Impact of broadly-protective vaccines on seasonal dynamics and variant escape of human influenza A

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Background

Human influenza A virus (HIAV) causes occasional potentially devastating pandemics and seasonal epidemics, resulting in substantial public health burden. HIAVs show rapid turnover of antigenic variants, due to continual immune selection and immune waning in the human population. They have two main clades, representative subtypes of which are H3N2 and H1N1, respectively. Therefore, current variant-specific influenza vaccines need to be updated yearly. Furthermore, these existing vaccines have low efficacy and cannot target potential pandemic influenza strains. To tackle this challenge, there have been great efforts to develop a new generation of BROADLY-PROTECTIVE INFLUENZA VACCINES. Three key characteristics of any such vaccine will be its efficacy, and breadth and duration of protection. Here we focus on the impact of CROSS-PROTECTION BREADTH on the seasonal dynamics of H3N2 and H1N1 subtypes, and the invasion of escape variants.

Methods

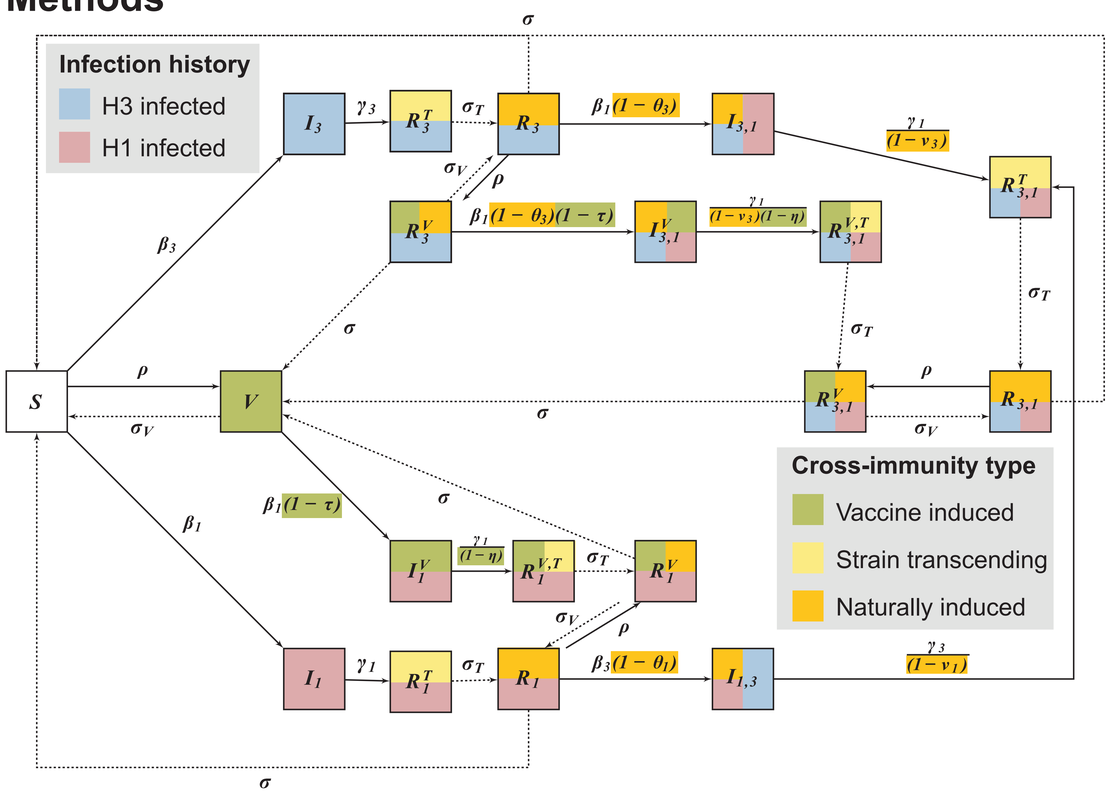

FIGURE 1: Model diagram. Births and deaths at rate μ per capita are not shown.

To illustrate the interacting immunity landscape from vaccines and natural infections, we construct a 2-strain Susceptible-Infected-Recovered-Susceptible (SIRS) model (FIGURE 1). Assuming the deployment of a vaccine that primarily protects against H3, we focus on the impact of vaccine breadth on 1) seasonal strain dynamics of endemic infections; 2) immune escape at inter- and intra-clades. We model the vaccine as providing strong within-clade cross-protection of influenza A, but weaker cross-protection across clades.

Results

Simulations show that subtype dynamics could be strongly affected by the interplay of natural and vaccine-induced cross-immunity against H1. Notably, when increasing the strength of vaccine-induced cross-immunity against H1, the critical vaccination threshold for H3 will increase (FIGURE 2). This is due to a decrease of natural cross-immunity against H3, when H1 infections drop.

Additionally, preliminary invasion analyses show that vaccine-induced cross-immunity against an invading new variant of HIAV has a significant impact on the success of invasion when the new variant evades natural immunity (FIGURE 3).

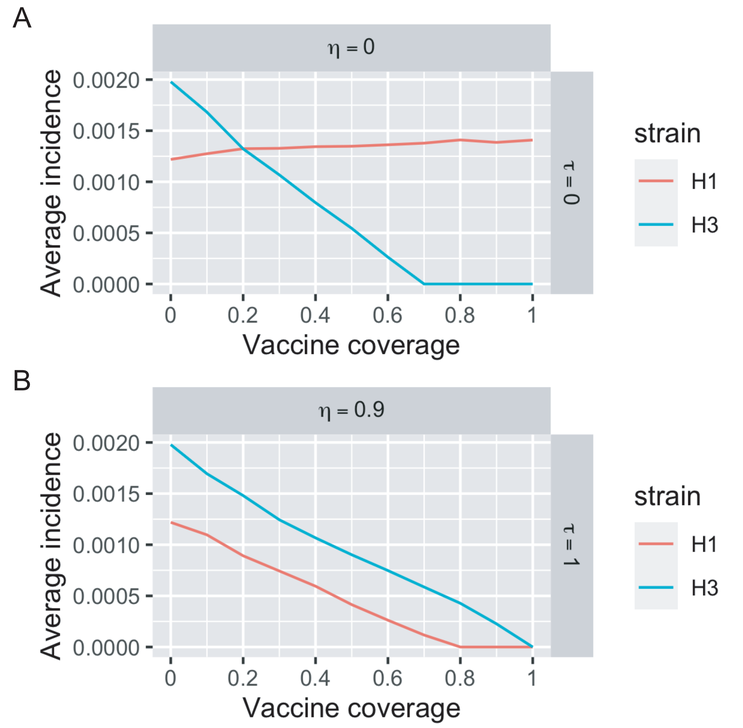

FIGURE 2: Average incidence of H1 and H3 based on simulation. While the vaccine provides full immunity to H3, it provides no cross-immunity (A) or strong cross-immunity against H1 (B). The vaccine-induced cross-immunity against H1 is characterized by η, reduction in infectious period of H1, and τ, reduction in susceptibility of H1.

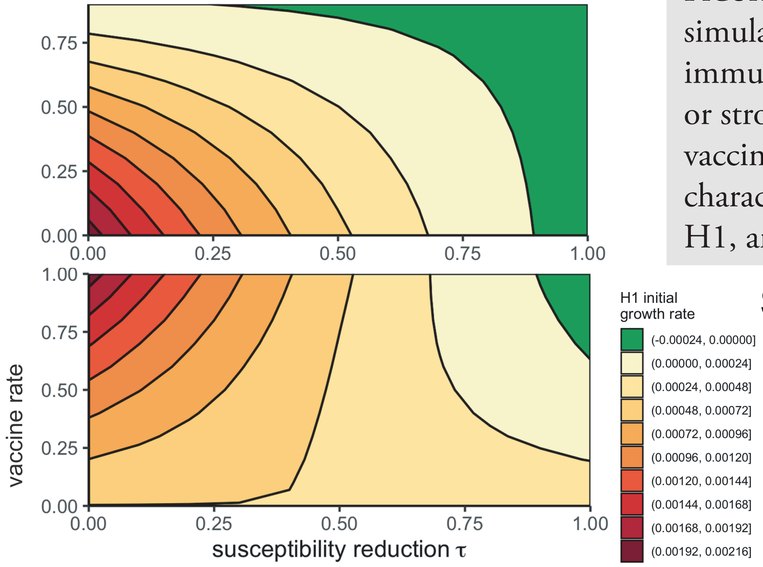

FIGURE 3: Initial growth rate of the new variant, when it invades H3-only epidemic equilibrium, as a function of cross immunity on susceptibility τ on the horizontal axis, and reduction in infectious period η (upper panel) or vaccine rate ρ (lower panel) on the vertical axis. In upper panel, vaccination rate ρ = 1; In lower panel, vaccine has no impact on reducing infectious period of the new variant, i.e. η=0.

Summary & Next steps

Our study underlines the importance of considering immuno-epidemiology in designing Target Product Profiles (TPPs) for future influenza vaccines, by translating individual-level immunological processes to population-level epidemiological processes. In future work, we will fit incidence data from the UK and the USA to model realistic seasonal epidemics.

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