Total Effect Analysis of Vaccination on Household Transmission in the Office for National Statistics COVID-19 Infection Survey

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Abstract

We investigate the distribution of numbers of secondary cases in households in the Office for National Statistics COVID-19 Infection Survey (ONS CIS), stratified by timing of vaccination and infection in the households. This shows a total effect of a statistically significant approximate halving of the secondary attack rate in households following vaccination.

Introduction

The ongoing COVID-19 pandemic has, at the time of writing, led to over 4 million confirmed deaths worldwide\textsuperscript{7}. This has in turn caused Governments to implement significant changes to the way in which societies function, often including compulsory isolation, implementation of test and trace systems, and closure of sectors of the economy\textsuperscript{1}. Since they became available, vaccines have been deployed in one of the fastest ever campaigns with over 3 billion doses administered to date\textsuperscript{7}.

In addition to questions about vaccine efficacy on recipient disease outcomes\textsuperscript{5,4}, there is a question about the impact of vaccination on onwards transmission. This was considered by Harris et al.\textsuperscript{2} using data from the HOSTED dataset, a passive surveillance system derived from England’s Test and Trace (T&T) system. They reported an overall secondary attack rate (SAR) in households of 10%, with adjusted odds ratios of 0.52 and 0.54 for index case vaccination with ChAdOx1 and BNT162b2 respectively. One potential concern about this study is the biases inherent in T&T data, and so we seek to see if the estimated vaccine efficacy can be reproduced under a different study design.

Here, we analyse data from the Office for National Statistics (ONS) COVID-19 Infection Survey (CIS), a large community-based longitudinal household survey of individuals aged 2 years and older living in randomly selected private households across the UK\textsuperscript{6}. Due to differences in study design we take a different analytical approach from that of Harris et al.\textsuperscript{2}, but address the same question of the impact of vaccination on transmission.
Methods

Data

In the ONS CIS, households are recruited from the general population and visited regularly for testing, which is independent of symptoms or vaccine status. For visits to be included in the current dataset, participants had to be aged 16 years or over and have either a positive or negative swab result from 1st December 2020 to 31 May 2021. We did not differentiate between vaccines since our aim is to obtain a total effect of the programme as implemented.

As PCR-positive results may be obtained at multiple visits after infection, positive tests were grouped into episodes. We defined the start of a new infection episode as the date of either: (1) the first PCR-positive test in the study or T&T positive (not preceded by any study PCR-positive test by definition); (2) a PCR-positive test after four or more consecutive negative CIS tests; or (3) a PCR-positive test at least 90 days after the start of a previous infection episode, with one or more negative tests immediately preceding this.

Visits were dropped if they were within a positive episode, unless the first positive in the episode was from T&T, in which case the first CIS positive (if any) within that episode was kept in the dataset (as T&T positives were not considered as positive outcomes in the dataset).

Households are stratified into the following three categories:

- Positive First & No Vaccine: First vaccine dose in household received more than 21 days after first positive episode in household and never vaccinated households.
- Intermediate: Difference in time between first vaccine dose in household and first positive episode in household less than 21 days.
- Vaccine first: First vaccine dose in household received more than 21 days before first positive episode in household.

As we will see, the ‘intermediate’ group is important to ensure that the net impact of a completed vaccination is captured appropriately.

This choice – i.e. stratification by overall household vaccination status – is necessary because the study design involves testing during a systematically scheduled visit, meaning the dates of first known positives in households are often simultaneous and an index case cannot be straightforwardly identified.

Analysis

Here we seek to calculate a total effect of having at least one completed vaccination in a household before introduction of infection, with no attempt to determine causation, mediation, confounding etc. We quantify uncertainty in the results using bootstrapping.

Standard bootstrapping involves repeatedly re-sampling the full dataset with replacement to quantify uncertainty. Here we are interested in the proportion of secondary cases generated (the Secondary Attack Rate, or SAR) and the more detailed distribution of secondary cases in households. If we have \(m\) households and the \(i\)-th household has size \(n_i\) and \(y_i\) positives, then let the set of households with at least one infection be \(I = \{ i \in [m] | y_i \geq 1 \}\), then the SAR is

\[
SAR = \frac{\sum_{i \in I} (y_i - 1)}{\sum_{i \in I} (n_i - 1)}
\]  

(1)

We will also be interested in the overall distribution of the \(y_i\)’s, split into the three vaccine status groups. To assess uncertainty in these, standard bootstrapping is not appropriate due to 0% and 100% counts, so we calculate generalised Jeffreys intervals by sampling from the conjugate Dirichlet distribution to the observed data and then sampling from a multinomial with the probability vector sampled from the Dirichlet. In each case we use 20,000 bootstraps.
Results and Discussion

The SAR estimates and 95% CIs are as below.

- Positive First & No Vaccine: SAR = 23.5[22.6,24.4]%.
- Intermediate: SAR = 29.7[22.8,37.1]%; one-sided p-value for hypothesis that this is larger than Positive First & No Vaccine = 0.040.
- Vaccine first: SAR = 12.5[4.0,23.3]%; one-sided p-value for hypothesis that this is larger than Positive First & No Vaccine = 0.023.

The interpretation of these results is that prior vaccination is significantly associated with lower secondary attack rates in households. The higher risks in intermediate households may be related to behaviour, although this would require further analysis, potentially using the regression methods of House et al. 3.

We now compare with the results from Harris et al. 2; while our overall SAR is over twice theirs due to different study design, we can determine if the relative effect is consistent in the following manner. If OR stands for the odds ratio in Harris et al., and SAR for the secondary attack rate in our positive first and no vaccine group, then the secondary attack rate that would follow from combination of these two numbers is, after some manipulation of the definitions of an odds ratio in logistic regression and the secondary attack rate,

\[ Q = \frac{\text{SAR} \times \text{OR}}{\text{SAR} \times \text{OR} + (1 - \text{SAR})} \]  

For the ChAdOx1 estimate in Harris et al. we obtain \( Q \approx 13.8[8.5,19.3]\% \), and for the BNT162b2 estimate, \( Q \approx 14.2[10.3,18.4]\% \). Both are consistent with our vaccine first group SAR estimate, meaning that both study designs are consistent in terms of the inferred relative secondary attack rate following vaccination.

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Figures

Figure 1: Household secondary attack rates (SARs) bootstrapped at the whole-dataset level.

Figure 2: Histograms of numbers positive in households stratified by household sizes with 50% and 95% CIs from whole-sample parametric bootstrapping shown.