Appearance of Waning Immunity in Studies of Influenza Vaccine Effectiveness due to Bias

Ivo M $\mathrm{Foppa}^{1,2,*}$ and Jill Ferdinands²

¹Battelle Memorial Institute, Atlanta, Georgia, USA

²Influenza Division, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Atlanta, 30333 Georgia, USA

^{*}Corresponding Author, Influenza Division, Centers for Disease Control and Prevention, 1600 Clifton Road NE, MS A-20, Atlanta, 30333 Georgia, USA, vor1@cdc.gov

${\bf Abstract}$

...

Introduction

In his enlightening editorial on the challenges faced by observational vaccine effectiveness (VE) studies, Lipsitch [1] spells out two mechanisms causing apparent waning in "leaky" vaccines: First, heterogeneous risk of infection will deplete the population of those with higher risk first, among the vaccinated slower than the unvaccinated [2]. This leads to relative increase in vaccinated case, resulting in lower VE estimates over time. The second mechanism, due to incomplete case ascertainment [3], is not further discussed by Lipsitch. Here, we consider that mechanism, but formulate it differently, for relevance in the context of observational influenza vaccine effectiveness studies.

uses the paper by Ray et al. [4] to highlight some of these challenges.

Acknowledgements

. . .

References

- [1] Lipsitch M. "Challenges of vaccine effectiveness and waning studies". In: *Clin Infect Dis* (2018). DOI: 10.1093/cid/ciy773. URL: https://www.ncbi.nlm.nih.gov/pubmed/30204853.
- [2] Margheri A, Rebelo C, and Gomes MGM. "Heterogeneity in disease risk induces falling vaccine protection with rising disease incidence". In: *Dynamical Systems* 32.1 (2017), pp. 148–163.
- [3] Wu Y et al. "The influence of incomplete case ascertainment on measures of vaccine efficacy". In: Vaccine 36.21 (2018), pp. 2946—2952. DOI: 10.1016/j.vaccine.2018.04.046. URL: https://www.ncbi.nlm.nih.gov/pubmed/29699788.
- [4] Ray GT et al. "Intra-season Waning of Influenza Vaccine Effectiveness". In: Clin Infect Dis (2018).

 DOI: 10.1093/cid/ciy770. URL: https://www.ncbi.nlm.nih.gov/pubmed/30204855.