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## **Potential opportunities and perils of imperfect dengue vaccines**

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### ABSTRACT

Dengue vaccine development efforts have focused on the development of tetravalent vaccines. However, a recent Phase IIb trial of the most advanced vaccine candidate indicates a protective effect against only 3 of the 4 serotypes. We developed a four-serotype, age-specific compartmental dengue transmission model that takes into account cross-protection and interaction between serotypes. We use the model to explore potential population effects of vaccination in settings of high and low transmission intensity. Crucially, we explore the effects that vaccines effective only against a subset of serotypes may have in the context of heterogeneities in pathogenicity, transmission intensity and enhancement between serotypes.

Our results show that partially effective vaccines have the potential to lead to 50% or greater reductions in the incidence of clinically apparent dengue, even in scenarios with high heterogeneity between serotypes. However, in instances where the serotype with highest transmission intensity is the one with lowest vaccine efficacy, direct effect of vaccination may be adverse (eg. vaccinated individuals may experience a higher incidence than unvaccinated individuals), despite protective indirect and total (counterfactual) effects (Figure 1). These results are dictated by the immunopathogenic effects of vaccine derived immunity that we assumed, and are even more prominent in settings of medium and low transmission intensity. These findings have important implications for dengue vaccine policy and raise issues regarding population vs. individual benefits of vaccination.