

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	The community paediatric respiratory infection surveillance study protocol: a feasibility, prospective inception cohort study
<b>AUTHORS</b>	Anderson, Emma; Ingle, Suzanne; Muir, Peter; Beck, Charles; Finn, Adam; Leeming, John; Cabral, Christie; Kesten, Joanna; Hay, Alastair

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Nick Francis Cardiff University, Wales
<b>REVIEW RETURNED</b>	30-Jun-2016

<b>GENERAL COMMENTS</b>	<p>I was delighted to read the protocol for what sounds like a very important and exciting study. My only comments are that I agree that the main concern is the representativeness of the cohort. In that regard I would like to see at least an attempt to attain a larger proportion recruited (this should be a key outcome). Furthermore, I do not feel that a comparison of age, gender and SES is sufficient to determine the representativeness of the cohort. I would like to see a comparison of consulting and prescribing rates. I realise that it may be challenging to get permission to access this data on non-consenting children, but there is certainly precedent for accessing anonymised aggregate data on non-consenting individuals, so it might be possible. Failing that, it would be helpful to compare consulting and antibiotic prescribing rates in the recruited cohort with rates calculated from routine data sources.</p> <p>I wish the authors the best of luck with the study.</p>
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<b>REVIEWER</b>	Beth Stuart University of Southampton UK
<b>REVIEW RETURNED</b>	02-Jul-2016

<b>GENERAL COMMENTS</b>	<p>This is a very well written manuscript that clearly describes an interesting feasibility study. The methods set out for examining the feasibility outcomes are appropriate for this sort of study and well described.</p> <p>The only aspect that I felt could be clarified was the treatment of the secondary outcomes. The study will allow multiple children from the same household. However, the transmission of illness and consultation rates are likely to be clustered by household (children within parents). This is a feasibility study and therefore the analyses will be primarily descriptive. However, in regression modelling, it might be appropriate to take this clustering into account.</p>
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## VERSION 1 – AUTHOR RESPONSE

Reviewer 1 comments (summarised):

Concerns about the representativeness of the cohort: proportion responding as well as measures of comparison (age and gender of children not enough). Address by:

1. Attempting to attain larger proportion recruited
2. Adding comparison of consulting and prescribing rates between recruited cohort and non-recruited - or routine data sources.

Study team response:

We thank the reviewer for their positive comments on our study. We agree on the importance of representativeness of the cohort and recognise this as a potential limitation of the study.

We aim to compare age, gender and index of multiple deprivation (IMD) levels between responders and non-responders, and, if this is not possible, at the very least compare IMD levels of responders with that of their GP practice population.

We have amended the manuscript as follows:

Page 6, line 11: We have added: “and a measure of index of multiple deprivation (IMD) for comparison with the recruited cohort.”

Page 6, line 12: We have tempered the statement of assessing representativeness by changing the wording from “enabling an assessment of how representative the recruited cohort is...” to “enabling some assessment...”

We address the reviewer’s two explicit suggestions below:

1. We agree that it would be preferable to attain a larger proportion taking part in the study from those invited. Estimates of response rates (circa 5%) were based on response rates attained within similar research within the wider infection research group at the University of Bristol, and response rates are a key outcome of this study. Attempts to maximise response rates were a part of the study design, which we agree would be good to highlight within the paper.

We have amended the manuscript as follows:

Page 6, line 1: We have added a section:

“Supplementary recruitment efforts

Attempts were made to maximise response rates through supplementing the initial letter mailout with non-responders receiving a reminder letter and (where the GP surgery had the facility) text (texts were not sent to the mobile numbers associated with older children’s medical records due to the risk of the number being the child’s own phone rather than the parents, who are the consenting participants). In addition, posters and recruitment cards were displayed in all GP surgeries, the team released a press release and set up a study website encouraging recruitment. Recruitment cards were also sent to all families identified as eligible during their welcome call, with a request to pass the message on to other parents who may be interested in the study (for ‘snowball’ recruitment).”

2. A strength of the current study is that it is the first time consultation rates will have been measured against the number (denominator) of unwell children. It also means we are able to look at the proportion of symptomatic children who consult and are given a prescription for antibiotics. Routine data and previous research can only tell us the proportion of registered children who consult – independently from community respiratory tract infection prevalence. For this reason it is not possible to find reliable comparable data on this measure for our cohort. While evidence of consultation and prescribing rates may be available by the denominator of the children, we would not be able to accurately compare our cohort with these data due to the varying time spans of surveillance

involvement within this feasibility study, as opportunity to be involved in the ongoing surveillance varied between one and four months due to sequential recruitment methods.

This study is a feasibility study, and as such its purpose is to inform the design of a future larger-scale cohort study. It is therefore very helpful to receive this comment as for our future study, we will now plan to seek ethical permission and the necessary budget for practices to run a routine search on (respiratory tract infection) consultation and prescribing rates and thereby allow a comparison of these important characteristics by responders and non-responders.

We have amended the manuscript to make this point more explicit in the paper as follows:

Page 5, line 19: We added “for reported symptoms” to the sentence: ‘Secondary aims are to provide evidence regarding the proportion choosing to consult \* and the duration of RTI symptoms in the community.’

Page 6, line 34: We have added (to sample size) “while equivalent rates in children are unknown (a research gap that this study addresses)”

Page 7, line 7: We have added (to secondary outcomes): “as a proportion of reported episodes of RTI symptoms”

Reviewer 2 comments (summarised):

Clustering of transmission of illness and consultation rates likely by household. Although this is feasibility (descriptive results), would need to take this clustering into account in regression modelling

Study team response:

We thank the reviewer for their positive comments on our study. The reviewer is correct that consultation rates are likely to be clustered within families. We will report the intraclass correlation coefficient (ICC), which will help us in designing the next phase of the study. It is also possible that we will have clustering at GP level (child within family within GP practice). In any reported regression analyses we will assess the extent to which clustering is an issue, and where appropriate, use multilevel modelling techniques to adjust the standard errors of regression coefficients.

We have amended the manuscript as follows:

Page 9 line 22: We have added “Regression analyses will be adjusted for clustering (children within families within GPs) where appropriate.”

Page 9 line 27: We have added “Again, regression analyses will be adjusted for clustering where appropriate.”