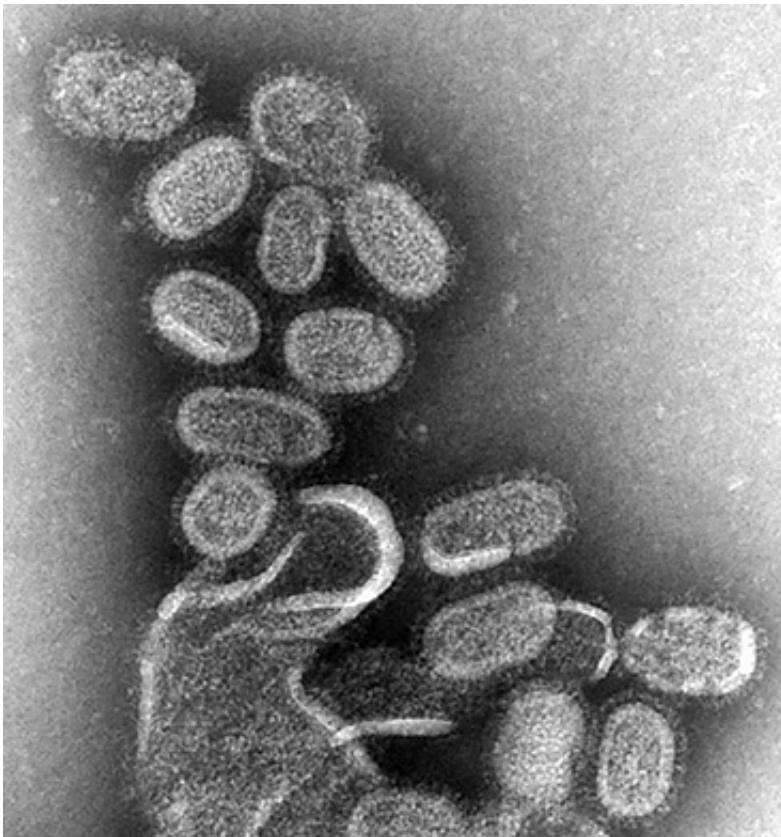


# New method to make deeper inferences about infection dynamics

July 14 2015, by Christopher Packham

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Electron microscopy of influenza virus. Credit: CDC

(Medical Xpress)—When influenza vaccinations are unavailable, public health policy favors nonpharmaceutical household interventions. So households also present perfect settings for researchers to study infection dynamics and test the efficacy of various interventions. But the analysis

of the accumulated data is complicated by such factors as the use of varying assays, with the result that researchers are often getting only partial results.

In known-index trials, symptomatic individuals and their families are recruited at [health care facilities](#), provide biological samples to the researchers, and are often asked to record symptoms in a diary. Researchers studying infection dynamics in these households rely on a measure of outcome called the household secondary attack rate (hSAR), defined as the proportion of nonindex household members who become infected during the study.

Significant reductions in hSAR are a sign of an intervention effect, but the amplitude of differences in effect is often difficult to measure, due to multiple complicating factors. Thus, a better yardstick than hSAR could potentially make fuller use of the data accumulated in countless past studies to reveal deeper and more detailed information about infection dynamics and the efficacy of interventions.

An international group of researchers recently applied a new analytic method to a 2008 household intervention study. Their Bayesian transmission model made inferences about the presence and timing of unobserved infections, and they report that this new assessment produced "more intuitively consistent attack rates" than hSAR by stratifying the participating households according to the speed of the tested interventions. They have published details of their method in the *Proceedings of the National Academy of Sciences*.

They analyzed the data collected from 322 households that participated in a known-index intervention study of influenza. The researchers conducting that study were attempting to determine if face masks and rigorous hand-hygiene interventions were efficacious in reducing infections in household settings. Using traditional hSAR analysis, the

researchers found a significant difference between control households and the households that adopted the hand-hygiene intervention.

By applying their inference technique, the researchers for the current study have inferred how the amplitude of infectiousness varies over time for household of four members. They write, "Leveraging our ability to infer infection events, we were also able to estimate the approximate generation time commonly reported from household studies—the time between the infection of the index case and the infection of the secondary cases." They estimated this time period to be 3.39 days on average, which was consistent with estimates for various strains of influenza.

They were also able to model the efficacy of interventions as the per-day reduction of infectiousness. "We suggest that [this] gives a more interpretable measure and could be a useful quantity to communicate as part of an overall health protection measure," they write.

In one of the intervention arms, they were able to refine the primary study analyses by using data from all the [households](#) rather than only one; they determined that efficacy of the [intervention](#) could be more accurately captured using rigorous statistical inferences. They were also able to describe transmission dynamics and how variable timing for the interventions affected outcomes.

They emphasize that this new framework is applicable to both the design of new studies and conducting secondary analyses of previous studies.

**More information:** "Inferring influenza dynamics and control in households." *PNAS* 2015 ; published ahead of print July 6, 2015, [DOI: 10.1073/pnas.1423339112](https://doi.org/10.1073/pnas.1423339112)

## **Abstract**

Household-based interventions are the mainstay of public health policy against epidemic respiratory pathogens when vaccination is not available. Although the efficacy of these interventions has traditionally been measured by their ability to reduce the proportion of household contacts who exhibit symptoms [household secondary attack rate (hSAR)], this metric is difficult to interpret and makes only partial use of data collected by modern field studies. Here, we use Bayesian transmission model inference to analyze jointly both symptom reporting and viral shedding data from a three-armed study of influenza interventions. The reduction in hazard of infection in the increased hand hygiene intervention arm was 37.0% [8.3%, 57.8%], whereas the equivalent reduction in the other intervention arm was 27.2% [−0.46%, 52.3%] (increased hand hygiene and face masks). By imputing the presence and timing of unobserved infection, we estimated that only 61.7% [43.1%, 76.9%] of infections met the case criteria and were thus detected by the study design. An assessment of interventions using inferred infections produced more intuitively consistent attack rates when households were stratified by the speed of intervention, compared with the crude hSAR. Compared with adults, children were 2.29 [1.66, 3.23] times as infectious and 3.36 [2.31, 4.82] times as susceptible. The mean generation time was 3.39 d [3.06, 3.70]. Laboratory confirmation of infections by RT-PCR was only able to detect 79.6% [76.5%, 83.0%] of symptomatic infections, even at the peak of shedding. Our results highlight the potential use of robust inference with well-designed mechanistic transmission models to improve the design of intervention studies.

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