Guiding COVID-19 Booster Vaccinations by COVID-19 Quantitative Spike Ig Antibody Titers Regardless of HIV Status, Immunosuppression, and Age

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Background

- Limited real-world data are available on the antibody (Ab) response after COVID-19 vaccination, comparing HIV-negative and HIV-positive individuals
- Post vaccination waning Ab levels are highly correlated with risk of re-infection, severe disease, and hospitalization[1,2]
- In-vitro neutralizing antibody (Ab) titers correlated with ~250 IU/mL Spike Ig Ab level for the Delta COVID-19 variant[1]
  - This correlation helped establish the 2021 French and Swiss cutoff for booster guidance
  - This guidance was adopted in a New York City healthcare clinic caring for both people with and without HIV during the COVID-19 pandemic
- A better understanding of vaccination responses in people with and without HIV may inform the use of quantitative Ab testing to determine those at greatest risk for infection and could help in guiding the timing of additional vaccinations

Objectives

Among people with and without HIV:

- To quantify early vaccination response
- To assess the rate of antibody decline over time

Methods

Study Population

- AIDS Healthcare Foundation Manhattan Midtown Healthcare Clinic
  - Prospectively captured, routine clinical data from electronic medical records (EMR)
  - Immunization data abstracted manually from pharmacy and EHR data
- Inclusion criteria
  - Aged 18+
  - Fully vaccinated against SARS-CoV-2 virus (i.e., 2 Pfizer, 2 Moderna or 1 J&J vaccine) between 14Dec2020 and 31OCT2021
  - >1 Roche SARS-CoV-2 Semi-Quant Spike Ig Ab test performed >21 days after vaccination and before a SARS-CoV-2 booster

Stratification

- Vaccine type (Pfizer, Moderna, J&J)
- HIV status (HIV-positive, HIV-negative)
- CD4 cell count (high: >200 cells/μL, low: ≤200 cells/μL)

Vaccine Response

- Assessed at the first Ab test
- Response level
  - Adequate: >250 IU/mL (correlates with in-vitro neutralizing Ab for the Delta COVID-19 variant[1])
  - Inadequate
    - Low: ≥51 to ≤250 IU/mL
    - No response: <51 IU/mL

Antibody decline

- Including all sequential Ab tests over the first 6 months between vaccination and boosting
- Rate of Ab decline over time assessed with linear regression
- Among individuals with ≥2 Ab tests within 6 months between vaccination and boosting

Results

Table 1. Demographic and clinical characteristics at the last dose of initial vaccination, by HIV status

	HIV-negative N = 313	HIV-positive N = 512
Age, n (%)		
18-49	171 (55)	191 (37)
50-64	97 (31)	239 (47)
65+	32 (10)	82 (16)
Female, n (%)	17 (5)	11 (2)
Race, n (%)		
Asian	15 (5)	21 (4)
Black	40 (13)	90 (18)
White	183 (58)	293 (57)
Mixed race/Other	8 (3)	17 (3)
Unknown	67 (21)	91 (18)
Ethnicity, n (%)		
Hispanic	61 (20)	99 (19)
Non-Hispanic	197 (63)	346 (68)
Unknown	55 (18)	67 (13)
Comorbidities,[a] n (%)	213 (68)	448 (88)
Viral load <200 copies/mL, n (%)	NA	471 (92)

[a] Cardiovascular disease, malignancy, hypertension, endocrine disorder (diabetes mellitus, dyslipidemia, thyroid disease), mental health conditions, liver disease (HBC, HCV, chronic liver disease), renal disease (moderate/severe), autoimmune disease (rheumatoid arthritis, lupus, Crohn's disease, ulcerative colitis), substance abuse (alcohol, drugs, marijuana)

Figure 1. Antibody response level by vaccine type among **HIV-negative** individuals (N = 313)

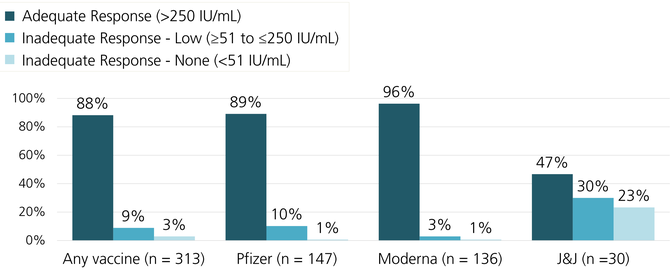


Figure 2. Changes in antibody level in the first six months after vaccination and before any booster dose, among **HIV-negative** individuals with ≥2 Ab tests (N = 38)

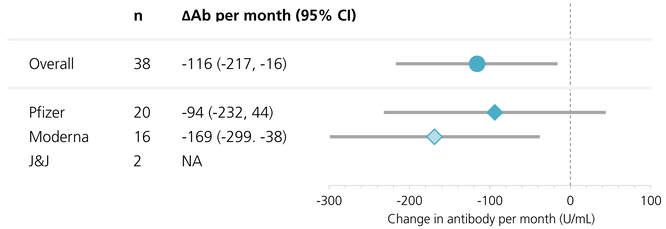
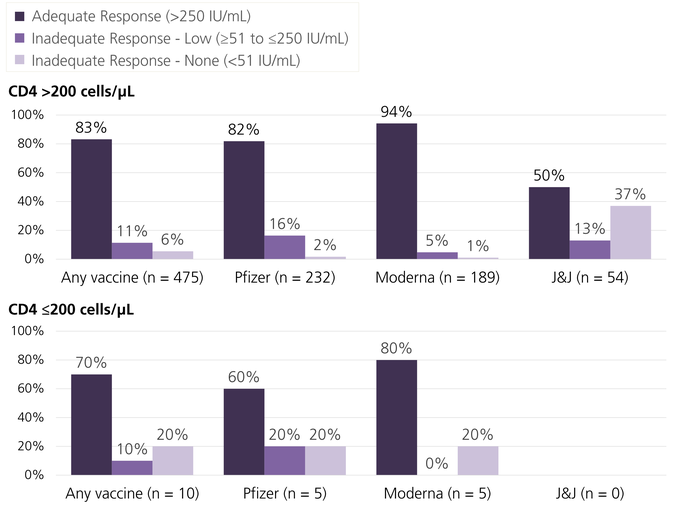
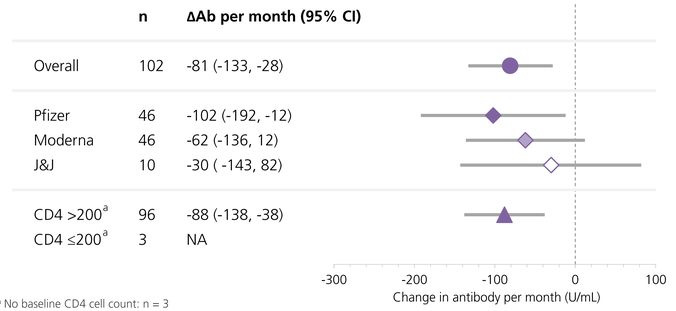


Figure 3. Antibody response level by vaccine type and CD4 cell count among **HIV-positive** individuals (N = 485)[a]



[a] No baseline CD4 cell count: n = 27

Figure 4. Changes in antibody level in the first six months after vaccination and before any booster dose, among **HIV-positive** individuals with ≥2 Ab tests (N = 102)



[a] No baseline CD4 cell count: n = 3

Table 2. Antibody response and changes in antibody levels overall and by HIV status

	Overall N = 825	Pfizer N = 390	Moderna N = 344	J&J N = 91
Antibody response, n (%)				
Adequate (>250 IU/mL)	700 (85)	329 (84)	326 (95)	45 (49)
Inadequate - Low (≥51 to ≤250 IU/mL)	86 (10)	55 (14)	14 (4)	17 (19)
Inadequate - None (<51 IU/mL)	39 (16)	6 (2)	4 (1)	29 (32)
≥2 Ab <6 months after vaccination, N	140	66	62	12
ΔAb per month (95% CI)	-91 (-138, -44)	-100 (-175, -25)	-91 (-156, -26)	-42 (-174, 90)

Δ, delta (change); Ab, antibody; CI, confidence interval; IU, international unit; mL, milliliter; N, number

Discussion

- Overall, 85% of vaccine recipients had an adequate immune response to primary COVID immunization (**Table 2**)
  - mRNA vaccines generally yielded adequate Ab responses, although an inadequate response was observed in 16% of Pfizer and 5% of Moderna recipients
  - The response to the J&J vaccine was more modest, with 51% of recipients experiencing an inadequate response
  - Findings were similar across strata of HIV status and CD4 cell count (**Fig 1, Fig 3**)
- Overall, Ab levels decreased at an average rate of 91 IU/mL per month (95% CI: -138, -44) after primary immunization (**Table 2**)
  - While some variation was observed across strata of HIV status, vaccine type and CD4 cell count, rates of Ab decay were generally consistent (**Fig 2, Fig 4**)
- No relationship between age and Ab levels was observed (not shown)
- Variability in vaccine responses and Ab declines show the utility of measuring spike Ig Ab levels rather than using empiric time frames for booster guidance
- This study focused on primary immunization in the pre-omicron era, with follow-up extending beyond the arrival of the Omicron wave in the US. Findings may thus not be applicable to infection with new variants.
  - Omicron-specific quantitative IgG neutralization levels must be established to inform therapeutic prevention of COVID-19 by vaccination and the optimal timing for booster vaccinations

Key Findings

- An adequate vaccine response was more likely with mRNA vaccines, although 5-16% of mRNA had inadequate vaccine responses to the primary COVID-19 vaccine series
- Antibody levels declined over time after initial vaccination at an approximate rate of 100 IU/ml/month
- Antibody levels may represent a useful tool when assessing the adequacy of vaccine response as well as the timing of additional booster doses

References

1. Bergwerk, M. et al., Covid-19 Breakthrough Infections in Vaccinated Health Care Workers NEJM 7/28/21
2. Goldberg et al. Waning immunity of the BNT162b2 vaccine: A nationwide study from Israel. https://www.medrxiv.org/content/10.1101/2021.08.24.21262423v1.full-text
3. Planas, Delphine, Veyer, David, Schwartz, Olivier, et al., "Reduced sensitivity of SARS-CoV2Variant Delta to antibody neutralization," NATURE, Vol. 596, 08 July 2021, 276-280.

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