

Quantification of influenza antibody vaccine responses accounting for both vaccine strength and breadth



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Background

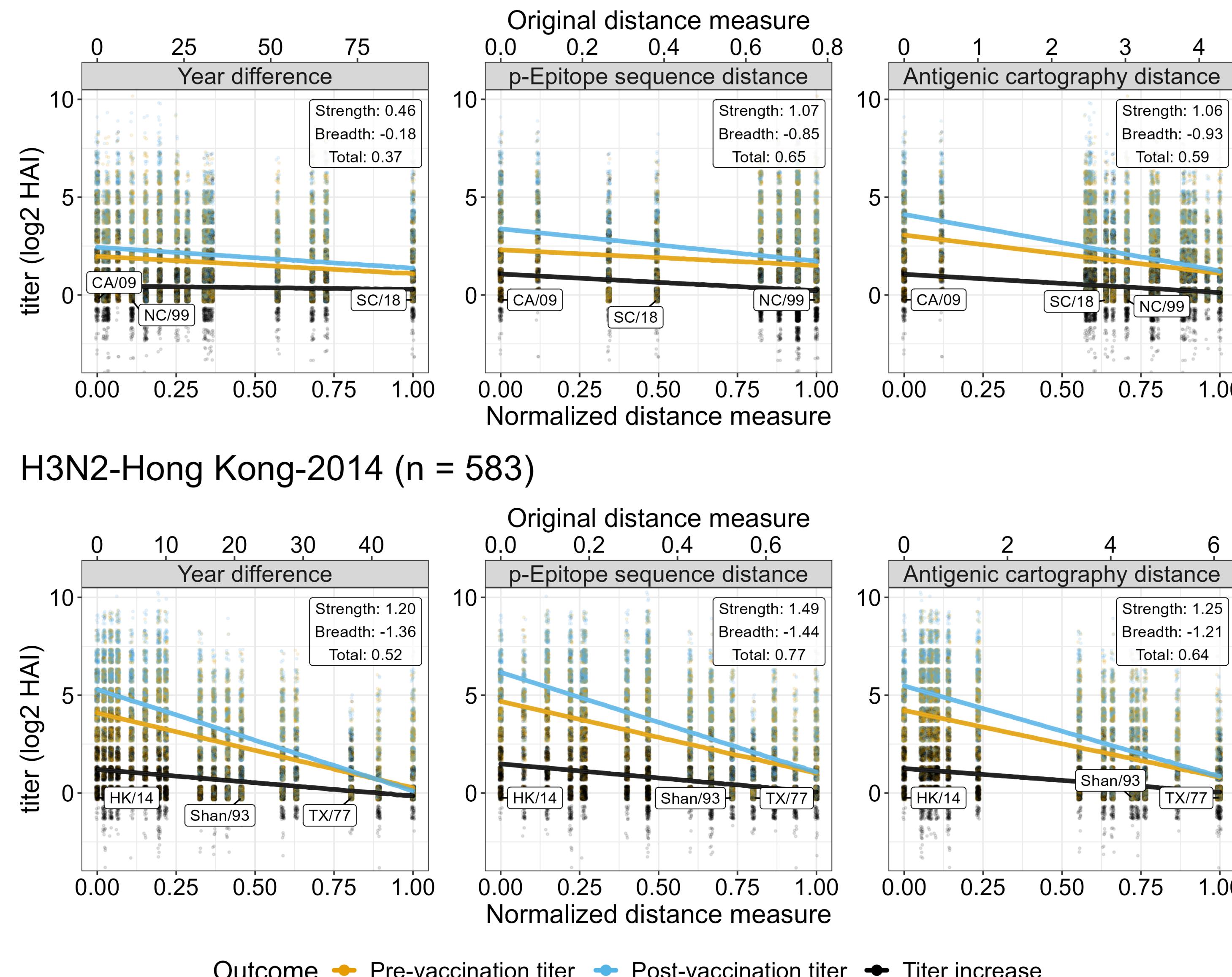
- For future universal influenza vaccine candidates, it will be important to quantify protective immunity against not just the vaccine components, but a broad range of genetically different influenza strains.
- HAI antibody titer is the most commonly used correlate of protection for influenza.
- To determine vaccine **strength**, HAI increase or post-HAI titers against the homologous vaccine components are measured.
- To determine vaccine **breadth**, HAI titers against heterologous strains are measured.
- Unless the panel of heterologous strains are the same, it is difficult to compare between vaccines/studies.
- Quantifying homologous **strength**, heterologous **breadth**, and **total** vaccine response will be useful.

Approach

- We analyzed HAI data pre- and post-vaccination for vaccine and heterologous strains from the UGAFluVac cohort study.
- We determined the distance between vaccine strains and heterologous test strains using 3 measures: 1) Years, 2) Genetic Distance, 3) Antigenic Distance.
- We fitted linear models and computed intercept, slope, and area under the titer increase curve to determine **strength**, **breadth** and **total** vaccine response.
- We illustrated how this framework can be applied to compare Standard Dose (SD) with High Dose (HD) FluZone vaccines.

Distance measure comparison

H1N1-California-2009 (n = 773)



H3N2-Hong Kong-2014 (n = 583)

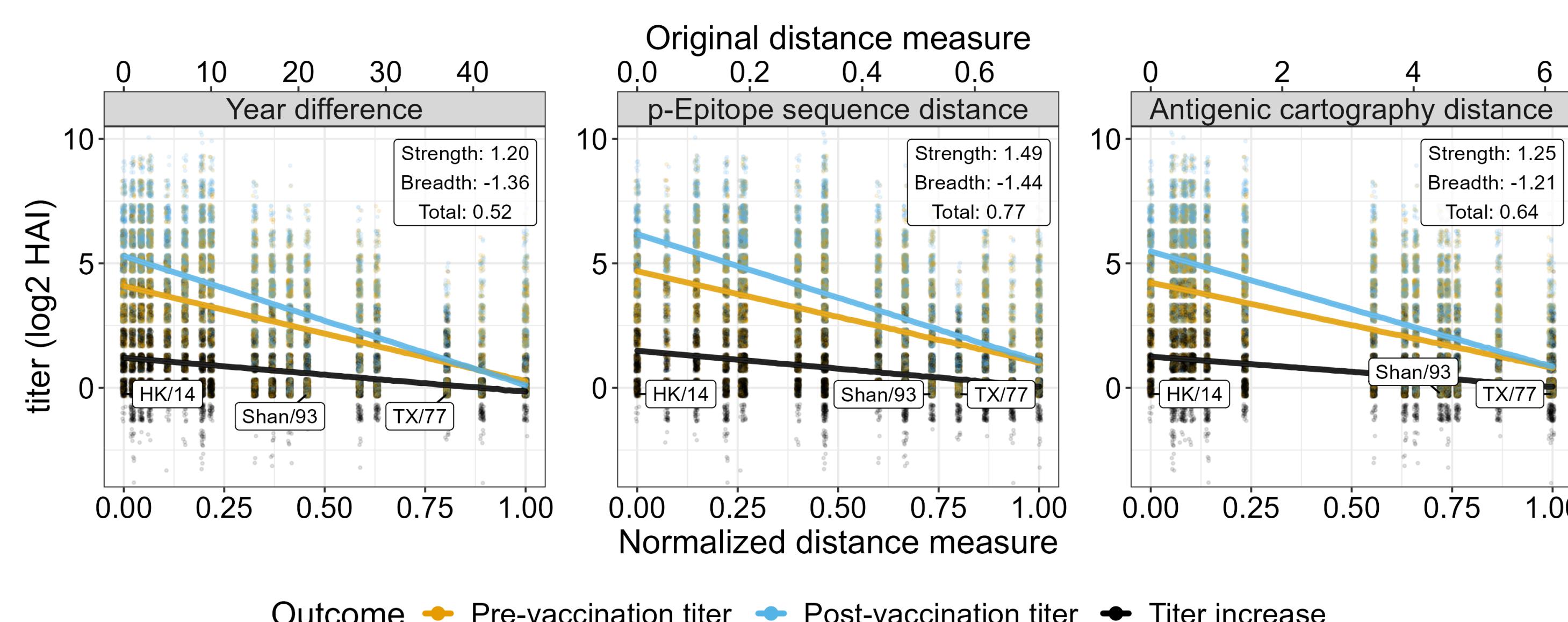


Figure 1: HAI titers for the three distance measures: 1) Years; 2) Genetic distance as quantified by p-epitope; 3) Antigenic distance quantified by shortest path on an antigenic cartography map. Each distance measure was normalized to have comparable ranges between 0 and 1. (Homologous) Strength = Intercept of fitted line. (Heterologous) Breadth = Slope of fitted line. Total response = Area under the curve/line. Standard dose vaccine recipients only.

Dose comparison example

H1N1-California-2009 (SD = 127; HD = 174)

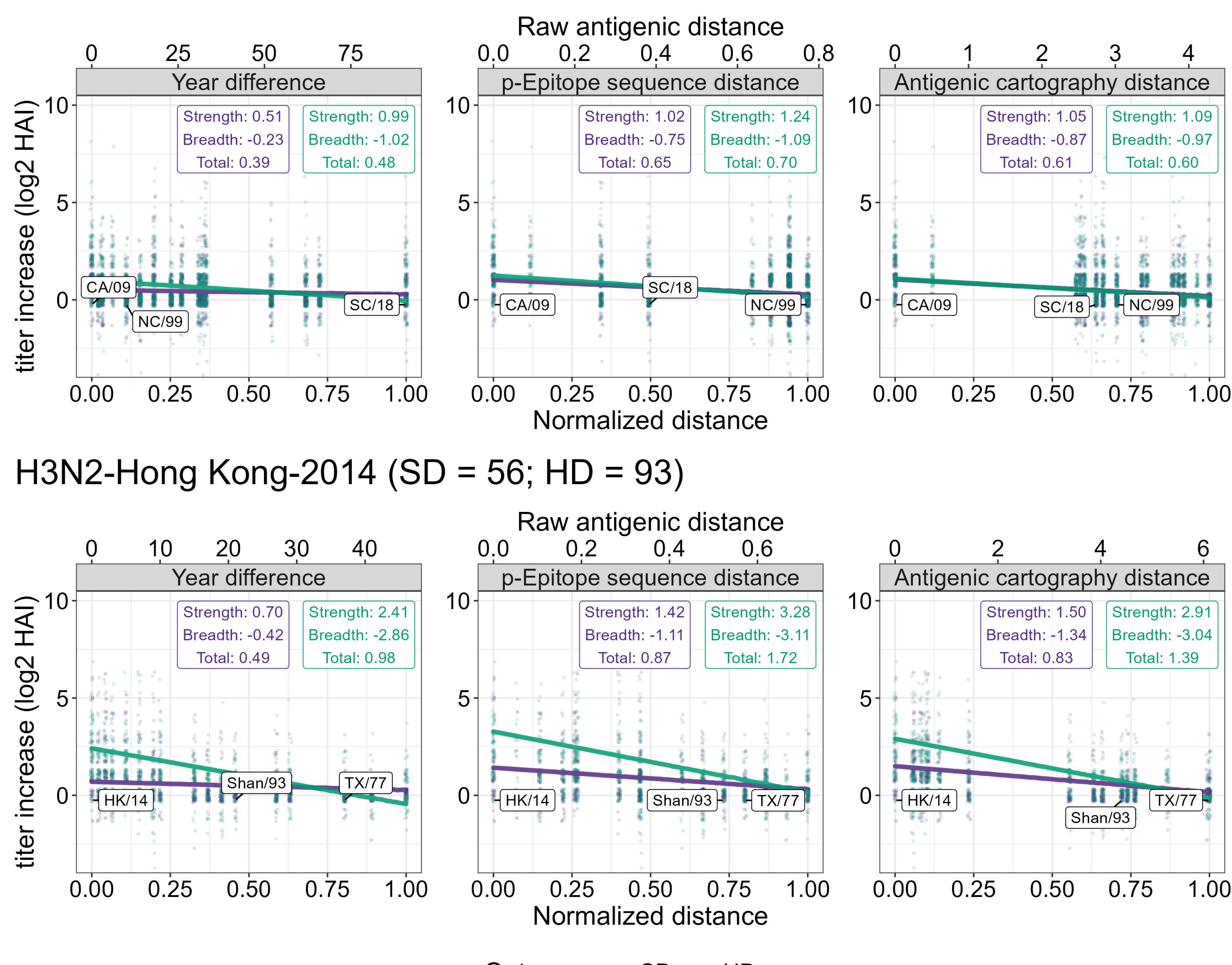
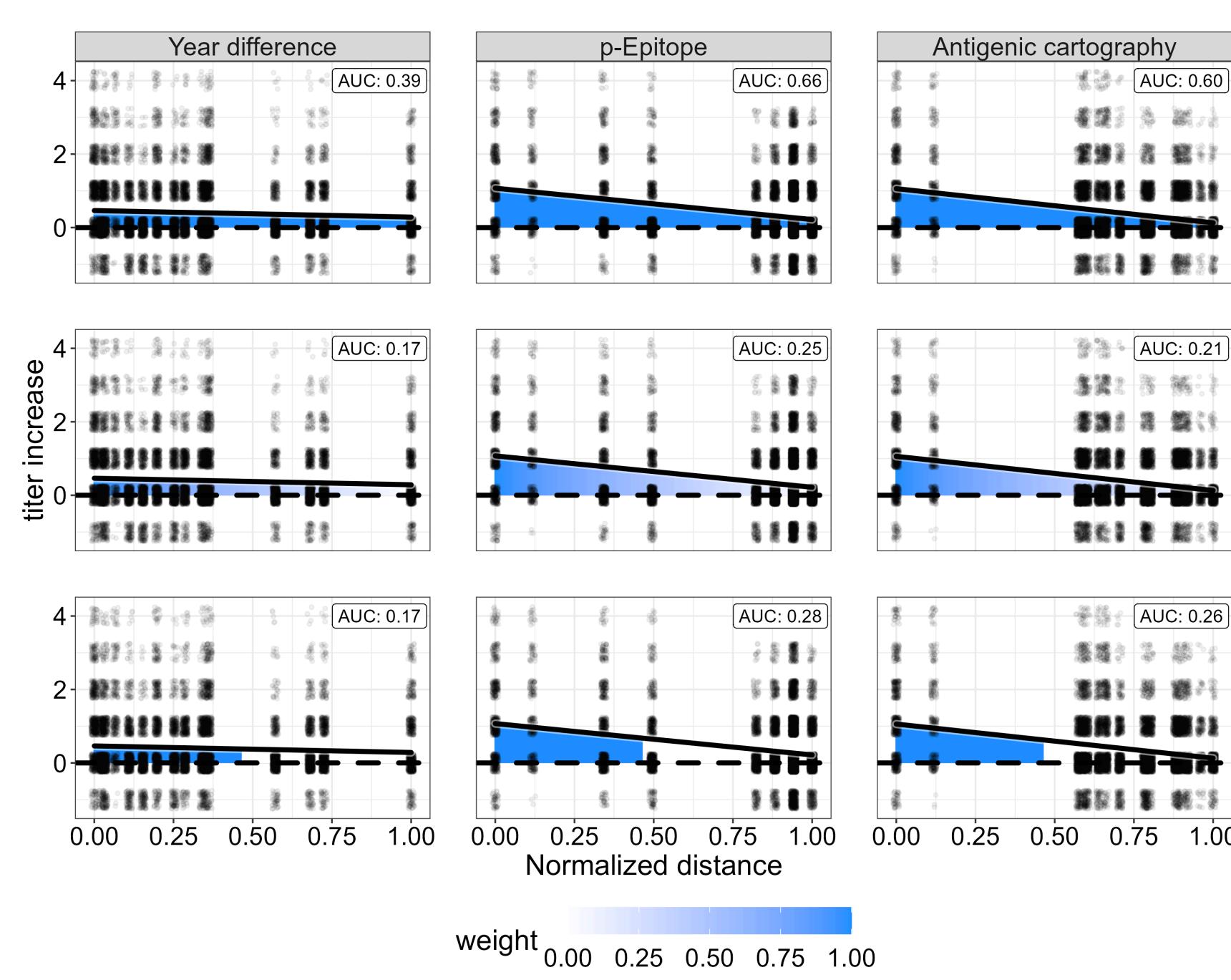


Figure 2: Strength, breadth and total amounts of HAI titer increase for standard dose (SD) and high dose (HD) vaccine recipients. Only individuals 65 years and above are included.

Extensions

- Multi-level statistical models might help further refine the estimates.
- Models that are more flexible than linear models can be explored.
- Interaction between **strength** and **breadth** needs consideration.
- Different weighting for **total** response calculations are possible.



Acknowledgements

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