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Silent spread of H5N1 in vaccinated poultry

A chink in the protection of a caged flock can dramatically increase the chances of a flu outbreak.

International debate on the merits of vaccinating poultry against the H5N1 influenza A virus[1–3] has raised concerns about the possibility of an increased risk of between-flock transmission before outbreaks are detected[4]. Here we show that this 'silent spread' can occur because of incomplete protection at the flock level, even if a vaccine is effective in individual birds. The use of unvaccinated sentinels can mitigate, although not completely eliminate, the problem.

We use an individual-based mathematical model, parameterized from experimental and observational data[5] (for details, see supplementary information), that tracks within-flock spread of a highly pathogenic avian influenza (HPAI) virus such as H5N1 to explore the impact of prophylactic vaccination on silent spread between flocks. We calculated the probability of outbreak occurrence and detection, as well as the contribution of flock infectiousness during, and at the end of, a flock's production cycle to transmission to other flocks (expressed as the case reproduction ratio, $R_{between}$). We determined the quantitative effects on these variables of different flock structure, within-flock transmission potential of HPAI, detection thresholds, vaccine effectiveness and fraction of the flock successfully vaccinated.

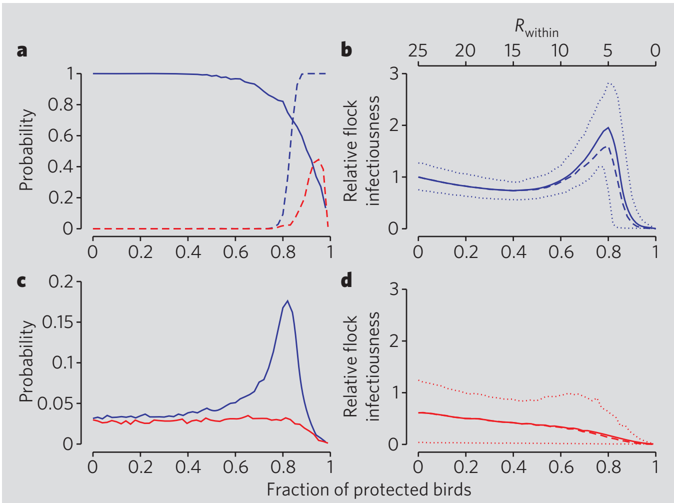

Figure 1 | Effects of vaccination protection levels in a flock. **a**, Probability of an outbreak (solid line) and probability that an outbreak will ever be detected (dashed lines) in caged flocks of 10,000 birds. Line colours: blue, no sentinels; red, 100 sentinels. **b**, Mean (solid line) and 95 percentiles (dotted lines) of the infectiousness of infected vaccinated flocks during the production cycle, relative to infected unvaccinated flocks (no sentinels). Dashed line: infected flock infectiousness weighted by probability of outbreak occurrence. For reference, the corresponding values of within-flock transmission potential, R_{within}, are shown. **c**, Probability that an outbreak occurs and is undetected at the end of the production cycle, assuming a cycle period of 365 days. Line colours: blue, no sentinels; red, 100 sentinels. **d**, Flock infectiousness as in **b**, but with 100 sentinels.

Outbreaks were modelled in caged flocks seeded with a small amount of infective faeces contaminating a single cage. The fraction of birds successfully vaccinated was considered[6], assuming a fully effective vaccine. We find that 90% of birds need to be protected to reduce the probability of an outbreak by 50% (Fig. 1a, solid line), but this can result in undetected outbreaks (Fig. 1a, blue dashed line). The infectiousness of an infected flock to other flocks (defined as the infectiousness of faeces integrated hourly over an outbreak) during the production cycle peaks at 80% protection (Fig. 1b, solid line). This is because, as the fraction protected rises, fewer birds become infected but outbreaks become harder to detect. Despite a reduced probability of outbreaks, vaccination can increase between-flock transmission at high flock-protection levels (Fig. 1b, dashed line). These results are qualitatively robust to uncertainties in parameter values (for details, see supplementary information).

The risk of between-flock transmission is greatest at the end of a flock's production cycle, when biological security can be compromised as birds are moved and housing units cleaned. High levels of flock protection can dramatically increase the probability that HPAI is undetected at this time because of the increased outbreak duration (Fig. 1c, blue line), thus contributing to between-flock transmission.

The negative effects of vaccination can be mitigated by monitoring unvaccinated sentinel birds placed into flocks[4] (although logistical problems arise[7]). Sentinels placed randomly among cages increase the probability of detection (although undetected outbreaks still occur; Fig. 1a, dashed red line), thereby reducing flock infectiousness (Fig. 1d) and the probability of undetected HPAI at the end of a production cycle (Fig. 1c, red line).

Between-flock transmission is related to flock infectiousness both during (Fig. 1b, d) and at the end of (Fig. 1c) a production cycle. Values of $R_{between}$ as high as 3 to 10 have been reported[8]. To prevent an epidemic, $R_{between}$ must be below 1 (ref. 9): to achieve this through vaccination, even with sentinels, would require very high levels of flock protection (Fig. 1c, d, red lines).

The main obstacle to achieving such protection is in ensuring that an adequate fraction of birds is properly vaccinated[7] (typically less than 90% of birds are protected in practice[2]). Vaccination can be highly effective in individual birds[10] and any minor deficiencies at that level are relatively unimportant (see supplementary information). A successful vaccination programme therefore requires not only a highly effective vaccine but also a highly effective vaccine-delivery system, combined with effective biological security and the rapid detection and removal of infected flocks.

Nicholas J. Savill*, Suzanne G. St Rose*, Matthew J. Keeling†, Mark E. J. Woolhouse*

*Centre for Infectious Diseases, University of Edinburgh, Ashworth Laboratories, The King's Buildings, Edinburgh EH9 3JT, UK
e-mail: nick.savill@ed.ac.uk
†Mathematics Institute and Department of Biological Sciences, University of Warwick, Coventry CV4 7AL, UK

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