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COVID-19 Vaccine Immunogenicity based on Immune Compromised Status: A Stop the Spread Ottawa (SSO) Analysis

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Introduction

- Questions remain regarding the immunogenicity of SARS-CoV-2 vaccines.
- Generalizability of COVID-19 vaccine clinical trials limited due to eligibility criteria.
- Observational research in diverse populations is valuable to fill knowledge gaps.

- SSO is a prospective longitudinal cohort created to address these gaps.

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Methods

- 1,034 adults in the Ottawa region at risk for or who have been infected with SARS-CoV-2 recruited beginning Sept 2020
- 10-months initial phase
- Optional 24-month extension phase.

- Convalescent Cohort:
  - COVID-19 infection or vaccination history - monthly blood draws.
- Surveillance Cohort:
  - no history of infection - blood draws at M0,3,10.

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Methods

- Specifically assessed immune compromised SSO participants
- Data cut Sept 2022
- IgG titres against SARS-CoV2 Spike (S) and receptor binding domain (RBD) proteins (BAU/mL).
- IgG titres were log-adjusted and predictors of vaccine immunogenicity were identified through multivariable quantile regression analysis.

Results

Table 1: Participant baseline characteristics.

Variable	Study Cohort (n=1,034)	Immune Compromised (n=316)	Non-Immune Compromised (n=718)	P value
Age				
Mean (SD)	45.0 (13.90)	50.6 (13.99)	42.5 (13.14)	<0.0001
Range (min, max)	61 (18, 79)	61 (18, 79)	58 (18, 76)	
Sex, n (%)				
Male	340 (32.9)	119 (37.7)	221 (30.8)	0.03
Female	694 (67.1)	197 (62.3)	497 (69.2)	
Race, n (%)				
Indigenous	19 (1.9)	4 (1.3)	15 (2.1)	0.21
Arab/West Asian	20 (1.9)	4 (1.3)	16 (2.2)	
Black	9 (0.9)	3 (1.0)	6 (0.8)	
Southeast Asian	17 (1.7)	10 (3.2)	7 (1.0)	
Latin American	9 (0.9)	1 (0.3)	8 (1.1)	
South Asian	15 (1.5)	5 (1.6)	10 (1.4)	
White	916 (89)	283 (89.6)	633 (88.8)	
Other	24 (2.33)	6 (1.9)	18 (2.5)	

Table 1: Participant baseline characteristics.

Variable	Study Cohort (n=1,034)	Immune Compromised (n=316)	Non-Immune Compromised (n=718)	P value
Immigration Status, n (%)				
Born in Canada	879 (87.2)	255 (83.3)	624 (88.8)	0.02
Immigrated to Canada	130 (12.9)	51 (16.7)	79 (11.2)	
Education level, n (%)				
Elementary School	1 (0.1)	0	1 (0.2)	0.20
High School	70 (7.1)	28 (9.2)	42 (6.1)	
Trade/Apprenticeship/Technical	35 (3.6)	12 (4.0)	23 (3.4)	
Community College	219 (22.2)	76 (25.1)	143 (20.9)	
University Certificate	28 (2.8)	10 (3.3)	18 (2.6)	
Bachelor's Degree	407 (41.2)	117 (38.6)	290 (42.4)	
Graduate Degree	227 (23.0)	60 (19.8)	167 (24.4)	
Employed, n (%)				
Yes	837 (83.3)	214 (69.3)	623 (89.5)	<0.0001
No	168 (16.7)	95 (30.7)	73 (10.5)	

Table 1: Participant baseline immune compromised conditions

Immune Compromising Condition [n(%)]	Study Cohort (n=1,034)	Immune Compromised (n=316)	Non-Immune Compromised (n=718)
Asthma/COPD on Medication		114 (36.1)	
Rheumatological Condition		36 (11.4)	
Diabetes		42 (13.3)	
Localized Autoimmune Diseases		12 (3.8)	
Localized Immune Dysfunction		18 (5.7)	
Inflammatory Condition		11 (3.5)	
Excessive Alcohol Consumption		68 (21.5)	
Immunosuppressant Medication*		66 (20.9)	
Organ/Tissue Recipient*		22 (7.0)	
Cancer*		24 (7.6)	
Primary Immunodeficiency*		9 (2.9)	
Neuromuscular Autoimmune Diseases*		3 (1.0)	
HIV**		32 (10.1)	

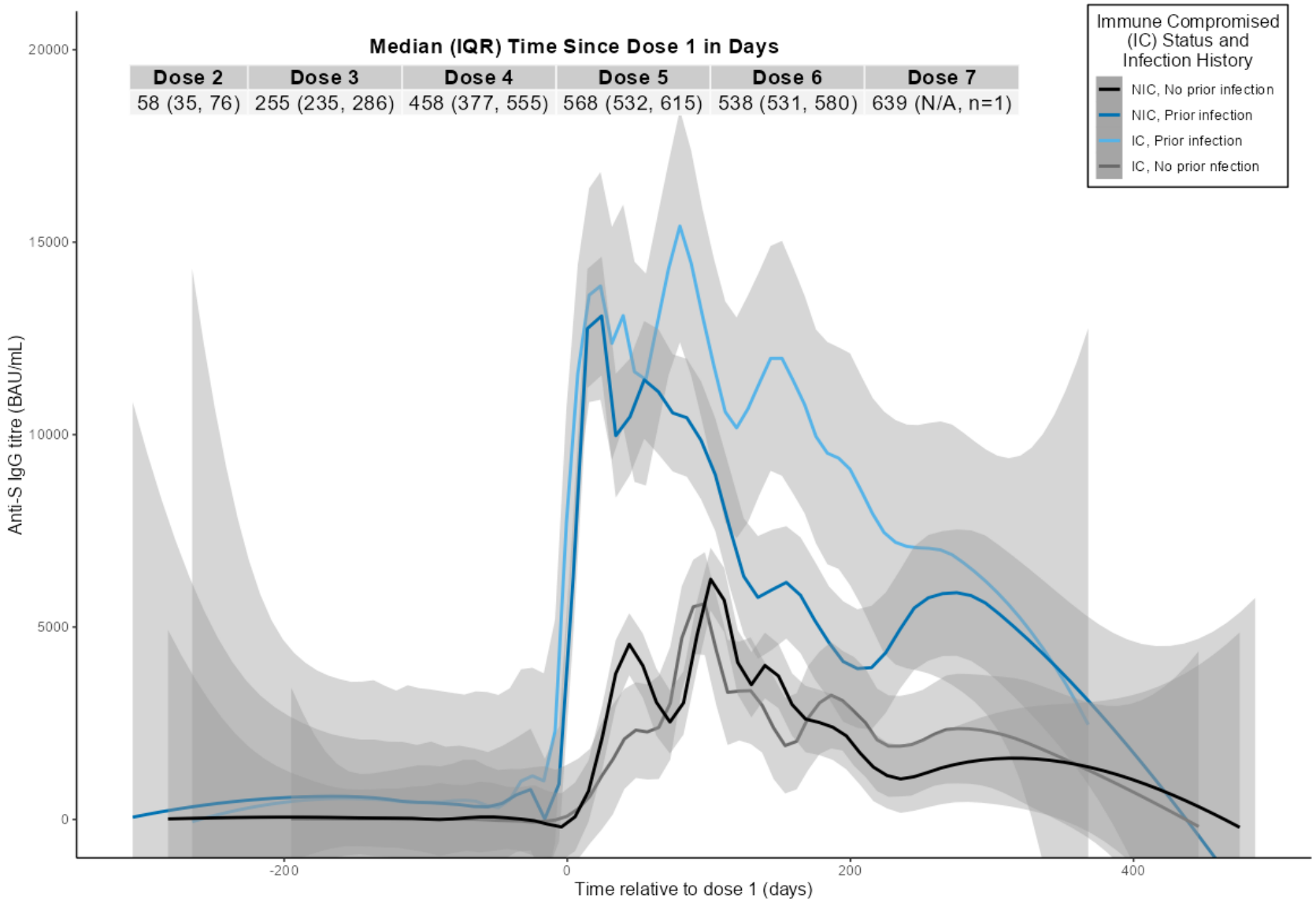
* High-level immune comprised

** Unsuppressed HIV RNA included as high-level IC

Table 1: Participant vaccination history

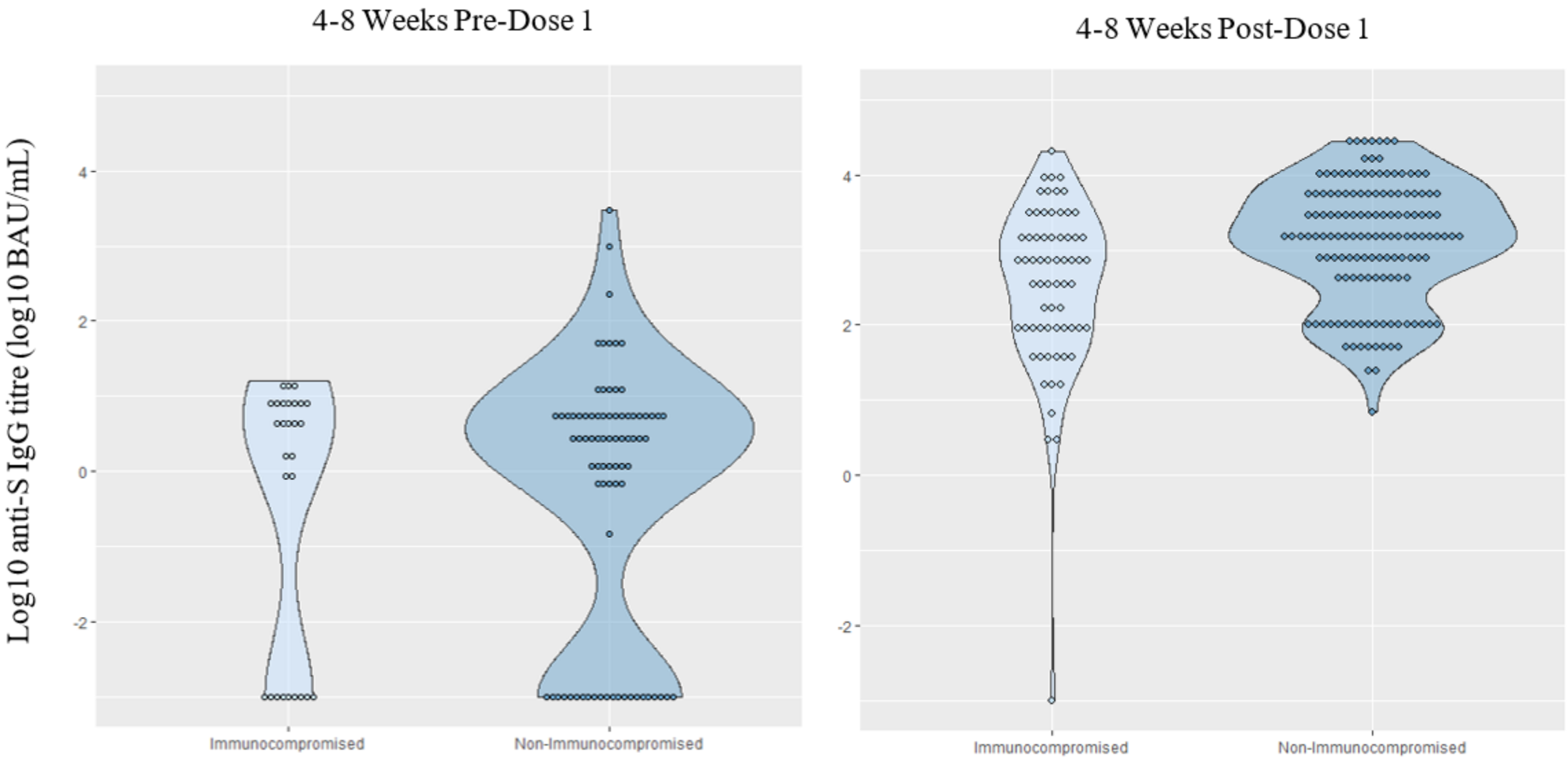
Variable	Study Cohort (n=1,034)	Immune Compromised (n=316)	Non-Immune Compromised (n=718)	P value
Vaccinated at time of analysis (self-reported), n (%)				
Yes	952 (98.7)	293 (98.7)	659 (98.7)	1.00
No	13 (1.4)	4 (1.4)	9 (1.4)	
Number of COVID-19 vaccine doses received at time of analysis (self-reported), n (%)				
None	13 (1.4)	4 (1.4)	9 (1.4)	<0.0001
1	8 (0.8)	1 (0.3)	7 (1.1)	
2	259 (26.8)	56 (18.9)	203 (30.4)	
3	562 (58.2)	171 (57.6)	391 (58.5)	
4	119 (12.3)	61 (20.5)	58 (8.7)	
5	4 (0.4)	4 (1.4)	0	
Time between first and second doses in days	n=928	n=289	n=639	
Median (IQR)	58 (35, 76)	58 (35, 71)	58 (35, 77)	0.52
Range	333 (11, 223)	128 (19, 147)	333 (11, 223)	

Figure 1: Loess curve of anti-S IgG titres (BAU/mL) over time



Data following infections following vaccination excluded.

Figure 2: Violin plots of IgG titres (log10 BAU/mL) against the SARS-CoV-2 **spike** protein at time points prior to and following COVID-19 vaccination, according to immune compromised or non-immune compromised status at baseline (no prior COVID infection).



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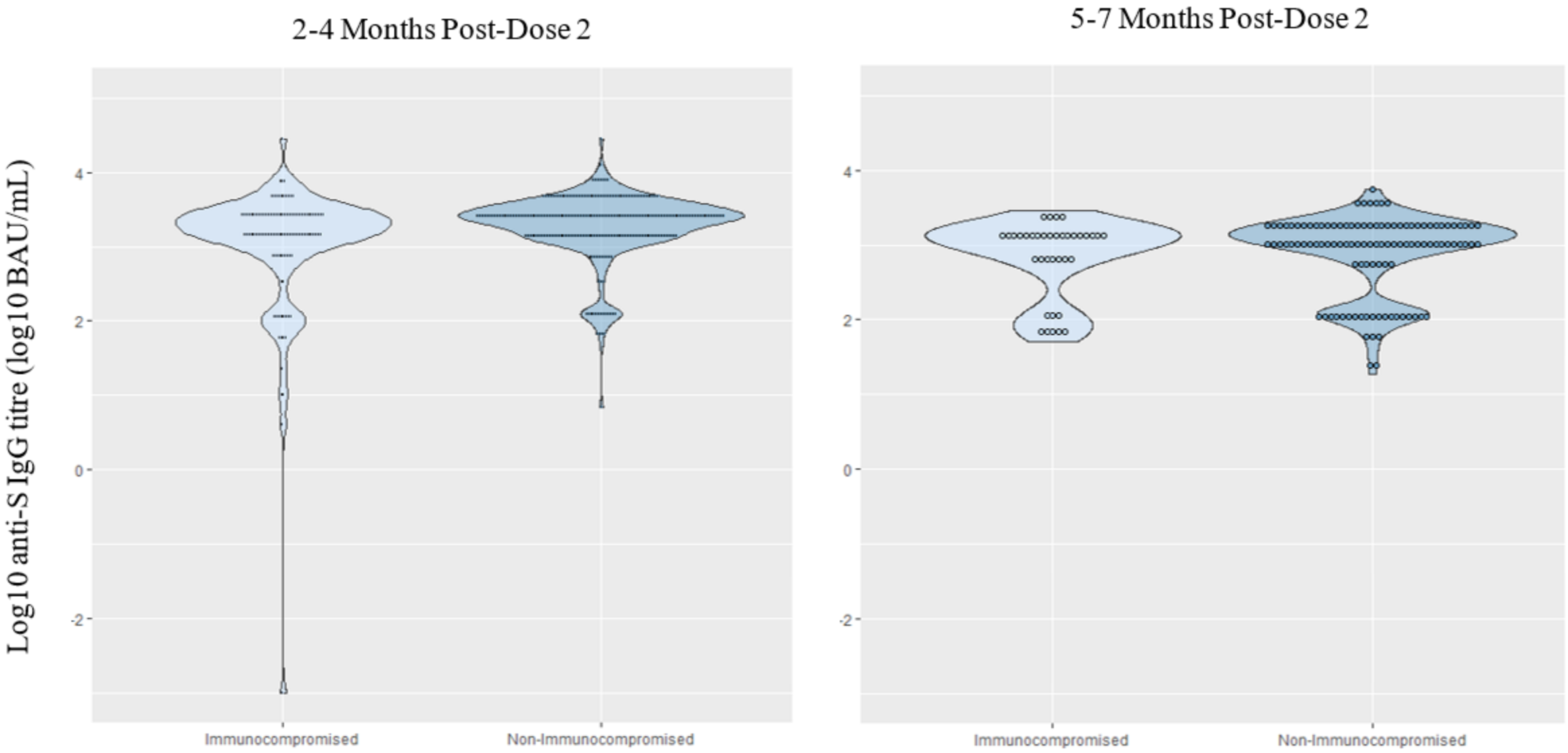


Table 2a: Difference in median log-adjusted IgG titres (log10 BAU/mL) against the SARS-CoV-2 **Spike** protein following the initial two COVID-19 vaccine doses by multivariable quantile regression: **No history of SARS-CoV-2 infection**

IgG Spike (log10 BAU/mL)				
Variable	3 months post dose 2 (±1 month)		6 months post dose 2 (±2 months)	
	Difference (95% CI)	P value	Difference (95% CI)	P value
Age (per 1 year increase)	-0.0049 (-0.0101, 0.0002)	0.06	0.0016 (-0.0039, 0.0071)	0.57
Sex				
Male	0.0974 (0.0035, 0.1913)	0.09	0.0316 (-0.1799, 0.2431)	0.77
Female	Referent		Referent	
Race				
Non-White	-0.0051 (-0.2193 0.2091)	0.96	-0.0226 (-0.6573, 0.6121)	0.94
White	Referent		Referent	
Body Mass Index	-0.0034 (-0.0119 0.0051)	0.43	-0.0032 (-0.0132, 0.0068)	0.53
Immune Compromised				
High	-0.1972 (-0.3818 -0.0126)	0.04	-0.1000 (-0.4477, 0.2478)	0.57
Low	-0.0859 (-0.1932 0.0213)	0.12	-0.0873 (-0.2203, 0.0458)	0.20
No	Referent		Referent	
Tobacco Smoking				
Current or former smoker	-0.1563 (-0.2443 -0.0683)	<0.001	-0.0391 (-0.1656 0.0874	0.54
Never smoker	Referent		Referent	
Allergies				
Yes	0.0941 (0.0120 0.1763)	0.03	0.0813 (-0.0242, 0.1868)	0.13
No	Referent		Referent	
Types of COVID-19 vaccines received, dose 1 & 2				
ChAdOx1-mRNA	0.0885 (-0.0652 0.2421)	0.26	-	
mRNA-mRNA	Referent		-	
Time between first and second doses, in days	-0.0001 (-0.0022 0.0020)	0.91	0.0032 (-0.0000, 0.0064)	0.05

Specific Immune Compromising Conditions

- IgG Spike 3 months post Dose 2 in those without prior COVID at baseline – univariate analysis
  - High Level Immune Suppression - yes
  - Organ/Tissue Transplant - yes
  - Excess Alcohol - yes
  - HIV - no

Table 2b: Difference in median log-adjusted IgG titres (log10 BAU/mL) against the SARS-CoV-2 **Spike protein** following the initial two COVID-19 vaccine doses by multivariable quantile regression:
History of SARS-CoV-2 infection prior to vaccination.

IgG Spike (log10 BAU/mL)				
Variable	3 months post dose 2 (±1 month)		6 months post dose 2 (±2 months)	
	Difference (95% CI)	P value	Difference (95% CI)	P value
Age (per 1 year increase)	0.0038 (-0.0046, 0.0122)	0.37	0.0102 (-0.0015, 0.0218)	0.09
Sex				
Male	-0.0166 (-0.2198, 0.1867)	0.87	0.1455 (-0.0626, 0.3536)	0.17
Female	Referent		Referent	
Race				
Non-White	0.6247 (-0.3077, 1.5571)	0.19	-0.0758 (-1.6848, 1.5332)	0.93
White	Referent		Referent	
Body Mass Index	0.0169 (-0.0050, 0.0388)	0.13	0.0062 (-0.0284, 0.0408)	0.72
Immune Compromised				
High	0.0855 (-0.3396, 0.5105)	0.69	-0.1633 (-0.4716, 0.1451)	0.29
Low	-0.0356 (-0.3051, 0.2339)	0.79	0.2818 (-0.6421, 1.2058)	0.55
No	Referent		Referent	
Types of COVID-19 vaccines received, dose 1 & 2				
At least one ChAdOx1 dose	-0.1773 (-0.5204, 0.1658)	0.31	-	
mRNA-mRNA	Referent		-	
Time between first and second doses, in days	-0.0014 (-0.0060, 0.0031)	0.54	-0.0026 (-0.0091, 0.0039)	0.42
Time from SARS-CoV-2 infection to dose 1	0.0006 (-0.0004, 0.0015)	0.23	0.0002 (-0.0011, 0.0015)	0.72

Similar results for RBD

Immunogenicity with Subsequence Vaccine Doses

- 3rd Dose – 3 months post without prior COVID infection
  - IgG Spike diminished in IC (p=0.05)
  - no difference in those with prior COVID infection
- 4th Dose - nil
- 5th Dose - nil

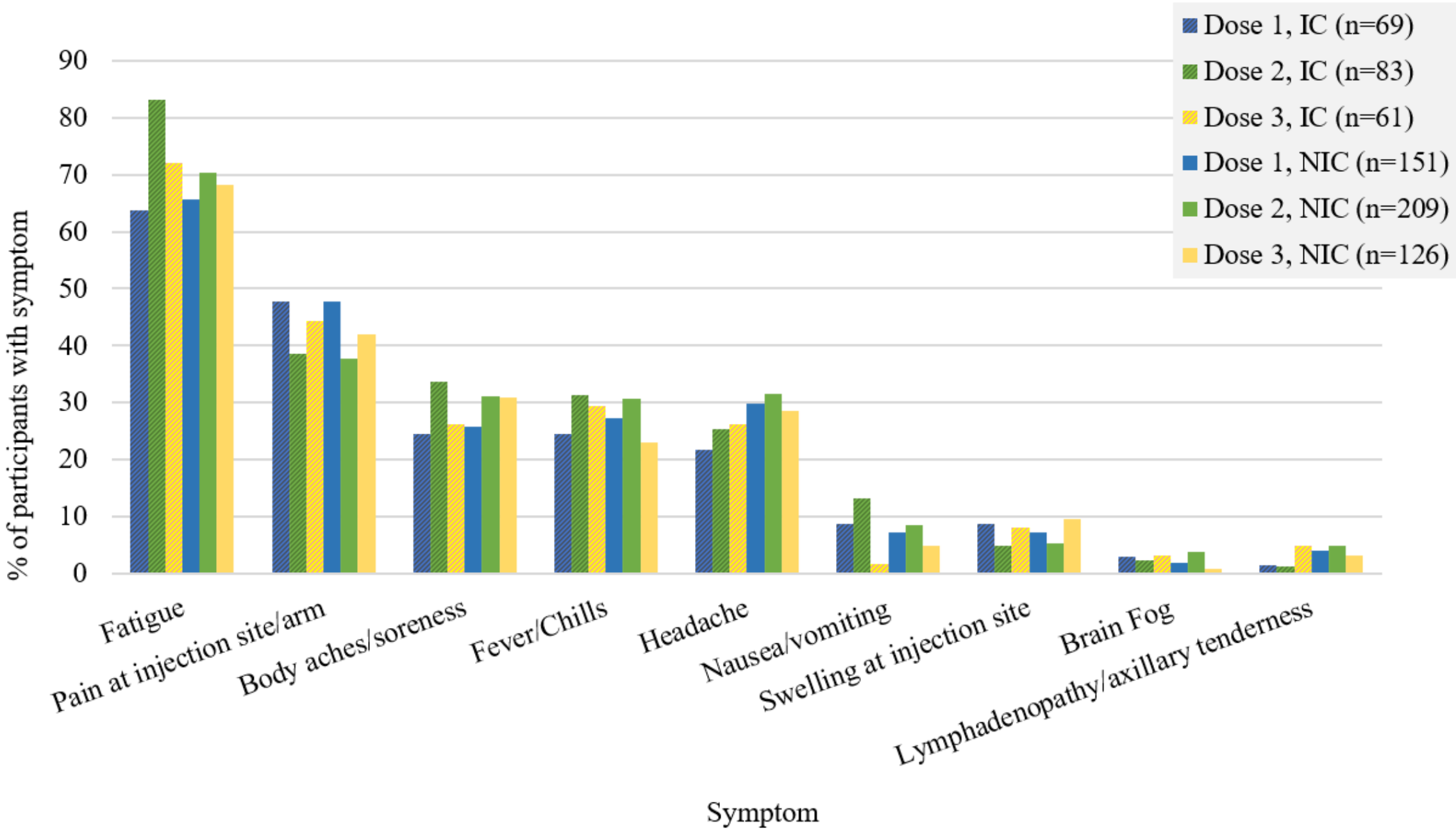
Table 3: Vaccination status of immune compromised (IC) and non-immune compromised (NIC) participants following COVID-19 vaccination.

- Vaccine-based immunity if IgG+ (SCO>1) for SARS-CoV-2 spike and RBD proteins
- No COVID infection at baseline

Adjusted for age, sex, ethnicity, and time between vaccine doses

Time point	Proportion with vaccine-based immunity (%)		Unadjusted odds ratio of vaccine-based immunity		Adjusted odds ratio of vaccine-based immunity	
	IC	NIC	IC vs NIC (95% CI), n	P value	IC vs NIC (95% CI), n	P value
6 weeks post dose 1 (±2 week)	55/62 (**88.7%**)	134/135 (**99.3%**)	0.083 (0.009, 0.39) n=197 (IC=62, NIC=135)	<0.01*	0.126 (0.013, 0.61) n=195 (IC=62, NIC=133)	<0.01*
3 months post dose 2 (±1 month)	73/78 (**93.6%**)	182/183 (**99.5%**)	0.110 (0.011, 0.56) n=261 (IC=78, NIC=183)	<0.01*	0.174 (0.016, 1.06) n=260 (IC=78, NIC=182)	0.06
6 months post dose 2 (±2 months)	37/38 (**97.4%**)	91/91 (**100%**)	0.137 (0.00093, 2.620) n=129 (IC=38, NIC=91)	0.18	0.2293 (0.0016, 5.74) n=129 (IC=38, NIC=91)	0.36
3 months post dose 3 (±1 month)	47/47 (**100%**)	86/86 (**100%**)	-	-	-	-
3 months post dose 4 (±1 month)	20/20 (**100%**)	24/24 (**100%**)	-	-	-	-
3 months post dose 5 (±1 month)	8/8 (**100%**)	3/3 (**100%**)	-	-	-	-

Figure 3: Reactogenicity by dose number and immune compromised status.



Limitations

- Immune Compromised Classification
- Degree of Immune Compromise
- Missing data and missing time points
- Small samples
- Analysis of vaccine dose 3 and beyond

Conclusions

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- COVID-19 vaccination is safe, well-tolerated
- Highly immunogenic across a broad spectrum of vaccine recipients including those with a range of immune comprising conditions

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Lessons Learned

- Never-ending data catch-up
- Recruitment strategy
- Study team communication