PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Do hospital pressures change following rotavirus vaccine introduction? A retrospective database analysis in a large paediatric hospital in the United Kingdom.
AUTHORS	Heinsbroek, Ellen; Hungerford, Daniel; Cooke, Richard; Chowdhury, Margaret; Cargill, James; Bar-Zeev, Naor; French, Neil; Theodorou, Eleni; Standaert, Baudouin; Cunliffe, Nigel

VERSION 1 - REVIEW

REVIEWER	Khitam Muhsen Tel Aviv University, Israel
REVIEW RETURNED	30-Nov-2018

GENERAL COMMENTS	This well-designed ecological study assessed changes in “hospital pressure” following the introduction of rotavirus immunization program in the UK, using medical records of a large pediatric hospital. Several outcomes were evaluated including any infection, rotavirus gastroenteritis, acute gastroenteritis, and hospital-acquired infections. The authors nicely discuss the study limitations and factors not-related to rotavirus immunization that can explain the study findings. It will be helpful to comment on changes in the population size (growth?) in the catchment area of the study hospital. Another inevitable question is whether changes in referral policy took place during the study period. Additional comments * The terms “impact” and “effect” imply causal association. As discussed by the authors, other factors, not only rotavirus immunization program, can explain at least in part, the findings /changes in the various study outcomes. It is recommended to revise the title and text accordingly. * Page 7 Setting: Please describe the study population in the catchment area of the Adler Hey Children’s hospital. Likewise, it can be useful if information on referral patterns is presented. * Presentation of the point estimates and confidence intervals in text/ tables and abstract should be uniform (e.g., using the minus sign in the point estimate and CI). * Page 5, line 70: Please explain the term “finished consultant episodes”

	* Page 11 line 192: Please present median and interquartile range for the number of rotavirus tests.

REVIEWER	Scott Grytdal Division of Viral Diseases Centers for Disease Control and Prevention USA
REVIEW RETURNED	18-Dec-2018

GENERAL COMMENTS	This is a well-written article describing the possible impact of rotavirus vaccination on hospital resources at a UK pediatric hospital. The premise of the article is interesting and timely given the amount of pressures placed on hospital resources worldwide. While the expected drops in rotavirus gastroenteritis admissions was observed, it is somewhat disappointing to see that the impact of vaccination did not seem to affect other hospital measures of pressures such as bed occupancy. However, the authors did a thorough examination of attempting to explain this apparent lack of impact. This reviewer would recommend that they re-examine this topic after additional years have passed since the introduction of rotavirus vaccine to see if a longer-term impact in vaccination can be observed later. Specific comments on this manuscript include: --Regarding the use of “non-infectious gastroenteritis” among the “any infection” and “acute gastroenteritis” categories of interest: consider adding the “unspecified diarrhea” (ICD-10 code R19.7) to capture additional acute gastroenteritis admissions that are not specifically coded as having an infectious cause. --It is unclear why HA bloodstream infection rate was used as an outcome measure of interest. Perhaps the authors can provide a brief explanation for the use of this outcome measure.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

The authors nicely discuss the study limitations and factors not-related to rotavirus immunization that can explain the study findings. It will be helpful to comment on changes in the population size (growth?) in the catchment area of the study hospital. Another inevitable question is whether changes in referral policy took place during the study period.

We have added the following sentence to the discussion, page 18 line 339-345

A further consideration is how changes to the catchment population size and referral patterns during the study period could affect our findings and their interpretation. There has been a small but steady population growth in the surrounding region consistent with a national trend, which could increase demand upon the hospital and dampen any effect of rotavirus vaccination on reducing these pressures. Finally, the impact of any changes in referral policy during the study period is difficult to quantity as Alder Hey serves a region of over 7.1 million people.

* The terms “impact” and “effect” imply causal association. As discussed by the authors, other factors, not only rotavirus immunization program, can explain at least in part, the findings /changes in the various study outcomes. It is recommended to revise the title and text accordingly.

The title has been changed to reflect this and the word impact removed from the manuscript.

“Do hospital pressures change following rotavirus vaccine introduction? A retrospective database analysis in a large paediatric hospital in the United Kingdom”

* Page 7 Setting: Please describe the study population in the catchment area of the Adler Hey Children’s hospital. Likewise, it can be useful if information on referral patterns is presented.

We have added the following detail to page 7 line 99

“Alder Hey Children’s NHS foundation Trust (Alder Hey) is located in Liverpool, UK and is one of the largest paediatric hospitals in Europe, with a catchment population of over 7.1 million.”

* Presentation of the point estimates and confidence intervals in text/ tables and abstract should be uniform (e.g., using the minus sign in the point estimate and CI).

This has been altered so that point estimates present a minus sign and CIs are separated by a comma.

* Page 5, line 70: Please explain the term “finished consultant episodes”

This is defined as consultant episode with a patient during hospital admission that has finished due to discharge, transfer or death. For global clarity we have changed the terminology in the manuscript to “hospital admission episodes”

* Page 11 line 192: Please present median and interquartile range for the number of rotavirus tests.

This has been added to the manuscript page 11 line 205

Reviewer: 2

This reviewer would recommend that they re-examine this topic after additional years have passed since the introduction of rotavirus vaccine to see if a longer-term impact in vaccination can be observed later.

Whilst ideally we would re-examine the topic, Alder Hey Children’s hospital has now moved to a new modern site with many single occupancy rooms. So conducting an extended analysis using the same methodology across the two sites would be fundamentally flawed. However, the use of other sites in the UK and in Europe may be pursued in the future.

Specific comments on this manuscript include:

 --Regarding the use of “non-infectious gastroenteritis” among the “any infection” and “acute gastroenteritis” categories of interest: consider adding the “unspecified diarrhea” (ICD-10 code R19.7) to capture additional acute gastroenteritis admissions that are not specifically coded as having an infectious cause.

Thank you for the suggestion. This code was not identified in the original case definition of this or other associated studies we have conducted. However, we have checked for the use of this code over the study period and R19.7 was not used at all. Therefore, inclusion of this code would not yield any additional data.

 --It is unclear why HA bloodstream infection rate was used as an outcome measure of interest. Perhaps the authors can provide a brief explanation for the use of this outcome measure.

An explanation below and added to line 156-159 pg 9 of the manuscript/

We chose to use HA Bloodstream infection rate as an outcome measure since, as for other outcome measures we examined such as HA rotavirus, this may be an indicator of how changes in hospital pressures could influence infection control practices and subsequent nosocomial transmission.

VERSION 2 – REVIEW

REVIEWER	Khitam Muhsen Tel Aviv University, Sackler Faculty of Medicine
REVIEW RETURNED	20-Feb-2019

GENERAL COMMENTS	The authors addressed all comments.