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Atkins, KE; Flasche, S; (2018) Vaccination to reduce antimicrobial resistance. *The Lancet Global health*, 6 (3). e252. ISSN 2214-109X DOI: [https://doi.org/10.1016/S2214-109X\(18\)30043-3](https://doi.org/10.1016/S2214-109X(18)30043-3)

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## 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.<sup>1</sup> Amy Ginsburg and Keith Klugman (November 2017, e1176–77)<sup>2</sup> 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.<sup>3</sup> 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.<sup>4,5</sup> Meanwhile, vaccines against non-focal pathogens (ie, pathogens which themselves are not the targets of resistance control) might have similar and substantial benefits.<sup>4,5</sup> 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.<sup>4</sup>

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.<sup>6</sup> 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.<sup>7–9</sup> 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.

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\**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

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