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Infection-acquired versus vaccine-acquired immunity in an SIRWS model

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ABSTRACT

In some disease systems, the process of waning immunity can be subtle, involving a complex relationship between the duration of immunity—acquired either through natural infection or vaccination—and subsequent boosting of immunity through asymptomatic re-exposure. We present and analyse a model of infectious disease transmission where primary and secondary infections are distinguished to examine the interplay between infection and immunity. Additionally we allow the duration of infection-acquired immunity to differ from that of vaccine-acquired immunity to explore the impact on long-term disease patterns and prevalence of infection in the presence of immune boosting.

Our model demonstrates that vaccination may induce cyclic behaviour, and the ability of vaccinations to reduce primary infections may not lead to decreased transmission. Where the boosting of vaccine-acquired immunity delays a primary infection, the driver of transmission largely remains primary infections. In contrast, if the immune boosting bypasses a primary infection, secondary infections become the main driver of transmission under a sufficiently long duration of immunity.

Our results show that the epidemiological patterns of an infectious disease may change considerably when the duration of vaccine-acquired immunity differs from that of infection-acquired immunity. Our study highlights that for any particular disease and associated vaccine, a detailed understanding of the waning and boosting of immunity and how the duration of protection is influenced by infection prevalence are important as we seek to optimise vaccination strategies.

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1. Introduction

The persistence of immunity following natural infection or vaccination plays a key role in shaping the epidemiological patterns of infectious disease. As immunity wanes over time, it may be boosted upon asymptomatic re-exposure, as observed for measles (Whittle et al., 1999) and pertussis (Cattaneo, Reed, Haase, Wills, & Edwards, 1996). Mathematical models of vaccine-preventable infectious diseases (Águas, Gonçalves, & Gomes, 2006; Barbarossa & Röst, 2015; Glass & Grenfell, 2003; Lavine, King, & Bjørnstad, 2011; Wearing & Rohani, 2009) are often based on the susceptible-infectious-recovered-susceptible (SIRS) framework (Keeling & Rohani, 2008), where every individual in a population is categorised into one of three compartments based on their immune status: susceptible (S) to infection, infected and infectious (I) if they can transmit the infection, and recovered (R) from infection and immune. As immunity wanes, recovered individuals become susceptible to infection again.

Mathematical models have been invaluable to vaccination programme design. Key contributions include the introduction of the concept of the basic reproductive ratio R_0 (Diekmann, Heesterbeek, & Metz, 1990; Heesterbeek, 2002; Heffernan, Smith, & Wahl, 2005) and herd immunity thresholds (Fine, 1993). Models provide guidance on optimal vaccination strategies (Campbell, McVernon, & Geard, 2017; Hethcote, Horby, & McIntyre, 2004; Magpantay, 2017) and reveal insights into the impact of vaccination programmes that may seem counter-intuitive due to nonlinearities in the transmission process (Águas et al., 2006; van Boven, Mooi, Schellekens, de Melker, & Kretzschmar, 2005; Heesterbeek et al., 2015).

Vaccines can induce protection against infection, against severe disease, against infectiousness, or a combination of these (Préziosi & Halloran, 2003a, b; Siegrist, 2008, ch. 2). There are multiple ways through which a vaccine may fail to provide sterilising immunity, such as degree of protection and duration of protection (McLean & Blower, 1993, 1995). Vaccines can provide incomplete protection by, for example, reducing one's susceptibility by some degree. Furthermore, the protection provided may wane over time. Importantly the duration of protection acquired through a vaccine may be considerably shorter than that provided through a natural infection, as appears to be the case for pertussis (Broutin, Simondon, Rohani, Guégan, & Grenfell, 2004; Chen & He, 2017; Wendelboe, Van Rie, Salmaso, & Englund, 2005). Moreover, infections following either vaccination or natural infection may occur, and these secondary infections may be less severe or asymptomatic (Klein, Bartlett, Rowhani-Rahbar, Fireman, & Baxter, 2012; Warfel, Zimmerman, & Merkel, 2014; Wendelboe et al., 2005). The vaccine failure mechanism through which a vaccinated individual becomes infected may be difficult to determine.

Here we introduce and analyse a mathematical model that includes the waning and boosting of immunity to study the long-term infection patterns when infection-acquired and vaccine-acquired immunity are distinguished. Our model differs from others (Althouse & Scarpino, 2015; van Boven, de Melker, Schellekens, & Kretzschmar, 2000; Gomes, White, & Medley, 2004; Rozhnova & Nunes, 2012; Safan, Kretzschmar, & Hadeler, 2013) in that we include immune boosting, and it is the inclusion of immune boosting that allows our model to exhibit periodic cycles. Previous studies that included immune boosting focused on the age profiles of infection under a stationary steady state (Águas et al., 2006; Fabricius, Bergero, Ormazabal, Maltz, & Hozbor, 2013). Although we exclude age-structure from our model, we focus on the long-term infection dynamics, where both stationary states and periodic cycles can be encountered as parameters are varied through biologically sensible ranges. In the oscillatory case, the inherent nonlinearity of the system has interesting consequences for the long-term average infection prevalence.

We investigate the influence on infection prevalence as the difference between the duration of vaccine- and infection-acquired immunity is varied. We explore these ideas using a generalisation of our previously developed model (Dafilis, Frascoli, Wood, & McCaw, 2012) in which waning immunity may be boosted upon exposure to extend the duration of protection. We illustrate how infection prevalence changes with vaccination coverage and duration of immunity under two different mechanisms through which immune boosting may act to provide protection.

1.1. The SIRWS model with differences in duration of immunity after natural infection or vaccination

Our model is an extension to the susceptible-infectious-recovered-waning-susceptible (SIRWS) model of Lavine et al. (2011). We allow the duration of infection-acquired immunity to differ from the duration of vaccine-acquired immunity and distinguish between primary and secondary infections.

Here secondary infections are infections experienced by individuals who have had the infection at least once or who were previously vaccinated. In contrast, primary infections are experienced by those who are immunologically naive. Secondary infections are considered less severe than primary infections but equally infectious. We investigate how the prevalence of severe disease changes with differences in the duration of infection- and vaccine-acquired immunity to potentially impact case notifications of any particular disease.

Individuals are divided into eight compartments depending on their immune status. As shown in Fig. 1, the susceptible population is divided into those who can acquire a primary infection (S_1) and those who can acquire a secondary infection (S_2). Similarly, the infectious population is divided into those with a primary (I_1) or secondary (I_2) infection. The recovered (R) compartment represents those who have recovered from and are fully immune to infection. They transition to the waning (W) compartment when their immunity has waned sufficiently. From there, they can either become susceptible to secondary infections (transition to S_2), or have their immunity boosted upon re-exposure (return to R).