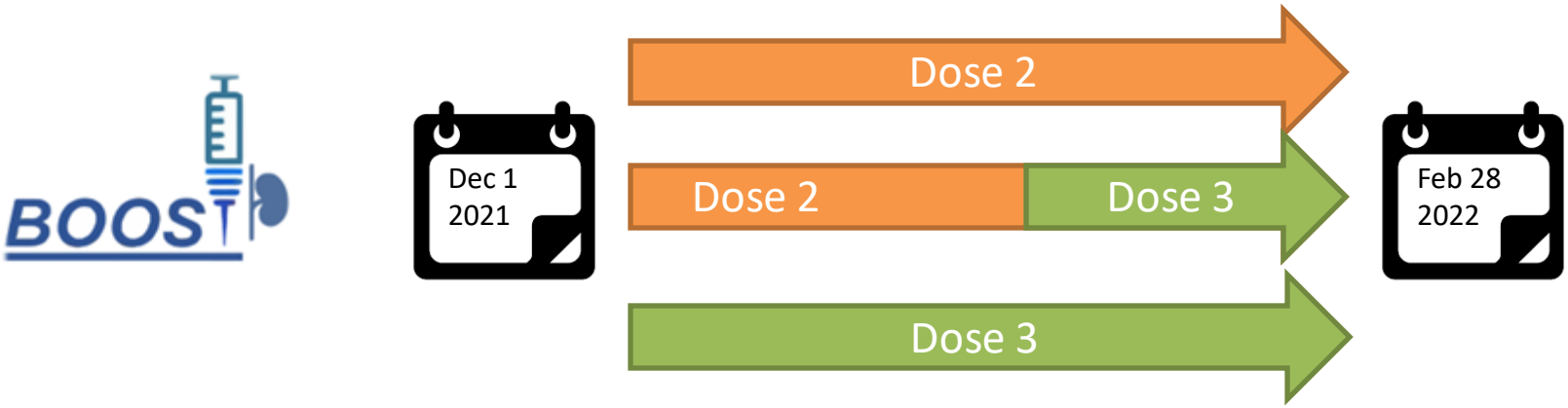
Vaccine Effectiveness of two doses of COVID-19 Vaccine in the pre-Omicron era in the maintenance dialysis population

HRs were adjusted for age, sex, ethnicity, dialysis modality, Charlson comorbidity index, economic dependency quintiles, long-term care residences, vintage, number of RT-PCR tests prior December 21, 2020 and monthly Public Health Unit Region SARS-CoV-2 infection rate. CI = confidence interval, HR = hazard ratio.

Oliver et al. JASN 33: 839–849, 2022.

The Omicron Era

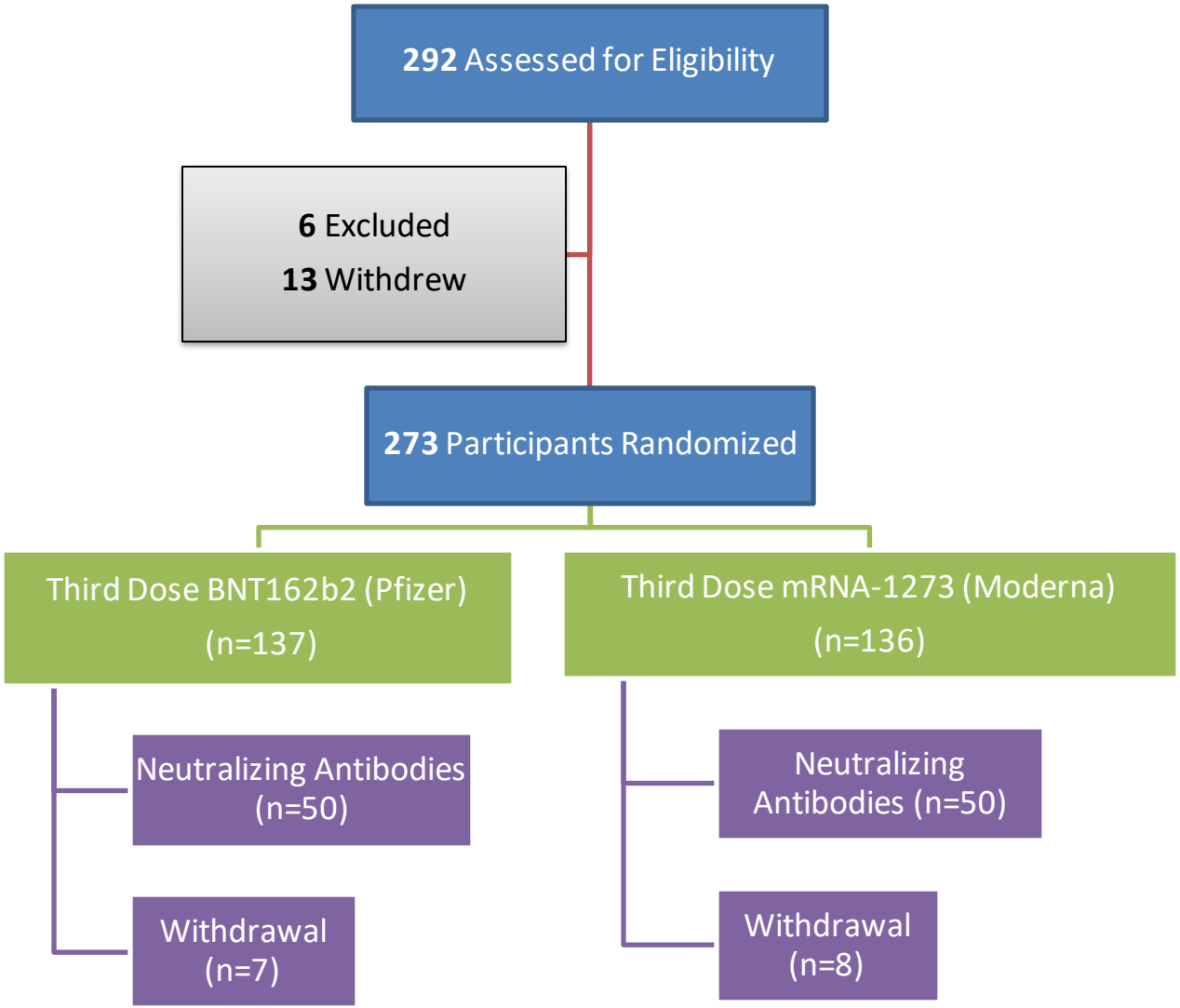
What is the vaccine effectiveness of a third dose of a mRNA COVID-19 vaccine in the maintenance dialysis population



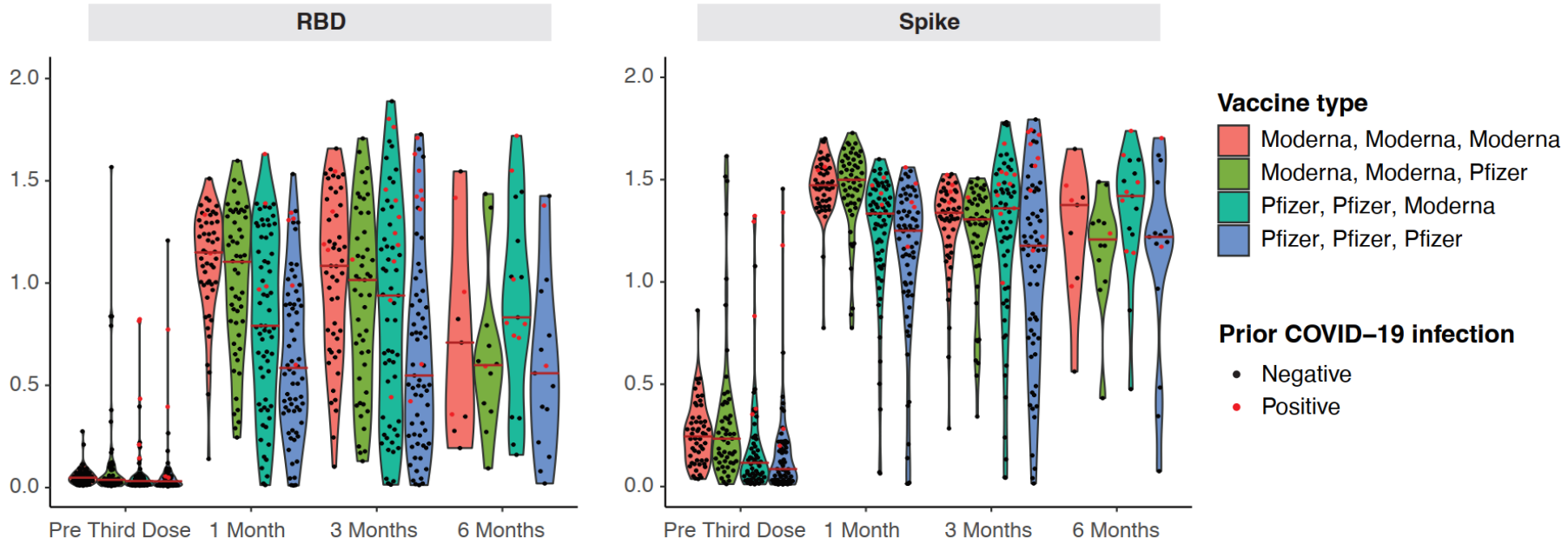
RCT of advanced chronic kidney disease patients (94% dialysis)
N= 273

Cohort study of in-centre hemodialysis patients in Ontario
N= 8457

The BOOST RCT

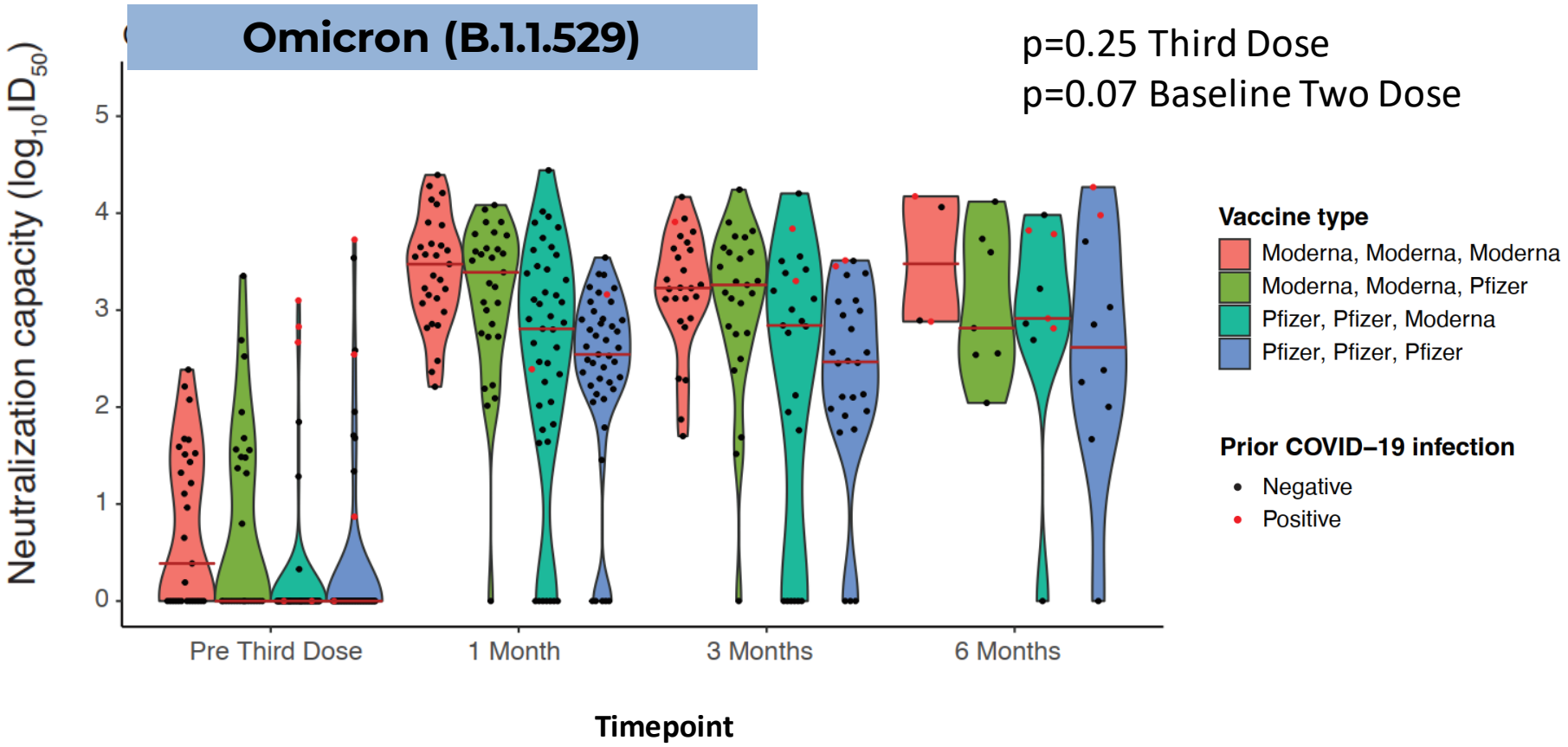


SARS-CoV-2 Binding Antibodies



A hird dose of mRNA-1273 was associated with higher anti-RBD levels (1871 BAU/mL) over a 6-month period in comparison to third dose BNT162b2 (1332 BAU/mL) with a difference of 539 BAU/mL (p=0.009). There was a trend for high levels of anti-spike levels (p=0.06)

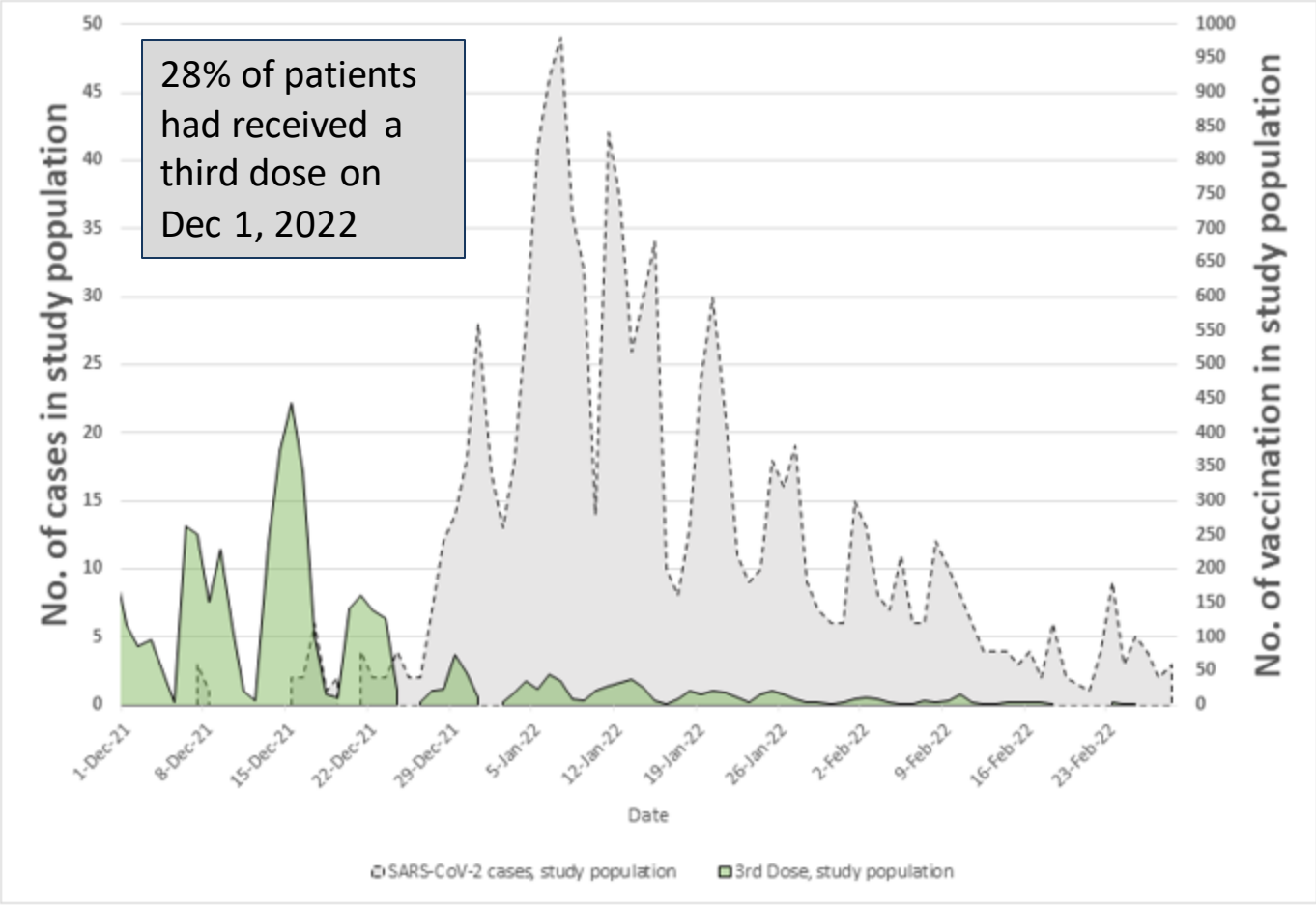
Omicron Neutralizing Antibodies



Neutralizing antibodies to wild-type (p=0.60), Delta (p=0.49), Omicron BA.1 (p=0.35) pseudoviruses were not statistically significantly higher in those receiving a third dose mRNA-1273 in comparison to third dose BNT162b2.

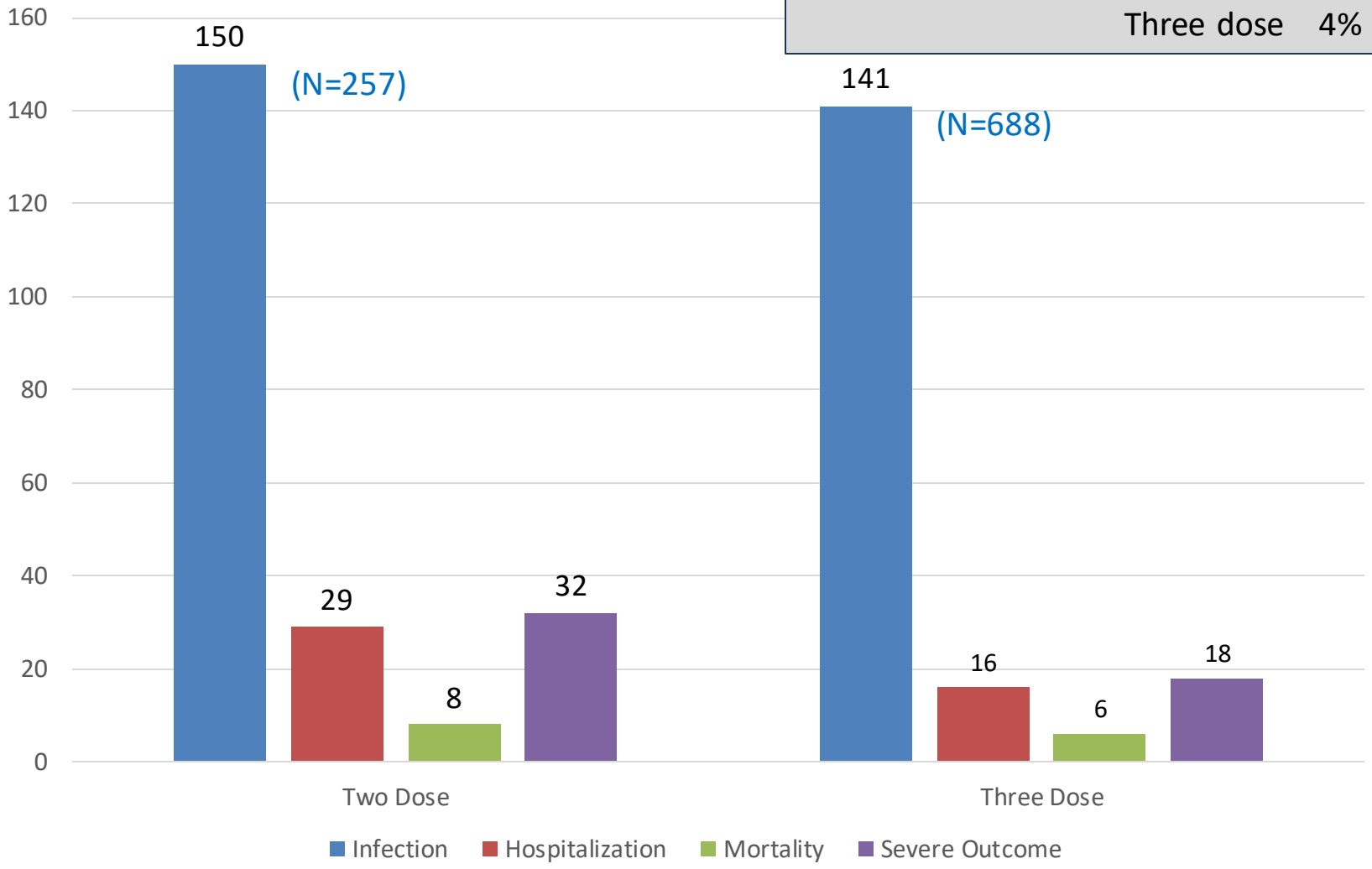
The cohort study

On that Dec 1, 2,334 individuals (28%) had received three doses, and by study completion, 7,468 individuals (88%) had received a third dose



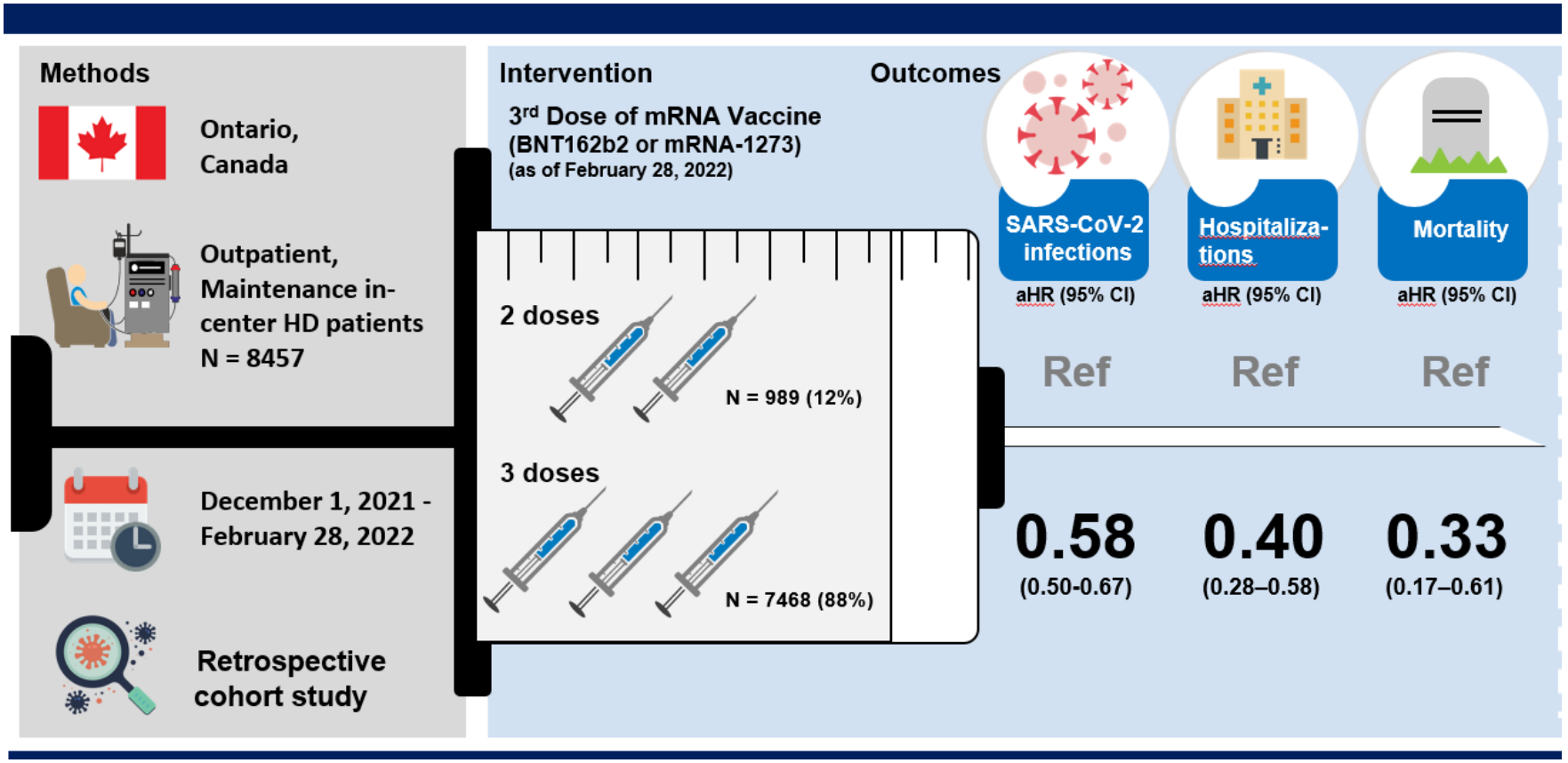
Rates of Infection and Serious Outcomes

Case fatality rate:		
	Two dose	6%
	Three dose	4%



* All rates per 100,000 person-days

Adjusted HR of Outcomes



Wing S et al. Clin J Am Soc Nephrol. 2023 Feb 1.

Prior infection and Vaccine type

Table 3. Subgroup analysis for SARS-CoV-2 infection on the basis of prior SARS-CoV-2 infection and vaccine type

Outcomes	Two Doses		Three Doses		HRs (Unadjusted)[a] (95% CI)	HRs (Adjusted)[a] (95% CI)
Subgroup	Infections, *N*	Rate (100,000 days)	Infections, *N*	Rate (100,000 days)		
No prior Infection	240	154	653	144	0.51 (0.44 to 0.59)	0.57 (0.48 to 0.66)
Prior infection	17	109	35	102	0.72 (0.40 to 1.31)	0.77 (0.39 to 1.54)
mRNA vaccine type[b]						
All BNT162b2	257	156	479	151	0.42 (0.36 to 0.48)	0.50 (0.43 to 0.59)
All mRNA-1273			139	124	0.32 (0.26 to 0.40)	0.34 (0.27 to 0.42)
2 BNT162b2 and 1 mRNA-1273			45	122	0.35 (0.25 to 0.48)	0.38 (0.27 to 0.54)

Reference is two doses.
[a]Data are shown as HRs (95% CI). HRs were adjusted for age, sex, ethnicity, Public Health Unit region, Charlson Comorbidity Index, long-term care residences, cumulative time on dialysis, and income quintile.
[b]mRNA vaccine subtypes reported for three doses. Combinations of mRNA vaccine described for the third dose: all BNT162b2, all mRNA-1272 and 2 BNT162b2/1 mRNA 1273. Additional vaccine combinations made up a minority, and not reported.

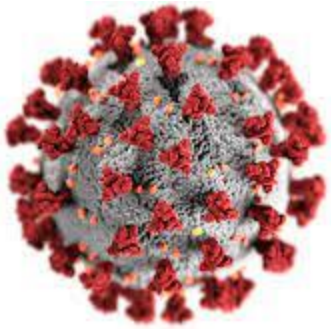
Prior SARS-CoV-2 infection was associated with a reduced risk of reinfection during the Omicron period (aHR, 0.44; 95% CI, 0.27 to 0.73) compared with those without prior infection (Cox model)

The aHR for SARS-CoV-2 infection for three doses of BNT162b2 was 0.50 (95% CI 0.43–0.59), while aHR for three doses of mRNA-1273 was 0.34 (95% CI 0.27–0.42) however this was not significantly different (interaction p-value=0.176).

Wing S et al. Clin J Am Soc Nephrol. 2023 Feb 1.

Prior infection and Vaccine type

Prior SARS-CoV-2 infection



aHR, 0.44; 95% CI, 0.27 to 0.73

aHR 0.17; 95% CI 0.12–0.25

Waning

≤ 3 months after a third dose compared to 2 doses > 6 months

aHR of 0.54 (95% CI, 0.46 to 0.64)

3–6 months after the third dose compared to 2 doses > 6 months

aHR, 0.92 (95% CI, 0.71 to 1.18)

Wing S et al. Clin J Am Soc Nephrol. 2023 Feb 1.

Conclusions

1. A 3rd dose of an mRNA COVID-19 vaccine caused a variable but robust antibody response for the majority of dialysis patients although a small number did not respond.
2. The mRNA-1273 vaccine had a greater level of antibody response but differences in clinical outcomes were not demonstrated in the RCT (not powered for clinical outcomes).
3. The 3rd dose significantly reduced infection and severe outcomes in the dialysis population but the vaccine effectiveness was less than with two doses of vaccine in the pre-Omicron era.
4. The case mortality in the Omicron era (4 to 6%) was substantially less than in the pre-vaccination period (26%) or in the pre-Omicron era with two dose of vaccine (10%).
5. Prior infection was protective and some evidence of waning was demonstrated although power is limited in this relatively small, although high risk population.

Challenges and Insights

1. Kidney disease researchers had to take a “crash course” on vaccine effectiveness to measure the vaccine effectiveness in their high risk population.
2. The dialysis population presented unique challenges for studying vaccine effectiveness including high rates of symptoms (often not recorded) and high rates of asymptomatic testing of during outbreaks.
3. Despite having access to provincial databases, we had limited power to examine subgroups (e.g. vaccine type, waning)
4. Measuring VE was a “moving target” as new variants emerged along with multiple vaccine doses over different time periods (waning).

Many Thanks

Levin A, Perl J, Chan CT, Dixon S, Naylor K, McArthur E, Kwong J, Gingras A, Hu Q, Abe KU, Qi F, Colwill K, Bolotin S, Leis J, Tsui H, Blake PG, Cooper R, Yau K, Thomas D, Balamchi S, Ip J, Atiquzzaman M, Djurdjev O, Lee E, Hladunewich MA.

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