



Background

Higher pre-vaccination antibodies have been associated with a lower immune response to influenza vaccine, a phenomenon known as "ceiling effects."

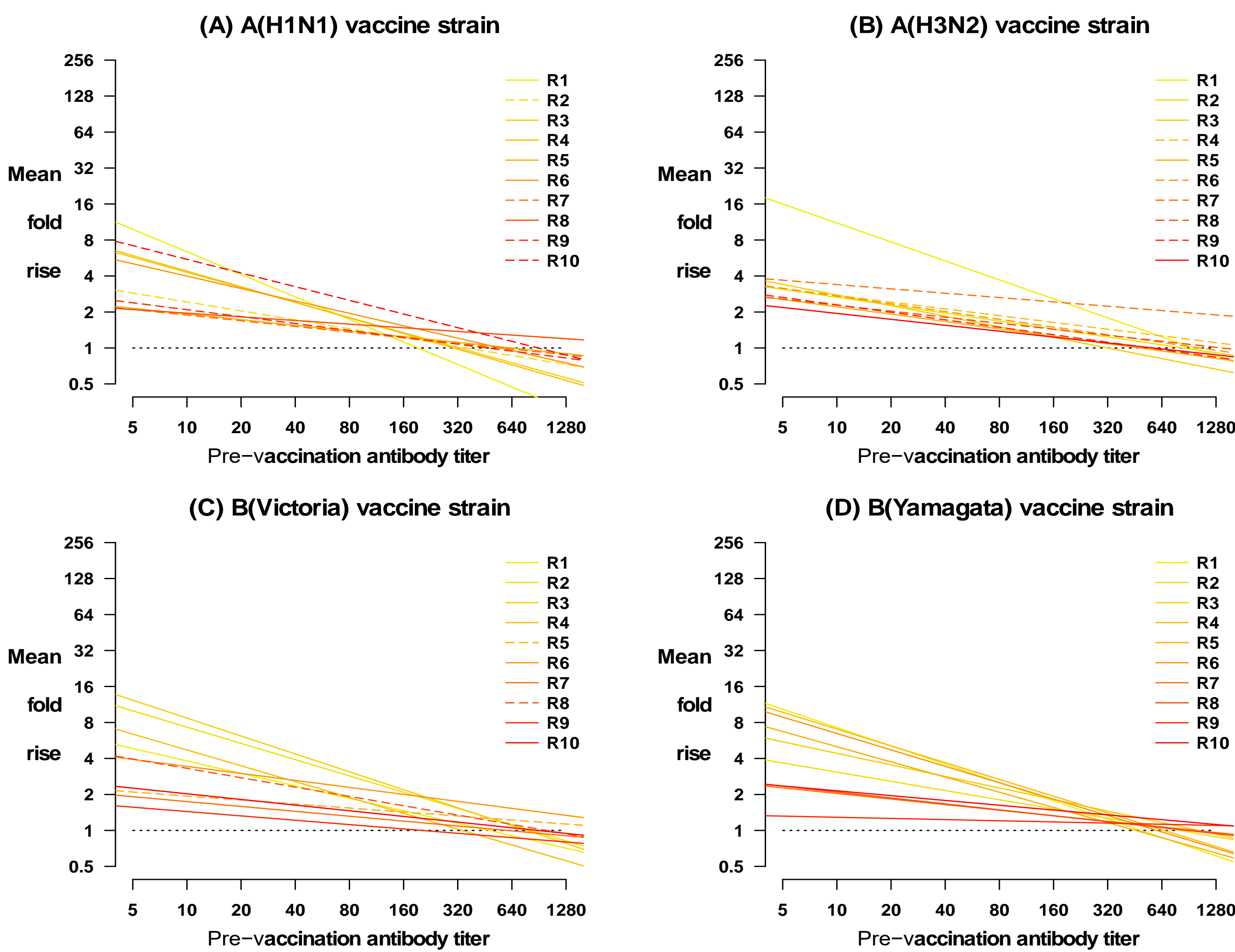


Figure 1. Repeated vaccination effects in twice-annual vaccination group. Dashed lines notated the updates of vaccine strains

Table 1. Association between repeated vaccination and scores in twice-annual group (mixed-effects model adjusted for age and sex)

Subtype	$\beta$ (95%CI) A(H1N1)	$\beta$ (95%CI) A(H3N2)
No. of vaccine	-0.33 (-0.57, -0.10)	-1.97 (-2.40, -1.54)
Strain update	-0.69 (-2.34, 0.96)	0.51 (-0.18, 1.19)
No. of vaccine $\times$ Strain update	0.52 ( 0.06, 0.97)	1.06 ( 0.39, 1.73)
Antigenic distance	0.52 (-0.27, 1.31)	1.10 ( 0.63, 1.56)

Methods

Adults aged 70-79 years in Hong Kong were enrolled and randomly assigned to receive twice- or once-annual influenza vaccinations from 2016-2021. Twice-annual group received influenza vaccine before the winter and summer influenza seasons, while once-annual group received vaccine before the winter and placebo before the summer. Sera were collected before and ~30 days after vaccination and tested using hemagglutination inhibition assay against vaccine strains. Antibody responses were assessed by a scoring system adjusting for pre-vaccination antibodies. Mixed-effects models were used to analyze the number of prior vaccinations, vaccine strain updates and antigenic distance between vaccine strains on the scores adjusting for age and sex.

Conclusion

Repeated vaccination was associated with reduced responses to the influenza vaccine, even after accounting for ceiling effects.

Objectives

We aimed to examine the effects of repeated twice- and once-annual influenza vaccination on antibody response, considering the ceiling effects.

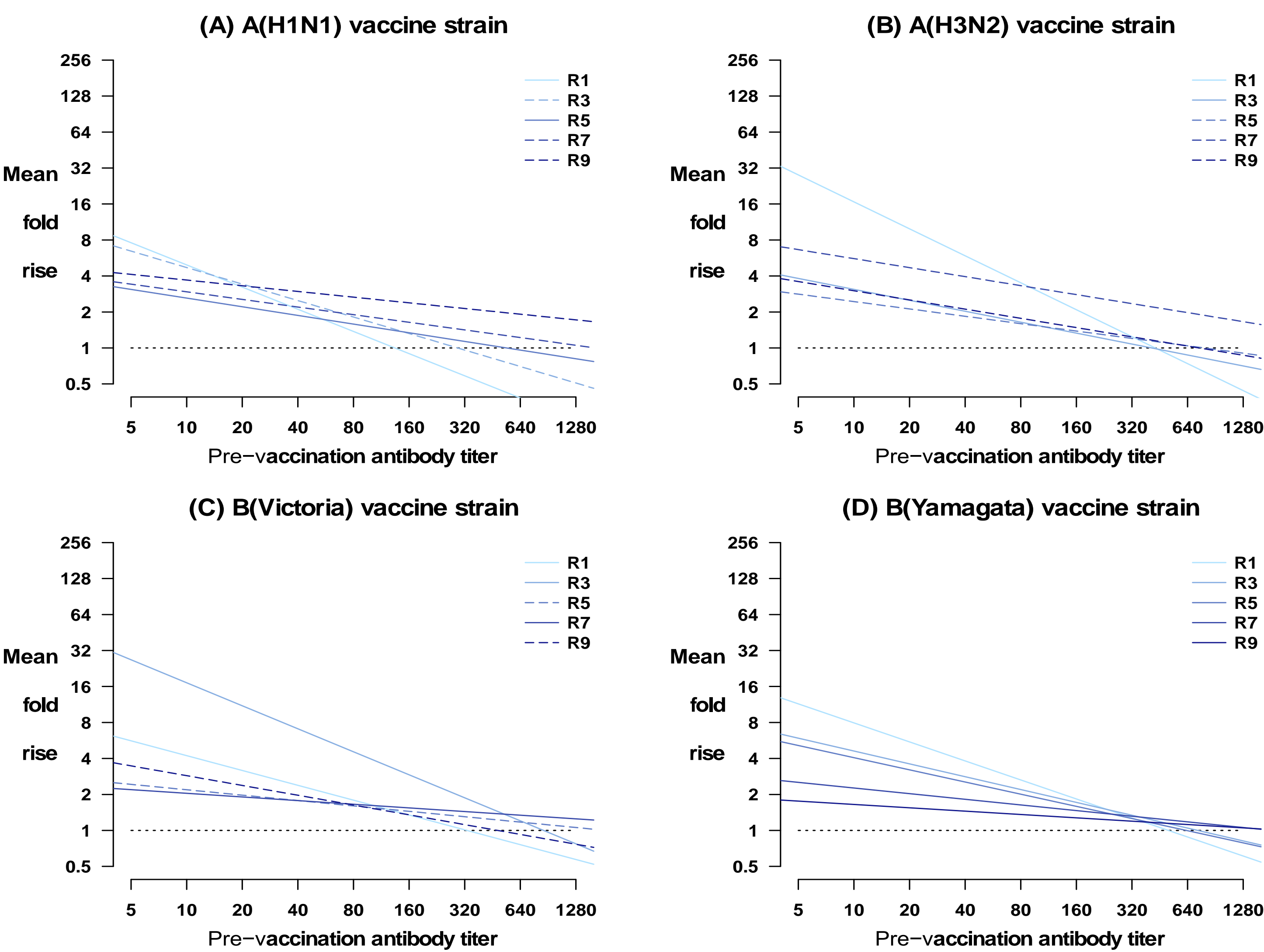


Figure 2. Repeated vaccination effects in once-annual vaccination group. Dashed lines notated the updates of vaccine strains

Table 2. Association between repeated vaccination and scores in once-annual group (mixed-effects model adjusted for age and sex)

Subtype	$\beta$ (95%CI) A(H1N1)	$\beta$ (95%CI) A(H3N2)
No. of vaccine	-0.29 (-0.42, -0.15)	-0.25 (-0.33, -0.17)
Strain update	-2.47 (-3.21, -1.73)	-0.09 (-0.37, 0.19)
No. of vaccine $\times$ Strain update	0.78 ( 0.59, 0.96)	-0.11 (-0.33, 0.10)
Antigenic distance	1.09 ( 0.74, 1.44)	0.27 ( 0.09, 0.45)

Results

Participants received twice- (n=205) and once-annual vaccination (n=199) for five seasons from 2016-2021. Number of prior vaccinations was associated with lower scores in both groups ( $\beta$  range, -1.97 to -0.25;  $P < 0.05$ ). Interaction terms between updates in vaccine strains and number of prior vaccinations were positively correlated with scores ( $\beta$  range, 0.52 to 1.06;  $P < 0.05$ ), except for A/H3N2 in twice-annual group ( $\beta = -0.11$ , 95%CI: -0.33, 0.10). Antigenic distance between vaccine strains were associated with higher scores ( $\beta$  range, 0.27 to 1.10;  $P < 0.05$ ), except for A/H1N1 in once-annual group ( $\beta = 0.52$ , 95%CI: -0.27, 1.31).

Acknowledgements

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