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Abstract

Background: People living with HIV (PWH) are at increased risk for complications from influenza and the antibody responses after influenza vaccination are lower in PWH than in general population. Our lab has previously reported on paradoxical aging in HIV: immune senescence of B Cells is most prominent in young age¹. High doses (HD) of influenza vaccine are being administered to people over age 65 to improve immunogenicity. In this study, we compared the standard dose (SD) and HD flu vaccine induced Ab responses in young (≤40 yrs) and old (≥60 yrs) PWH and people without HIV (PWoH) in a longitudinally followed FLORAH cohort.

Methods: Participants were divided into four groups based on age and HIV status as Young PWoH (YPWoH, n=53), Young PWH (YPWH, n=33), Old PWoH (OPWoH, n=57) and Old PWH (OPWH, n=51). All participants received SD vaccine in Year 1. A subset of participants, YPWoH n=14, YPWH n=8, OPWoH n=20, and OPWH n=23 received HD vaccine in the subsequent year. Hemagglutination inhibition (HAI) antibody responses specific to H1N1, H3N2, B1 (Washington/Michigan) and B2 (Phuket) lineages were measured at baseline (T0) and day 28 post-vaccination (T3). In a subset of participants (YPWoH n=7, YPWH n=5, OPWoH n=10, OPWH n=10) flu HA antigen-specific IgG antibody isotypes (Total IgG, IgG1, IgG2, IgG3, and IgG4) were measured by a bead-based multiplex assay. Data were compared using a two-tailed Kruskal Wallis test.

Results: Impaired HAI Ab response to SD vaccination was noted only for the group of YPWH for H3N2 and B2 antigens, that were collectively unaffected after HD vaccination. Baseline titers specific for each antigen or fold change in titers from baseline (FC) were similar for SD and HD vaccine groups. OPWH responded adequately to the SD vaccine and their response did not change after HD vaccination. Among IgG isotypes, no isotype was affected in either PWH or PWoH in young and old after SD vaccination and did not change after HD vaccination.

Conclusion: Our initial analysis concludes that HD vaccination did not significantly enhance the Ab responses in either young and old PWH and PWoH groups and increasing the antigen dose via HD vaccine resulted in increased FC of Ab in very few participants. A key observation was the weaker response to some antigens in YPWH, which supports the concept of premature immunosenescence. Further studies are warranted to understand the cell intrinsic T and B cell defects that could compromise the immunity in PWH.

Background

- People living with HIV (PWH) remain at greater risk from influenza-associated complications owing to lower antibody responses after influenza vaccination in PWH than in general population^{1, 2}
- We previously reported the paradox of immune function with aging in PWH, where immune senescence of B Cells is most prominent in young age³.
- High doses (HD) of influenza vaccine are being recommended to people over age 65 to improve immunogenicity.

Aim

To compare the standard dose (SD) and HD flu vaccine induced Ab responses in Young (≤40 yrs) and old (≥60 yrs) PWH and people without HIV (PWoH) to ascertain the effectiveness of HD vaccine in PWH.

Methodology

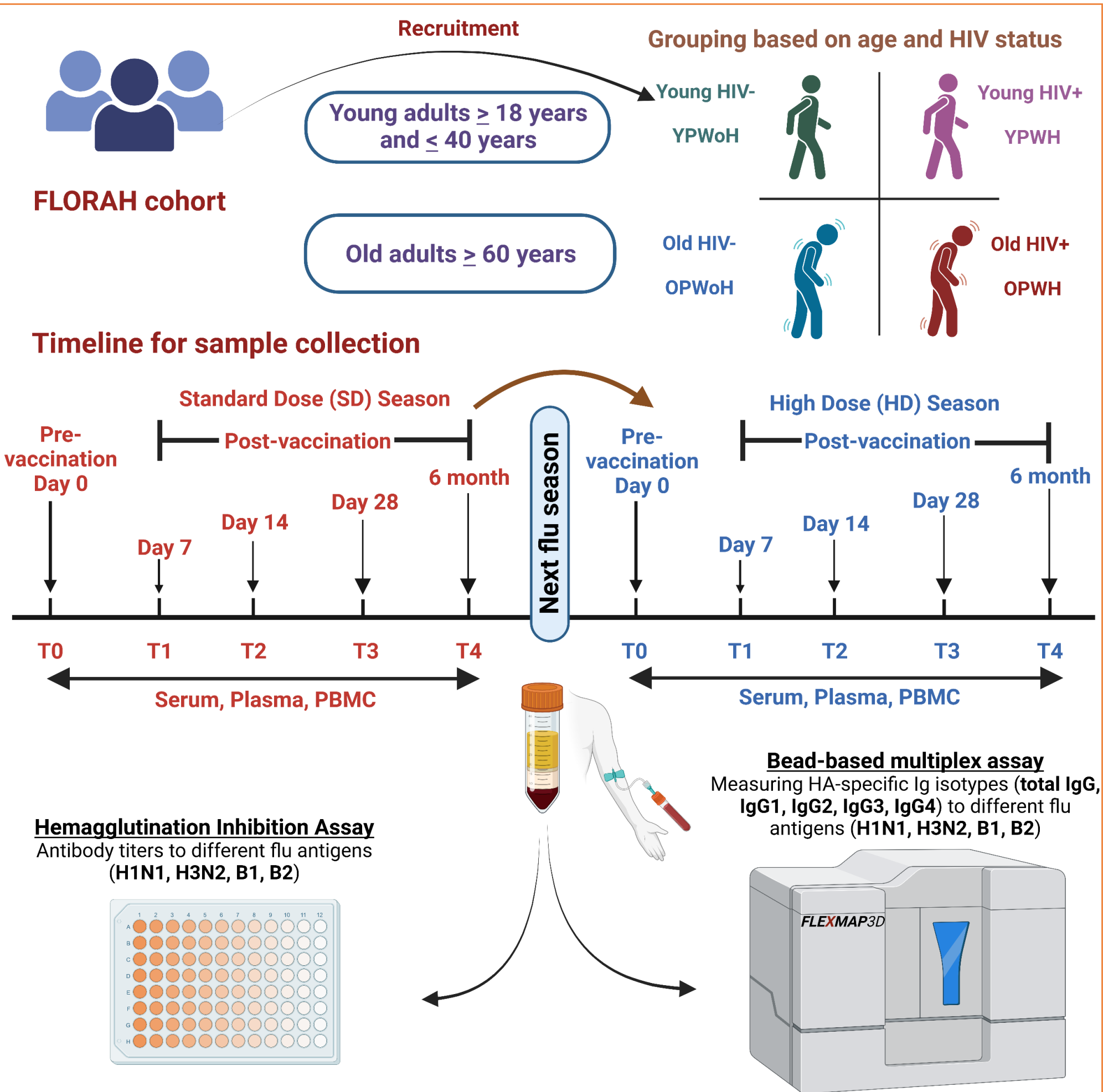


Table 1: Demographic characteristics of the study groups

Population	YPWoH	YPWH	OPWoH	OPWH
N	44	15	47	40
Median age in years (range)	30.5 (23-40)	29 (18-40)	64 (60-85)	64 (60-81)
Gender: Male/Female	20 / 24	10 / 5	32 / 15	26 / 14
Race: WC/AA/NA/A/M*	20/20/0/2/2	6/7/0/0/2	13/34/0/0/0	9/29/1/0/1
Ethnicity: HL/NHL/U**	15/29/0	7/8/0	4/40/0	12/27/1
Cell count-Median (IQR)				
Baseline CD4+ T cell (cells/uL)	1000 (809-1207)	787.5 (568-1022)	770.1 (564-1096)	812.2 (528-1079)
Baseline CD8+ T cell (cells/uL)	483 (359-694)	883.2 (663-1117)	524.4 (278-888)	711 (445-1089)
Baseline CD4/CD8 ratio	2.05 (1.6-2.4)	0.94 (0.6-1.3)	1.8 (1.2-3.2)	1.3 (0.6-1.8)

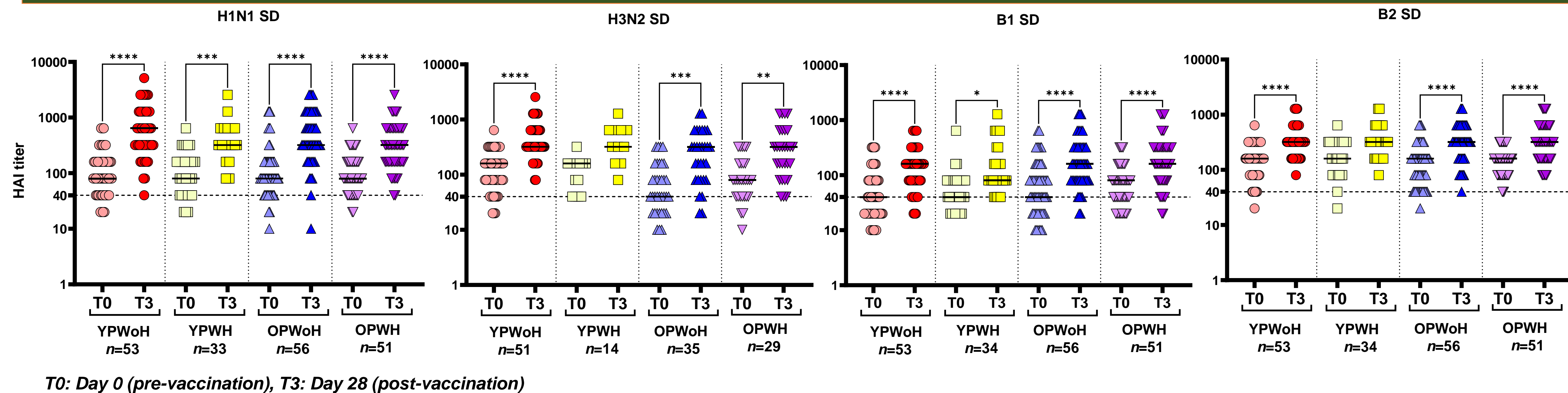
* WC White Caucasian, AA African American, NA Native American, A Asian, M Mixed; ** HL Hispanic/Latino, NHL Non-Hispanic/Non-Latino, U Unknown. A subset of participants from SD vaccine season (2021-2022), YPWoH n=14, YPWH n=8, OPWH n=20, OPWH n=23 received HD vaccine in the subsequent year (2022-2023).

References

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- George, V.K., et al., HIV infection worsens Age-Associated Defects in Antibody Responses to Influenza Vaccine. *J Infect Dis*, 2015.
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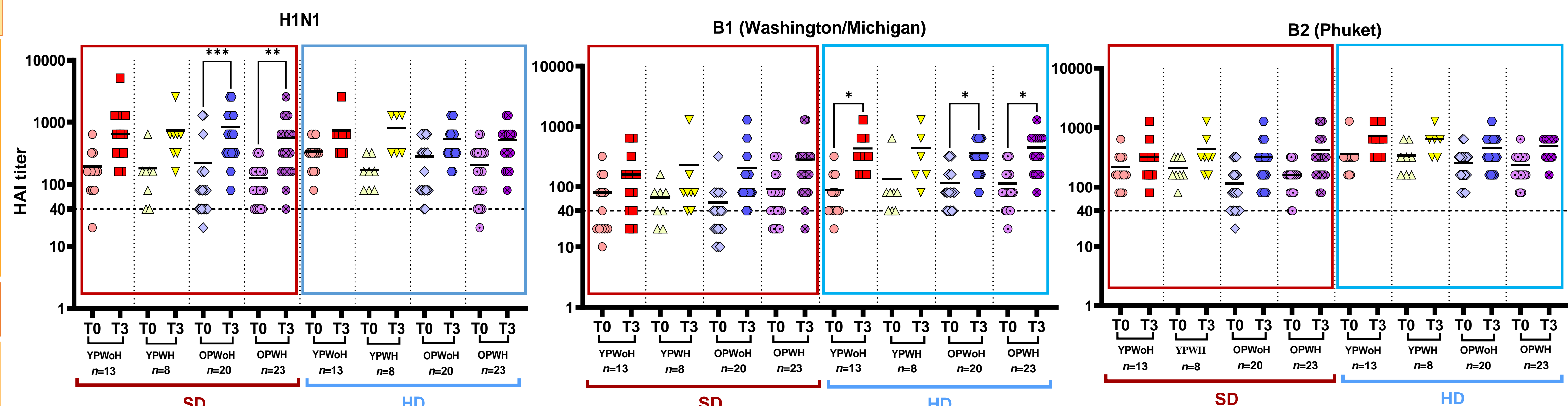
Results

Figure 1: SD Vaccination: All groups except YPWH (YH) showed significant increase in HAI titers to all flu antigens at T3 (Day 28) while YPWH responded only to H1N1 and B1 antigens.



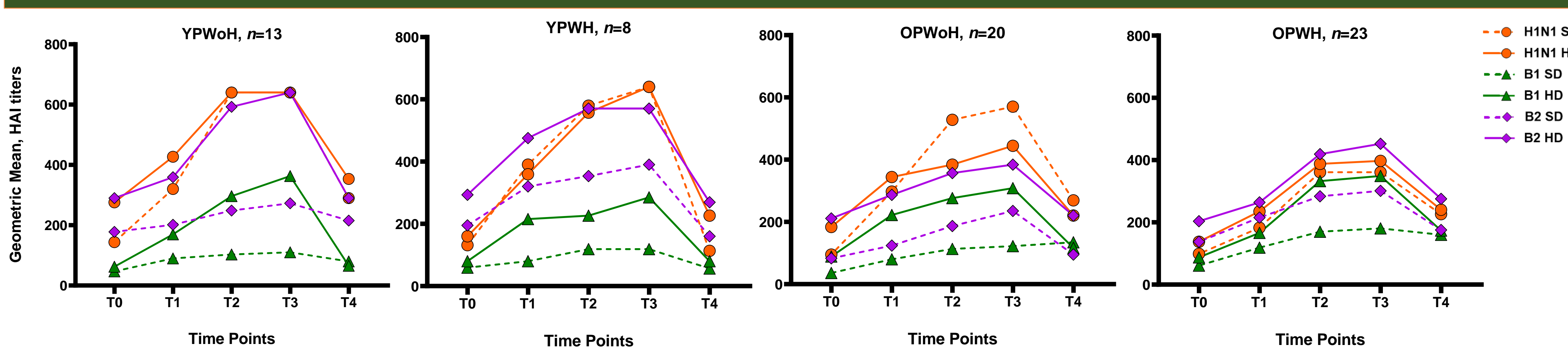
Antibody responses at pre (T0) and post (T3) post-SD vaccination was measured by hemagglutination inhibition (HAI) assay specific for H1N1, H3N2, B1 (Washington/Michigan) and B2 (Phuket) antigens. Data compared using Kruskal-Wallis test with Dunn's correction. Significance between time points and groups indicated by **** p<0.0001; *** P<0.001; **p<0.01; *p<0.05. Horizontal dotted line represents the HAI titer cut-off value.

Figure 2: HD vaccination: HAI titers did not significantly increase compared to SD vaccination



Antibody responses at pre (T0) and post (T3) post-SD vaccination was measured by hemagglutination inhibition (HAI) assay specific for H1N1, H3N2, B1 (Washington/Michigan) and B2 (Phuket) antigens. Data compared using Kruskal-Wallis test with Dunn's correction. Significance is indicated by **** p<0.0001; *** P<0.001; **p<0.01; *p<0.05. Comparison for H3N2 antigen could not be obtained owing to ineffective strain for titer testing during the HD season.

Fig 3: Enhanced antibody responses against B1 and B2 antigens following HD vaccination in both younger and older groups



Comparison of immune response curve between the SD and HD vaccination seasons. Results based on geometric mean of HAI titers (specific for H1N1, H3N2, B1 (Washington/Michigan) and B2 (Phuket) antigens) plotted for all five time points (T0-T4), for both SD and HD season.

Table 2: Correlation analysis between T3 (Day 28) HAI titers and HA-specific IgG isotypes: HD vaccine enhances the breadth of antibody responses by inducing IgG3 response in PWoH and PWH.

PWoH	Vaccine Season	Sample No.	HAI titer v/s Antibody Isotypes:					PWH	Vaccine Season	Sample No.	HAI titer v/s Antibody Isotypes:				
			Total IgG	IgG1	IgG2	IgG3	IgG4				Total IgG	IgG1	IgG2	IgG3	IgG4
H1N1	SD	n=24	*** (0.6)	* (0.4)	NS	NS	NS	H1N1	SD	n=32	* (0.3)	* (0.4)	NS	NS	NS
	HD	n=21	NS	NS	NS	** (0.6)	NS		HD	n=18	* (0.4)	NS	NS	* (0.5)	NS
B1	SD	n=24	NS	NS	NS	NS	NS	B1	SD	n=32	NS	NS	NS	NS	NS
	HD	n=21	NS	NS	NS	* (0.4)	NS		HD	n=18	NS	NS	NS	NS	NS
B2	SD	n=24	NS	NS	NS	NS	NS	B2	SD	n=32	* (0.3)	* (0.3)	NS	NS	NS
	HD	n=21	NS	* (0.5)	NS	NS	NS		HD	n=18	** (0.6)	NS	NS	NS	NS

Results based on Spearman's correlation. Data in parenthesis denotes the magnitude of coefficient of correlation. Significance of association is indicated by **** p<0.0001; *** P<0.001; **p<0.01; *p<0.05.

Summary and Conclusions

- SD vaccine showed significant increase in HAI titers to all 4 flu antigens at T3 (Day 28) for YPWoH, OPWoH and OPWH. YPWH showed the weakest response to SD vaccination with low response to H3N2 and B2 antigens.
- After HD vaccination, younger groups showed a major improvement while older groups showed a minor improvement in Day 28 antibody responses to B2 antigen. Both young and old groups showed similar improvement in antibody response to B1 antigen.
- Rate of decline in HAI titers observed at 6 months post-vaccination was similar for both SD and HD vaccination.
- HD vaccine increases the breadth of HA-specific IgG subtype by inducing IgG3 isotype to H1N1 and B1 antigens in PWoH and IgG3 to H1N1 in PWH.
- In conclusion, our preliminary analysis indicates that old PWH/PWoH showed lesser enhancement in Ab responses specific to B1 and B2 antigens with HD vaccine.
- Further, studies are warranted to understand the possible cell-intrinsic defects in T cells and B cells that could compromise the response to vaccination even with HD vaccination in old PWoH and PWH.

Acknowledgements

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