



THE UNIVERSITY *of* EDINBURGH

Edinburgh Research Explorer

Vaccination to reduce antimicrobial resistance

Citation for published version:

Atkins, KE & Flasche, S 2018, 'Vaccination to reduce antimicrobial resistance', *The Lancet Global Health*, vol. 6, no. 3, pp. e252. [https://doi.org/10.1016/S2214-109X\(18\)30043-3](https://doi.org/10.1016/S2214-109X(18)30043-3)

Digital Object Identifier (DOI):

[10.1016/S2214-109X\(18\)30043-3](https://doi.org/10.1016/S2214-109X(18)30043-3)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Publisher's PDF, also known as Version of record

Published In:

The Lancet Global Health

General rights

Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.



Vaccination to reduce antimicrobial resistance

With the pipeline of new antibiotics running dry, vaccines are being proposed as a key part of the toolkit used to fight antimicrobial resistance.¹ Amy Ginsburg and Keith Klugman (November 2017, e1176–77)² suggest that a reduction in resistant pathogens might be easier to achieve in many countries via vaccines than through other interventions, such as improved hygiene and sanitation. However, vaccines are rarely designed to target resistant pathogens directly, with the notable exception of pneumococcal conjugate vaccines (PCVs) that protect against serotypes of *Streptococcus pneumoniae* displaying high resistance frequency. Hence, vaccines' effect of reducing antimicrobial resistance has been mostly regarded as a highly desirable byproduct. The scale of the problem of antimicrobial resistance now requires us to formally integrate the effect of vaccines on antimicrobial resistance into decision-making in public health.

Vaccines, arguably more than any other public health intervention, are subject to rigorous evaluations before integration into national immunisation programmes. Because of the non-linear effects of transmission-reducing vaccines, embedding mathematical modelling forecasts in economic evaluations is the gold standard for impact predictions.³ Similarly, the interplay between vaccination and the emergence and spread of antimicrobial resistance will probably yield complex dynamics that require mathematical modelling analysis. The characteristics and efficacy of a particular vaccine will influence the linked direct and indirect reductions in resistance burden and antibiotic use.^{4,5} Meanwhile, vaccines against non-focal pathogens (ie, pathogens which themselves are not the targets of resistance control) might have similar and substantial benefits.^{4,5} However, there is a scarcity of modelling studies that aim to quantify

the public health effect of vaccines on antimicrobial resistance. Furthermore, none of these models have integrated an economic framework.⁴

Mathematical models have been able to reflect both the fall of penicillin-resistant *S pneumoniae* and the subsequent rise in resistance in non-vaccine serotypes after the introduction of PCVs.⁶ Notwithstanding these post-hoc studies, developing mechanistic models that show the empirical relation between an antibiotic's use and the rising frequency of resistance against the antibiotic has been challenging.^{7–9} Without an accurate quantification of the selection mechanisms through which resistance frequency is maintained, it will be impossible to base policy decisions on model forecasts.

To couple vaccine programmes with an evidence-based strategy for antimicrobial resistance, we must now move from blanket recommendations of vaccine use for antimicrobial resistance control to a vaccine-specific, pathogen-specific, and setting-specific quantification of vaccine policy. This crucial shift will rely on a new generation of mathematical models and of the economic frameworks in which these models will be embedded.

We declare no competing interests.

Copyright © The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.

*Katherine E Atkins, Stefan Flasche
katherine.atkins@lshtm.ac.uk

Centre for Mathematical Modelling of Infectious Diseases (KEA, SF), The Vaccine Centre and Department of Infectious Disease Epidemiology (KEA, SF), and Faculty of Epidemiology and Population Health (KEA, SF), London School of Hygiene and Tropical Medicine, London WC1E 7HT, UK

- 1 Review on Antimicrobial Resistance. Vaccines and alternative approaches: reducing our dependence on antimicrobials. https://amr-review.org/sites/default/files/Vaccines%20and%20alternatives_v4_LR.pdf (accessed Nov 21, 2017).
- 2 Ginsburg AS, Klugman KP. Vaccination to reduce antimicrobial resistance. *Lancet Glob Health* 2017; **5**: e1176–77.
- 3 Wilder-Smith A, Longini J, Zuber PL, et al. The public health value of vaccines beyond efficacy: methods, measures and outcomes. *BMC Med* 2017; **15**: 138.

- 4 Atkins KE, Lafferty E, Deeny SR, Davies, NG, Robotham JV, Jit M. Use of mathematical modelling to assess the impact of vaccines on antibiotic resistance. *Lancet Infect Dis* 2017; published online Nov 13. [https://doi.org/10.1016/S1473-3099\(17\)30478-4](https://doi.org/10.1016/S1473-3099(17)30478-4).
- 5 Lipsitch M, Siber GR. How can vaccines contribute to solving the antimicrobial resistance problem? *MBio* 2016; **7**: e00428–16.
- 6 Opatowski L, Mandel J, Varon E, Boëlle PY, Temime L, Guillemot D. Antibiotic dose impact on resistance selection in the community: a mathematical model of beta-lactams and streptococcus pneumoniae dynamics. *Antimicrob Agents Chemother* 2010; **54**: 2330–37.
- 7 Lehtinen S, Blanquart F, Croucher NJ, Turner P, Lipsitch M, Fraser C. Evolution of antibiotic resistance is linked to any genetic mechanism affecting bacterial duration of carriage. *Proc Natl Acad Sci USA* 2017; **114**: 1075–80.
- 8 Lipsitch M, Colijn C, Cohen T, Hanage WP, Fraser C. No coexistence for free: neutral null models for multistrain pathogens. *Epidemics* 2009; **1**: 2–13.
- 9 Davies NG, Flasche S, Jit M, Atkins, KE. Within-host dynamics explain the coexistence of antibiotic-sensitive and resistant bacteria. *bioRxiv* 2017; published online Nov 10. DOI:10.1101/217232.

