Predictors of SARS-CoV-2 antibody levels following two COVID-19 vaccine doses: Results from the CHILD COVID-19 Add-on Study

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BACKGROUND

- **COVID-19 vaccine-induced immune antibody responses** vary among individuals and wane over time[1].
- The **variation** and **timing** of this immune response is **not fully understood**, particularly in children.

OBJECTIVE

To identify health and sociodemographic factors associated with vaccine-induced SARS-CoV-2 antibody levels among Canadian families after two COVID-19 vaccine doses.

METHODS

We studied a subset of **children** (**n= 172**; mean age: 12.5±1.5 years) and **adults** (**n=1159**, 43.7±5.9 years) vaccinated with **two doses** of the COVID-19 vaccine recruited from the **CHILD Cohort Study**.

The CHILD Study: A general population birth cohort of 3455 families recruited from 2008-12 across four Canadian sites.
The CHILD COVID-19 Add-On Study (Jan 2020 - Mar 2021) is embedded in the CHILD Study and was designed to understand the impact of the COVID-19 pandemic on Canadian families
www.childstudy.ca

Demographic, vaccination, and health information: online questionnaires.

Blood samples: Dried Blood Spot kits between March 2021 and January 2022.

SARS-CoV-2 anti-spike IgG **antibody levels**: automated chemiluminescent ELISAs.

Associations determined by **multivariable linear regression**.

REFERENCE:
1. Collier, D.A. et al. Age-related immune response heterogeneity to SARS-CoV-2 vaccine.... Nature 596 (2021).

RESULTS

Fig. 1 Age and biological sex of participants (n= 1331)

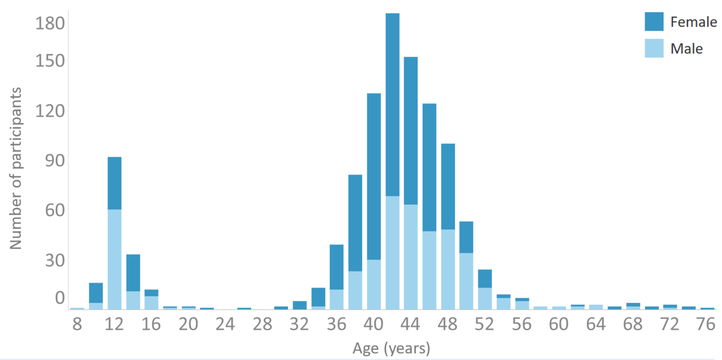
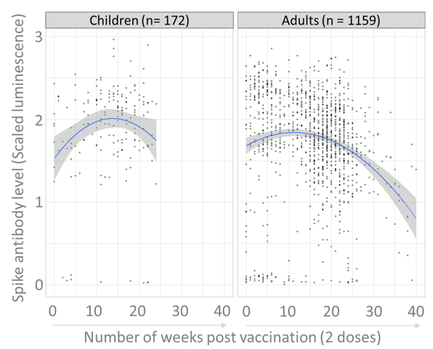


Fig. 2 Antibody levels after two COVID-19 vaccine doses



- Lines and shaded bands represent fit and 95% confidence intervals from polynomial linear regression.
- For both adults and children, the highest antibody levels were observed around 3 months post-vaccination.

Fig. 3 Multivariable linear regression: predictors of SARS-CoV-2 antibody levels following two COVID-19 vaccine doses (n= 1329)

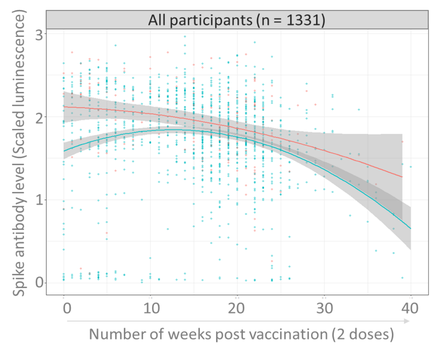
Predictors	n (%)	β - Estimates	95% CI
Vaccine type			
Mixed mRNA-viral vector vaccine	327 (25)	0.00	[reference]
AstraZeneca-Oxford vaccine	37 (3)	-0.54	(-0.73,-0.35)***
Mixed mRNA vaccine	92 (7)	0.12	(-0.01, 0.25)
Moderna mRNA vaccine	131 (10)	0.17	(0.06, 0.29)**
Pfizer-BioNTech vaccine	725 (55)	0.07	(-0.01, 0.15)
SARS-CoV-2 infection status			
No previous infection	1143 (86)	0.00	[reference]
Previous SARS-CoV-2 infection	186 (14)	0.20	(0.11, 0.29)***
†**Comorbidities**			
No immunosuppressive comorbidities	1159 (87)	0.00	[reference]
Underlying immunosuppressive comorbidities	170 (13)	-0.08	(-0.18, 0.02)
Age-group			
Adults	1159 (87)	0.00	[reference]
Children	172 (13)	0.11	(0.01, 0.21)*
Biological sex			
Female	786 (59)	0.00	[reference]
Male	543 (41)	0.01	(-0.05, 0.08)
Interval between vaccine doses			
9 - 16 weeks	710 (55)	0.00	[reference]
3 – 8 weeks	581 (45)	0.02	(-0.05, 0.09)
Elapsed time post-vaccination			
0 - 1 months	168 (13)	0.00	[reference]
2 - 3 months	270 (20)	0.18	(0.07, 0.30)**
4 - 6 months	807 (61)	0.07	(-0.03, 0.17)
> 6 months	83 (6)	-0.28	(-0.44,-0.12)**

-0.5 0 0.5 *p*-value *** ≤0.001; ** ≤0.01; * ≤0.05

*Immunosuppressive comorbidities include current diagnosis of cancer, diabetes, pneumonia and severe obesity.

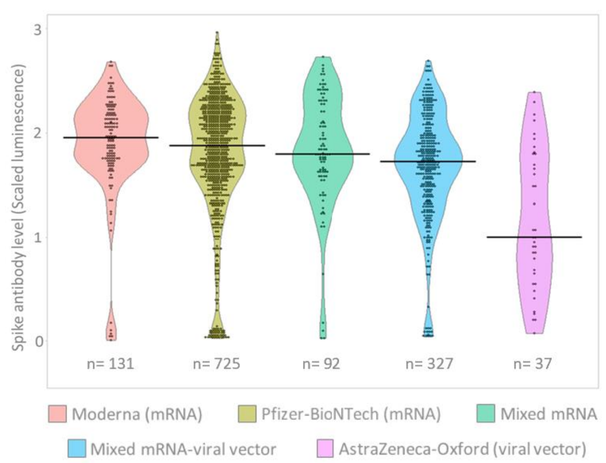
Lower SARS-CoV-2 antibodies — Higher SARS-CoV-2 antibodies

Fig. 4 Antibody levels after two COVID-19 vaccine doses in infected & infection-naïve participants



- Individuals with prior SARS-CoV-2 infection (by self-report or serology) had higher antibody levels compared to infection-naïve individuals.

Fig. 5 Antibody levels by COVID-19 vaccine received (n= 1331)



KEY FINDINGS

- **Multiple factors** contribute to the **heterogeneity** of COVID-19 vaccine-induced **antibody response**.
- SARS-CoV-2 anti-spike IgG antibodies are **highest approximately 3 months post-vaccination** in both adults and children (cross-sectional data). **Fig. 2**

In a multivariate model **Fig. 3** :

- **HIGHER antibody levels** were associated with: **previous SARS-CoV-2 infection** **Fig. 4** (β=0.20), **age <18 years** (β= 0.11), and receiving the **Moderna vaccine** for both doses (vs. a combination of Moderna or Pfizer or AstraZeneca vaccines; β=0.17).
- **LOWER antibody levels** were associated with: receiving the **AstraZeneca vaccine** **Fig. 5** for both doses (β= -0.20;) and being **>6 months post-vaccination** (vs <1 month; β= -0.28).

CONCLUSION

Antibody levels following two doses of COVID-19 vaccination are associated with age, previous SARS-CoV-2 infection, vaccine type, and time since vaccination.

RELEVANCE & NEXT STEPS

This study uniquely offers the opportunity to study COVID-19 vaccine-induced antibody immune response in an established, deeply-phenotyped general population longitudinal cohort.

Next steps will include investigating:

- Other potential correlates of vaccine responses
- Whether predictors differ among children vs. adults
- The role of pre-existing health conditions

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