Estimating Vaccine Efficacy against Recurrent, Multi-Strain Pathogens

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Pathogens with multiple strains present a challenge for vaccine design, as polyvalent vaccines may only be effective against some strains of the pathogen. In addition, some bacteria such as Streptococcus pneumonia, may recurrently and asymptomatically colonize the nasopharynx in a carrier state which is necessary for transmission. Identifying vaccine efficacy against this carrier state is important. Because of the potential for individual strain colonization to be cleared and then recur, longitudinal sampling provides the best measure of vaccine efficacy; however, such sampling is prohibitively invasive for most studies. In a recent paper published in Biometrics, M. Elizabeth Halloran (Vaccine and Infectious Disease Division) and collaborators Kari Auranen and Hanna Rinta-Kokko (National Institute for Health and Welfare, Finland), describe a framework to estimate strain-specific and aggregate vaccine efficacy for pathogens which can be acquired and carried repeatedly.

The team developed two models of colonization and competition with multiple strains of a pathogen. In Model A, an individual may be susceptible, colonized by either strain, or co-colonized by both strains. Transition between any of these colonization states is associated with a transition hazard, which is the likelihood of a patient in any given state transitioning to a different state, e.g. from colonization with strain 1 to clearance. Model B is similar, however, it does not allow for co-colonization of the patient. Model A led to the derivation of two estimands of vaccine efficacy; one at an individual level, and one at a population level. For both of these estimands, total vaccine efficacy is a weighted average of the strain-specific efficacies, and they are similar when co-colonization is rare and competition between strains is equivalent.

The team used these estimands to re-examine the vaccine efficacy against nasopharyngeal colonization in infants from two polyvalent pneumococcal vaccine studies based on a single colonization measurement. For both of these studies, vaccine efficacy was approximately 0.4-0.8 for each vaccine strain. This result is slightly higher than estimates based on a simple odds ratio measurement which, unlike the model presented in this study, does not account for time-at-risk of colonization. Interestingly, vaccine efficacy for non-vaccine strains was negative, suggesting that replacement colonization by these strains may occur as competition by vaccine strains is reduced.

This study presents a framework to estimate the efficacy of vaccination against colonization. Importantly, the models described in this study take into account whether or not an individual is susceptible to colonization, and by which strains. Future development of this work will focus on unequal competition between strains, changes in rates of colonization over time, and differential responses to vaccination.

Auranen K, Rinta-Kokko H, Halloran ME. 2013. Estimating Strain-Specific and Overall Efficacy of Polyvalent Vaccines Against Recurrent Pathogens From a Cross-Sectional Study. Biometrics. Epub ahead of print, doi: 10.1111/j.1541-0420.2012.01826.x.

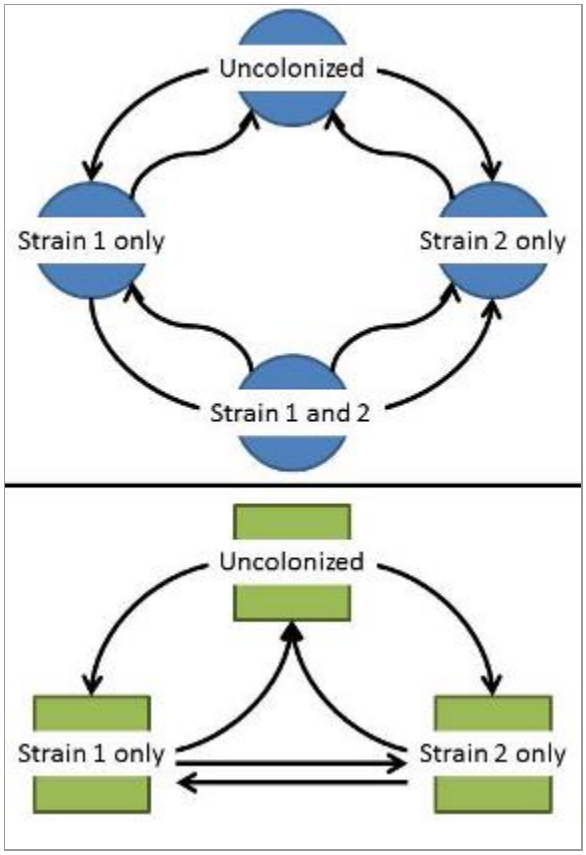

Image courtesy Greg Brennan

Schematic of the two models of bacterial colonization. Model A (top) describes a system which allows for co-colonization, while Model B (bottom) allows only single colonization. Black arrows indicate the allowed transitions between colonization states.