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## **Persistence, fade-outs and re-introduction of dengue viruses in the presence of serotype heterogeneities and mass vaccination**

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### ABSTRACT

Several projects for a tetravalent dengue vaccine have reached advanced stages of development and field testing. In all likelihood, a commercially-released dengue vaccine will have serotype-dependent efficacies that will modify the already-asymmetric competitive landscape that exists between serotypes. One possible consequence of mass-vaccination campaigns is that serotype fade-outs and reintroductions become more probable. To analyze this situation, we first use a compartmental dengue transmission model with no vaccination to show that serotype fade-outs may be less frequent when two conditions hold: (a) the viruses have slightly different transmissibilities (as opposed to fully homogeneous viruses) and (b) there is some increased transmissibility of secondary infections through immune enhancement. Then, we extend our model to incorporate mass vaccination and investigate the likelihood of serotype reintroductions in locations where one or more serotypes are absent. We show that with strictly sterilizing vaccines, there exists a range of vaccination coverage that facilitates the reintroduction of missing serotypes, particularly in settings where circulating serotypes possess strong transmission intensities. This counterintuitive result is understood by examining the accumulation of individuals exclusively susceptible to the serotypes absent from circulation. We discuss the implications of our findings from a public health perspective.