

1 **1 Do hospital pressures change following rotavirus vaccine introduction? A retrospective**
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4 **2 database analysis in a large paediatric hospital in the United Kingdom.**

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41
42 20 **Abbreviated title:** Hospital pressures post rotavirus vaccination

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44 21 **Word count:** 3248

45
46 22 **ABSTRACT**

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48 23 **Objective** Hospitals in the United Kingdom are under increasing clinical and financial

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50 24 pressures. Post introduction of childhood rotavirus vaccination in the UK in 2013, rotavirus

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52 25 gastroenteritis (RVGE) hospitalisations reduced significantly. We evaluated changes in

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26 'hospital pressures' (demand on healthcare resources and staff) following rotavirus vaccine
27 introduction in a paediatric setting in the UK.

28 **Design** Retrospective hospital database analysis between July 2007 and June 2015.

29 **Setting** A large paediatric hospital providing primary, secondary and tertiary care in
30 Merseyside, UK.

31 **Participants** Hospital admissions aged < 15 years. Outcomes were calculated for four
32 different patient groups identified through diagnosis coding (ICD-10) and/or laboratory
33 confirmation: all admissions; any infection, acute gastroenteritis; and RVGE.

34 **Methods** Hospital pressures were compared before and after rotavirus vaccine
35 introduction: these included bed occupancy, hospital-acquired infection rate, unplanned
36 readmission rate, and outlier rate (medical patients admitted to surgical wards due to lack
37 of medical beds). Interrupted time-series analysis was used to evaluate changes in bed
38 occupancy.

39 **Results** There were 116,871 admissions during the study period. Lower bed occupancy in
40 the rotavirus season in the post-vaccination period was observed for RVGE (-89%, 95%CI
41 73%,95%), acute gastroenteritis (-63%, 95%CI 39%,78%) and any infection (-23%, 95%CI
42 15%,31%). No significant overall reduction in bed occupancy was observed (-4%, 95%CI -
43 1%,9%). No changes were observed for the other outcomes.

44 **Conclusions** Rotavirus vaccine introduction was not associated with reduced hospital
45 pressures. A reduction in RVGE hospitalisation without change in overall bed occupancy
46 suggests that beds available were used for a different patient population, possibly reflecting
47 a previously unmet need.

48 **Clinical trials identifier** ClinicalTrials.gov NCT03271593

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2 50 **'Strengths and limitations of this study'**
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- 4 51 • This study used 8 years of retrospective routinely collected data from a large
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6 52 paediatric hospital in the United Kingdom.
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8 53 • This is the first study to examine the effects of a vaccine on wider measures of
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10 54 hospital pressures in the United Kingdom.
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12 55 • Our analysis highlights the importance of the presentation of data from the full study
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14 56 period in a time series analysis, rather than restricting the results to a "before-after"
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16 57 comparison.
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18 58 • Our analysis was complicated by inevitable changes in hospital practices over the 8-
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20 59 year study period, in particular changes in patient flow, laboratory procedures,
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22 60 infection control and clinical coding.
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61 INTRODUCTION

62 In the context of increasing patient need and constrained resources, the United Kingdom's
63 (UK) National Health Service (NHS) faces growing clinical and financial pressures. Currently,
64 the NHS is failing to meet targets for urgent, emergency and planned care.[1, 2] Hospital
65 admission rates have been increasing for the past decade; if the increases continue at the
66 current rate an extra 22 hospitals with 800 beds each will be required by 2022.[3] Although
67 highest for the elderly, increases in admission rates are occurring across all age groups.[3] In
68 children aged 0-14 years, the number of hospital admission episodes increased from 1.7 to
69 2.0 million between 2004-05 and 2014-15 [4] and emergency department (ED) attendances
70 have risen by approximately 300,000 between 2011-12 and 2014-15,[5] leaving paediatric
71 services with increased demand but a short fall of medical staffing.[6]

72 While the problems the NHS faces are complex, there are ongoing disease prevention
73 mechanisms which can help alleviate some of the burden. Vaccines for example, are the
74 most effective defence against infectious diseases.[7] For highly efficacious vaccines
75 targeting childhood diseases with a large hospitalisation burden, it is possible that the
76 reduction in beds occupied for infections caused by the vaccine target pathogen reduces
77 hospital pressures, and potentially nosocomial infections.[8, 9]

78 Prior to vaccine introduction in the UK, rotavirus gastroenteritis (RVGE) was a major cause
79 of hospital admission in young children during the winter/spring months. It was estimated
80 that in children less than 5 years of age, 20% of ED attendances and 45% of hospitalisations
81 for acute gastroenteritis (AGE) were due to rotavirus infections.[10] The UK introduced the
82 monovalent two-dose rotavirus vaccination (*Rotarix*, GSK) into the routine childhood
83 immunisation schedule in July 2013. Rotavirus vaccine uptake increased rapidly to over 90%
84 for one dose [11] and early vaccine impact studies suggest a significantly reduced incidence
85 of RVGE hospitalisations in children.[7, 12, 13] The aim of this study was to assess hospital

1 86 pressures at a large UK NHS paediatric hospital pre- and post- rotavirus vaccine introduction
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4 87 using routinely collected data. As there are no direct measures of hospital clinical pressures
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6 88 (on healthcare resources and staff), evidenced proxy indicators were used: bed occupancy,
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9 89 hospital-acquired infection rate, unplanned readmission rate, and rate of outliers (medical
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11 90 patients admitted to surgical wards).
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92 **METHODS**

93 **Setting**

94 Alder Hey Children's NHS foundation Trust (Alder Hey) is located in Liverpool, UK and is one
95 of the largest paediatric hospitals in Europe, with a catchment population of over 7.1
96 million. Alder Hey provides primary, secondary and tertiary care facilities for >200,000
97 children each year and has approximately 240 inpatient beds; this study utilized data prior
98 to the opening of a new hospital premises in October 2016. General medicine, general
99 surgery, and a range of specialist services are provided. There is also a large ED. Patients
100 with a suspected or confirmed RVGE are admitted to a room within the cubicle areas of one
101 of the general medical wards. If no beds are available in the general medical wards, cubicle
102 areas in specialized medical wards or surgical wards are used.

103 **Data sources**

104 Retrospective hospital database analysis (ClinicalTrials.gov NCT03271593) was conducted at
105 Alder Hey. Anonymised bed admission and laboratory data were extracted by the hospital
106 informatics department from routine patient databases. Patient data were extracted for the
107 period July 2000 – June 2015; analysis was restricted to the period July 2007 – June 2015
108 since changes were made to clinical coding in 2006, and bed availability data were only
109 available from February 2006 onwards.

110 **Study population and definitions**

111 We included all inpatients aged 0-14 years admitted between 1st July 2007 and 30th June
112 2015, who attended at least one ward other than the ED. Excluded from analysis were any
113 patients 15 years or older at time of admission, day patients, and those who were admitted
114 and discharged from the ED or observation unit without attending another ward.

115 Outcomes were calculated for four different patient groups identified through ICD-10
116 (International Classification of Disease, tenth edition) hospital discharge diagnosis codes:

- 1 117 • *All admissions*
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- 4 118 • *Any infection:* Admissions coded as any infection (ICD-10 A00-B99 and J09-J22 in any
- 5
- 6 119 diagnostic code) or as non-infectious gastroenteritis (K52.9).[14]
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- 9 120 • *Acute gastroenteritis (AGE):* Admissions coded as acute gastroenteritis (ICD-10 A00-
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- 11 121 A09 in any diagnostic code) or as non-infectious gastroenteritis (K52.9).[14]
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- 14 122 • *Rotavirus gastroenteritis (RVGE):* Admissions coded as rotavirus gastroenteritis (ICD-
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- 16 123 10 A08.0 in any diagnostic code) and/or laboratory-confirmed as rotavirus.[14]
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- 18 124 Laboratory confirmation for RVGE was defined as rotavirus antigen detected by
- 19
- 20 125 either immunochromatographic test or by enzyme immunoassay in a faecal
- 21
- 22 126 specimen of a child with AGE. A distinction was made between community-acquired
- 23
- 24 127 (CA) and hospital-acquired (HA) RVGE: HA RVGE was defined as any patient with a
- 25
- 26 128 positive test for rotavirus infection with a sample date more than 2 days after
- 27
- 28 129 admission and no record of diarrhoea or vomiting on admission.[7] Testing for RVGE
- 29
- 30 130 was done on clinicians' request. The testing policy for RVGE did not change over the
- 31
- 32 131 study period.
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38 132 Diagnosis coding for non-infectious gastroenteritis (ICD-10 K52.9) was included since

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40 133 unspecified gastroenteritis was classified under this code until April 2012.[15]

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43 134 The pre-vaccination period was defined as 1st July 2007 - 30th June 2013; the post

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45 135 vaccination period was defined as 1st July 2013 – 30th June 2015. The rotavirus season was

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47 136 defined as 1st January – 31st May; the period when laboratory detection rate in the UK is

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49 137 highest.[16]

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52 138 **Outcomes**

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55 139 The following outcomes were calculated:

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- 1 140 • *Bed occupancy*: number of patients allocated a bed on a specific ward divided by
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4 141 number of available beds at that ward at 12.00 noon. Bed occupancy for any
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6 142 infection, AGE and RVGE were determined using the definitions above. For HA-RVGE,
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8 143 only bed occupancy on the ward where the patient tested positive for rotavirus was
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10 included. For CA-RVGE, total hospital stay was attributed to rotavirus. Sensitivity
11 144 analyses were done with bed availability data collected at 9am and 5pm.
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16 146 • *HA bloodstream infection rate*: number of HA bloodstream infections per 1,000
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18 147 admissions with length of stay >2 days. We used indicator organisms to describe HA
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20 infection: a HA bloodstream infection was defined as identification of methicillin-
21 148 sensitive *Staphylococcus aureus* or methicillin-resistant *Staphylococcus aureus* or
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23 149 *Escherichia coli* or *Candida* species in a blood sample obtained >2 days after
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25 admission. HA Bloodstream infection rate was used as an outcome measure since, as
26 150 for other outcome measures such as HA rotavirus, this may be an indicator of how
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28 151 changes in hospital pressures could influence infection control practices and
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30 subsequent nosocomial transmission.
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38 155 • *Unplanned readmission*: number of patients with an emergency readmission within 7
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40 156 days after discharge per 1,000 admissions.[8]
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43 157 • *Outlier rate*: number of medical patients admitted to a surgical ward per 1,000
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45 158 admissions. A medical patient was defined as any patient classified under
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47 haematology/oncology, general paediatrics, endocrinology, nephrology,
48 159 rheumatology, respiratory medicine, dermatology or accident & emergency.
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53 161 Calculations of bed occupancy, HA infection rate, and unplanned readmission rate were
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55 162 restricted to nine general medical wards. Several wards opened or closed during the study
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1 163 period. Changes in ward structure were taken into account in the outcomes calculated by
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4 164 including data according to the wards' opening periods.

6 165 **Descriptive analysis**

8 166 Data analyses were performed using R version 3.2.0 (R Core Team, Vienna). The number of
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11 167 admissions for each patient group, length of stay and age of RVGE patients was described
12
13 168 pre and post-vaccine introduction during the rotavirus season. Differences between
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16 169 continuous variables were tested using Student's t-test or Wilcoxon rank-sum test if not
17
18 170 normally distributed and χ^2 -test or Fisher's exact test for categorical variables.

21 171 **Statistical analysis**

23 172 To assess any changes in bed occupancy following rotavirus vaccine introduction,
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26 173 interrupted time-series analysis was used as previously described.[7] Monthly expected bed
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28 174 occupancy was estimated by fitting a negative binomial regression model to pre-vaccine
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30 175 monthly bed occupancy data, adjusted for seasonality and secular trends using calendar
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33 176 month and rotavirus year (July to June), respectively. A negative binomial model was chosen
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35 177 to account for overdispersion in the data. This model was used to predict the expected bed
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38 178 occupancy rate in the absence of vaccination, where the post-vaccine introduction change is
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40 179 expressed by the difference between the expected and observed bed occupancy. To
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43 180 quantify change in average bed occupancy in the rotavirus season as a result of introduction
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45 181 of the vaccine, a second model included a binary indicator variable for the vaccine period,
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47 182 enabling the computation of risk ratios (RR) and associated 95% confidence intervals (CI).
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50 183 This second model was restricted to the rotavirus season and adjusted for calendar month
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53 184 and rotavirus year. Percentage change in average bed occupancy was calculated as $100(1 -$
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55 185 $RR)$.

57 186 **Ethics**

1 187 Ethics approval was provided by the NHS Research Ethics Committee, North East –
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4 188 Newcastle & North Tyneside 2 and by the Alder Hey Children’s NHS Foundation Trust
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6 189 Research and Development Department.
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8 190 **Patient and public involvement statement**

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11 191 This study was conducted using secondary data and there was no new contact with patients
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13 192 throughout the study. No patients were directly involved in designing the research question,
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15 193 conducting the research or interpretation of the research findings. Investigators have
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17 194 presented these findings at national and international events
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20 21 **RESULTS**

22
23 196 In total, there were 116,871 admissions among 68,838 unique patients at any time in the
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25 197 year during the study period from 1st July 2007 – 30th June 2015. Of those admissions,
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27 198 48,852 occurred during the rotavirus season.
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30 199 Testing for rotavirus remained stable throughout the pre-vaccination study period, with a
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32 200 median of 509 (IQR=481-539) admissions tested each rotavirus season, of which a median of
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34 201 128 (25.2%) were positive (Figure 1). In the rotavirus seasons following rotavirus vaccine
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36 202 introduction, the proportion of rotavirus-positive test results amongst admissions tested
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38 203 dropped to 3.8% (13/338) and 5.9% (16/272) in 2014 and 2015 respectively.
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41 204 The median age of patients with RVGE was 11 months in the pre-vaccination period, and 22
42
43 205 months in the post-vaccination period ($p=0.06$). Median length of hospital stay for patients
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45 206 with CA RVGE did not differ between the pre- and post-vaccination period (2.2 vs. 2.4 days,
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47 207 $p=0.89$). Median length of stay from RVGE diagnosis to discharge for patients with HA RVGE
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49 208 was not significantly different between the pre- and post-vaccination period (8.5 days pre
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51 209 vs. 5.0 days post, $p=0.88$) (Figure 2).
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55 210 Length of stay for all admissions was highest during the respiratory virus season in
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57 211 November/December and slightly increased from 2007 to 2012 ($p<0.001$) (Supplementary
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1 212 Figure 1). No significant change in length of stay for all admissions was observed for the
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4 213 period 2012 to 2015 ($p=0.21$).

6 214 **Bed occupancy**

8 215 Figure 3 shows the average monthly bed occupancy for general medical wards for all
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11 216 admissions, admissions with a diagnosis of any infection, and admissions with a diagnosis of
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14 217 RVGE. Bed occupancy for AGE is shown in Supplementary Figure 2. Clear seasonal patterns
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16 218 were observed for total bed occupancy, with highest overall bed occupancy for the
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18 219 respiratory virus season in November/December, and lowest overall bed occupancy in the
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21 220 summer months. A year-on-year increase was observed for overall bed occupancy over the
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23 221 study period ($p<0.001$), from 79% bed occupancy in December 2007 to 90% in December
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26 222 2014.

28 223 Bed occupancy for RVGE showed clear seasonal peaks before introduction of the vaccine,
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30 224 with highest occupancy shown for February/March. After introduction of the rotavirus
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33 225 vaccine, bed occupancy for RVGE in the rotavirus season was reduced by 89% (95%CI
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35 226 73%,95%) (Table 1). Bed occupancy for any infectious disease increased year on year in the
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38 227 pre-vaccination period, both within and outside the rotavirus season ($p<0.001$ and $p<0.001$
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40 228 respectively), as did bed occupancy for AGE ($p<0.001$ within, $p=0.04$ outside rotavirus
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43 229 season). Post introduction of the vaccine, observed bed occupancy for AGE in the rotavirus
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45 230 season was reduced by 63% (95%CI 39%,78%) after adjustment for the positive trend in the
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48 231 pre-vaccination period. Observed bed occupancy for any infection in the rotavirus season
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50 232 was reduced by 23% (95%CI 15%,31%). No significant reduction was observed when
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53 233 considering observed vs. expected bed occupancy for any cause of admission (-4%, 95%CI -
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55 234 1%,9%). Sensitivity analyses with bed availability data taken at 9am and 5pm provided the
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57
58 235 similar results.

236 **Table 1:** Average monthly bed occupancy and decline in bed occupancy comparing the pre-
 237 and post-rotavirus vaccination period for any admission, any infection, acute gastroenteritis
 238 and rotavirus gastroenteritis on general medical wards in Alder Hey NHS Foundation Trust,
 239 July 2007 – June 2015.

Variable	Average bed occupancy		Crude Risk ratio (95% CI)	Adjusted Risk ratio (95% CI) ¹	Decline in bed occupancy (95% CI)	P-value
	Pre-vaccination n	Post-vaccination n				
All	77% (70% - 85%)	79% (67% - 87%)	1.03 (0.99,1.08)	0.96 (0.91,1.01)	4% (-1%,9%)	0.15
Any infection ²	39% (25% - 56%)	42% (33% - 51%)	1.09 (0.95,1.25)	0.77 (0.69,0.85)	23% (15%,31%)	<0.001
AGE ²	5% (1% - 16%)	3% (1% - 8%)	0.72 (0.45,1.13)	0.37 (0.22,0.61)	63% (39%,78%)	<0.001
RVGE ³	5% (0% - 17%)	1% (0% - 4%)	0.18 (0.09,0.35)	0.11 (0.05,0.27)	89% (73%,95%)	<0.001

240 AGE: acute gastroenteritis; CI: confidence interval; NHS: National Health Service; RVGE:
 241 rotavirus gastroenteritis.

242 ¹ Adjusted for seasonality and secular trend. ² Diagnosis of any infection and AGE by clinical
 243 coding only. ³ Diagnosis of RVGE by clinical coding and laboratory results.

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4 **245 Hospital-acquired (HA) bloodstream infection rate**5
6 246 A decrease in HA bloodstream infection was observed in the post-vaccination period,
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9 247 although this did not appear different from secular trends in the pre-vaccination period
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11 248 (Figure 4).12
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14 **249 Unplanned readmission rate**15
16 250 No difference was observed between the unplanned readmission rate in the pre-vaccination
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18 251 period and the post-vaccination period (Figure 5).19
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21 **252 Outlier rate**22
23 253 Clear seasonal patterns were observed for the outlier rate, with the highest peak during the
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26 254 respiratory virus season in November/December, and a secondary peak during the rotavirus
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28 255 season in January-May (Figure 6). The outlier rate increased in 2012, and remained high
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30 256 throughout 2013-2015, both within and outside the rotavirus season. The increase in outlier
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32
33 257 rate is synchronous with the closure of one specific ward, a large general medical ward in
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35 258 November 2011, and the opening of a new medical admission unit (short-stay department
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38 259 prior to discharge or admission to other wards).
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1 260 **DISCUSSION**

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4 261 This is the first study to examine the effects of national vaccine introduction on wider
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6 262 measures of hospital pressures in the UK. The introduction of rotavirus vaccine has led to a
7
8 263 large reduction in RVGE hospitalisation,[7] reflected in the reduction in proportion of
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10 264 admissions tested rotavirus-positive and the reduction in bed occupancy due to RVGE and
11
12 265 AGE as described here. Lower bed occupancy for RVGE and AGE in the rotavirus season
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14 266 post-vaccine introduction was concordant with lower bed occupancy for any infection in the
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16 267 rotavirus season in the post-vaccination period. Despite the reduction in RVGE
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18 268 hospitalisation, overall bed occupancy was not reduced. This suggests that a large, busy NHS
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20 269 Trust, such as Alder Hey, operates at full capacity and that the beds that became available
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22 270 by the reduction of RVGE hospitalisations were occupied by a different patient population,
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24 271 probably reflecting a previously unmet need and/or physicians having greater freedom to
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26 272 admit patients if beds have become available. The absence of a reduction in overall bed
27
28 273 occupancy could explain why reductions in the other proxy measures (HA-infection rate,
29
30 274 unplanned readmission rate, outlier rate) were not observed.
31
32 275 Two other studies have examined hospital pressures since rotavirus vaccination
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34 276 introduction. A study conducted in two Finnish hospitals concluded that bed occupancy for
35
36 277 RVGE and AGE decreased since introduction of the vaccine.[17] There is no discussion of
37
38 278 changes in total bed occupancy, or on other proxy measures for hospital pressures following
39
40 279 rotavirus vaccine introduction. A study conducted in a general hospital in Belgium (36
41
42 280 paediatric beds) concluded that bed-day occupancy, bed-day turnover and unplanned
43
44 281 readmissions for AGE were lower in the post-vaccination compared with the pre-vaccination
45
46 282 periods, and that this resulted in improved quality of care for overall admissions.[8] In our
47
48 283 study, the reduction of bed occupancy for RVGE did not result in a change in overall bed
49
50 284 occupancy or other measures of hospital pressure. No change in hospital length of stay for

1 285 RVGE patients was observed. Median hospital stay for CA RVGE was shorter in Alder Hey
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4 286 NHS Foundation Trust than reported in the Belgian study (2.2 vs. 4.1 days), suggesting a
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6 287 difference in management of RVGE cases, and could be an indicator of higher hospital
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9 288 pressure and more rapid patient turnover in Alder Hey.

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11 289 Several caveats need to be considered when using routinely collected data. Our analysis was
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13 290 complicated by changes in hospital practises, in particular changes in patient flow,
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16 291 laboratory procedures, infection control and clinical coding. Firstly, several wards relevant
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18 292 to this study opened or closed during the study period. Although ward closures were
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21 293 accounted for in the bed occupancy analysis, more subtle changes in patient dynamics still
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23 294 influenced our results. A steep increase was observed for the outlier rate in 2012, with the
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26 295 higher level sustained throughout 2013-2015. The increase in outlier rate is synchronous
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28 296 with the closure of a large general medical ward in November 2011, and the opening of a
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31 297 new medical admission. It is possible that the change in ward structure led to an increased
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33 298 bed usage in surgical and specialised medical wards.

34
35 299 Secondly, several changes in laboratory procedures were observed during the study period,
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37
38 300 most notably the introduction of polymerase chain reaction for the rapid testing of
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41 301 respiratory pathogens in 2013. Faster diagnosis of respiratory infection could have had
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43 302 implications for patient treatment, isolation practices and patient flow, and could have
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45 303 influenced the measured hospital pressure outcomes. The number of admissions tested for
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48 304 rotavirus did not change significantly over the study period, which provides confidence that
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50 305 the drop in RVGE in the post-vaccine era is a real effect, and not caused by a change in
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53 306 testing policy.

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55 307 Thirdly, there were changes in infection prevention and control (IPC) practices in later years
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57 308 of the study, including an increase in IPC staff; the introduction of isolation and hand
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60 309 hygiene posters, bed space dividers screens and infection control enclosure isolation pods;

1 310 and changes in environmental cleaning. Changes in IPC practices will most likely have
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4 311 resulted in changes in HA infection rates – it is difficult to disentangle their effect on HA
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6 312 infection from any effect due to a reduction in hospital pressures post-rotavirus vaccination
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8
9 313 introduction.

10
11 314 We observed that bed occupancy for any infectious disease increased in the pre-vaccination
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14 315 period, both within and outside the rotavirus season. An increase in bed occupancy for any
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16 316 respiratory infection (supplementary Figure 3) and any gastroenteritis was observed, but
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18 317 neither increase can fully account for the overall increase in any infection. It is possible that
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21 318 the increase in infection observed is due to an artefact of the recording of the data.

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23 319 Supplementary Figure 4 shows that all clinical diagnostic coding increased over the study
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26 320 period. Clinical diagnostic coding increased for both cases with and without any infection
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28 321 recorded. We observed that bed occupancy for any infection in the rotavirus season was
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31 322 lower than the expected bed occupancy for any infection based on pre-vaccination
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33 323 estimates. The increase in any clinical diagnostic coding was sustained in 2014 and 2015,
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35 324 providing confidence that our observation of lower than expected bed occupancy for any
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38 325 infection in the post-vaccination period is a true finding.

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40 326 Our analysis highlights the importance of the presentation of data from the full study period
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43 327 in a time-series analysis, rather than restricting the results to a “before-after” comparison,
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45 328 when there is non-homogeneity in disease management, hospital management and data
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48 329 collection over time. A long-term increase in bed occupancy for any infection could be
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50 330 observed (possibly due to an increase in clinical coding) that predated the introduction of
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53 331 vaccination: taking this ongoing increase in admissions coded as infection into account, a
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55 332 reduction in bed occupancy for any infection can be observed.

56
57 333 A further consideration is how changes to the catchment population size and referral
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60 334 patterns during the study period could affect our findings and their interpretation. There

1 335 has been a small but steady population growth in the surrounding region consistent with a
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4 336 national trend, which could increase demand upon the hospital and dampen any effect of
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6 337 rotavirus vaccination on reducing these pressures. Finally, the impact of any changes in
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9 338 referral policy during the study period is difficult to quantify as Alder Hey serves a region of
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11 339 over 7.1 million people.

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13 340 Routinely collected hospital data can be used for the evaluation of a (vaccination) policy, but
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16 341 our study highlights the difficulty of evaluating a (vaccination) policy in a period with
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18 342 concurrent changes in patient flow, laboratory procedures and IPC practices.

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21 343 The introduction of rotavirus vaccination has led to a dramatic reduction in hospitalisation
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23 344 for RVGE and thus a reduction in bed occupancy for RVGE. However, overall bed occupancy
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25 345 was not reduced further highlighting the severe strain the NHS is under and that demand is
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27 346 outstripping capacity. Bed occupancy continues to rise and even a highly effective routine
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29 347 vaccine only freed-up beds which were then filled by admissions, making no overall
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31 348 headway into reducing the overall pressures the NHS is facing.

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7
8 353 stages of study conduct. GlaxoSmithKline Biologicals SA also took in charge all costs
9
10
11 354 associated with the development and publication of this manuscript.

12
13 355 **Conflicts of interest**

14
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16
17 356 Rotarix is a trademark of the GSK group of companies.

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21 357 NC, NF, and DH are in receipt of research grant support from the GSK group of companies

22
23 358 for the conduct of the present study. NC has received honoraria for participation in GSK

24
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26
27 360 Watermark Research Partners for participation in independent data monitoring committee

28
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30
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32
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34
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36
37 365 the GSK group of companies and from Takeda Pharmaceuticals outside the submitted work.

38
39 366 BS and ET are employees of the GSK group of companies. EH, RC, MC and JC have nothing to

40
41 367 disclose.

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49 368 **Authorship and manuscript preparation**

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51
52 369 DH, RPDC, MC, NC, NF designed the study and wrote the protocol. EH performed the

53
54 370 analyses and wrote the manuscript. JSC and MC provided data for the study. NBZ provided

55
56 371 statistical support. DH, RPDC, MC, JSC, NBZ, NF, NAC provided advice on the understanding

1 372 of the findings. ET and BS provided external advice. All authors approved the final version of
2
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4 373 the paper for submission.

5
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7

8
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12
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14
15
16 378 manuscript coordination, on behalf of GSK. Stephanie Garcia coordinated manuscript
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18 379 development and editorial support.
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22
23 381 **Data sharing**
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25
26 382 The results summary for this study (GSK study identifier: 205369 - ClinicalTrials.gov
27
28 383 identifier: NCT03271593) is available on the GSK Clinical Study Register and can be accessed
29
30 384 at www.gsk-clinicalstudyregister.com. The full data that support the findings of this study
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32 385 are held by Alder Hey Children's NHS Foundation Trust and restrictions apply to the
33
34 386 availability of these data as they are not publicly available. Aggregated data may be
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36 387 available from the authors/ Alder Hey Children's NHS Foundation Trust on reasonable
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38 388 request and with permission of Alder Hey Children's NHS Foundation Trust.
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1 434 **Figures Captions**

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4 435 **Figure 1. Number of admissions tested for rotavirus in the rotavirus season in Alder Hey**
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6 436 **NHS Foundation Trust, July 2007 – June 2015.**

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8 437 *NHS: National Health Service.*

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11 438 **Figure 2. Total length of stay for CA and HA RVGE.**

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14 439 For HA RVGE, length of stay was calculated from date of first positive test.

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16 440 *CA: community-acquired; HA: hospital-acquired.*

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18 441 **Figure 3. Observed and expected bed occupancy for any admission, any infection and**
19
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21 442 **rotavirus gastroenteritis on general medical wards in Alder Hey NHS Foundation Trust,**
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23 443 **July 2007 – June 2015.**

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26 444 The coloured shading represents the 95% confidence intervals for the expected incidence.

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28 445 Grey shading represents the rotavirus season (January-May). The vertical hashed line
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30 446 represents the introduction of rotavirus vaccine in the UK in July 2013.

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33 447 *NHS: National Health Service.*

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35 448 **Figure 4. Hospital acquired bloodstream infection rate on general medical wards in Alder**
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38 449 **Hey NHS Foundation Trust, July 2007 – June 2015.**

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40 450 Black line shows raw data, red line shows smoothed data. Grey shading represents the
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42 451 rotavirus season (January-May). The vertical hashed line represents the introduction of
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44 452 rotavirus vaccine in the UK in July 2013.

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47 453 *HA: hospital-acquired; NHS: National Health Service.*

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50 454 **Figure 5. Unplanned readmission rate for any admission on general medical wards in Alder**
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53 455 **Hey NHS Foundation Trust, July 2007 – June 2015.**

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55 456 Raw data in black, smoothed data in red. Grey shading represents the rotavirus season
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57 457 (January-May). The vertical hashed line represents the introduction of rotavirus vaccine in
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59 458 the UK in July 2013.

1 459 *NHS: National Health Service.*

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4 460 **Figure 6. Outlier rate for any admission in Alder Hey NHS Foundation Trust, July 2007 –**
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6 461 **June 2015.**

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9 462 Raw data in black, smoothed data in red. Grey shading represents the rotavirus season

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11 463 (January-May). The vertical hashed line represents the introduction of rotavirus vaccine in

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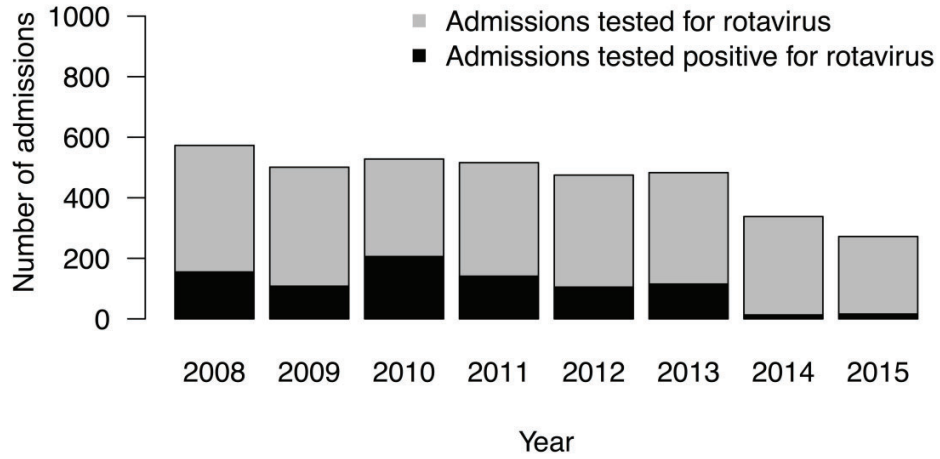


Figure 1. Number of admissions tested for rotavirus in the rotavirus season in Alder Hey NHS Foundation Trust, July 2007 – June 2015.
 NHS: National Health Service.

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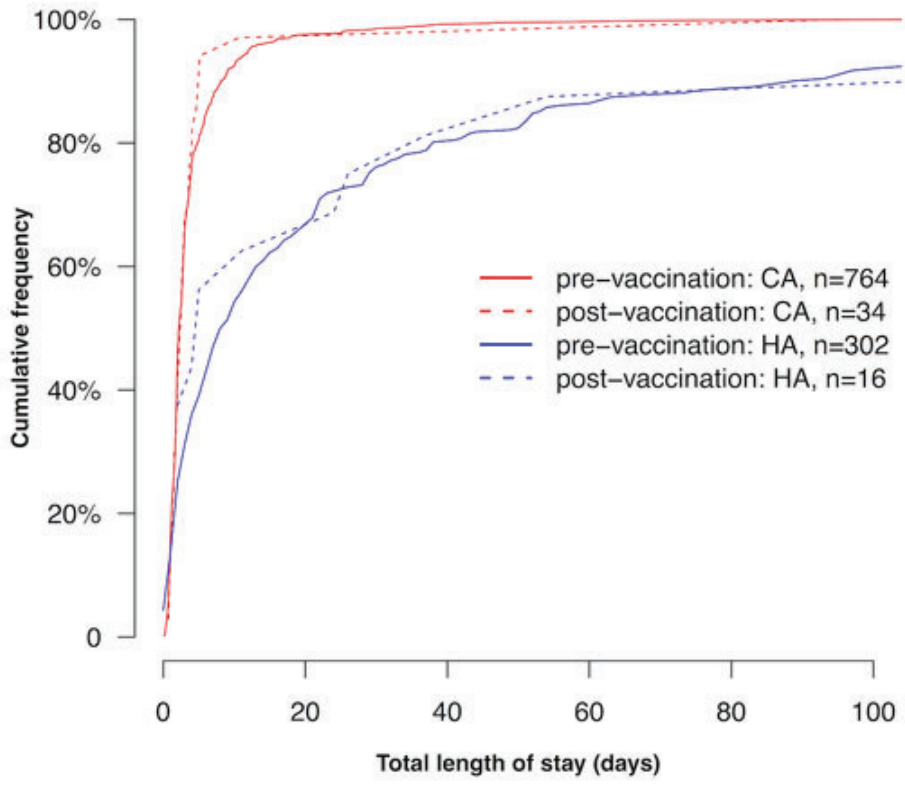


Figure 2. Total length of stay for CA and HA RVGE.
For HA RVGE, length of stay was calculated from date of first positive test.
CA: community-acquired; HA: hospital-acquired.

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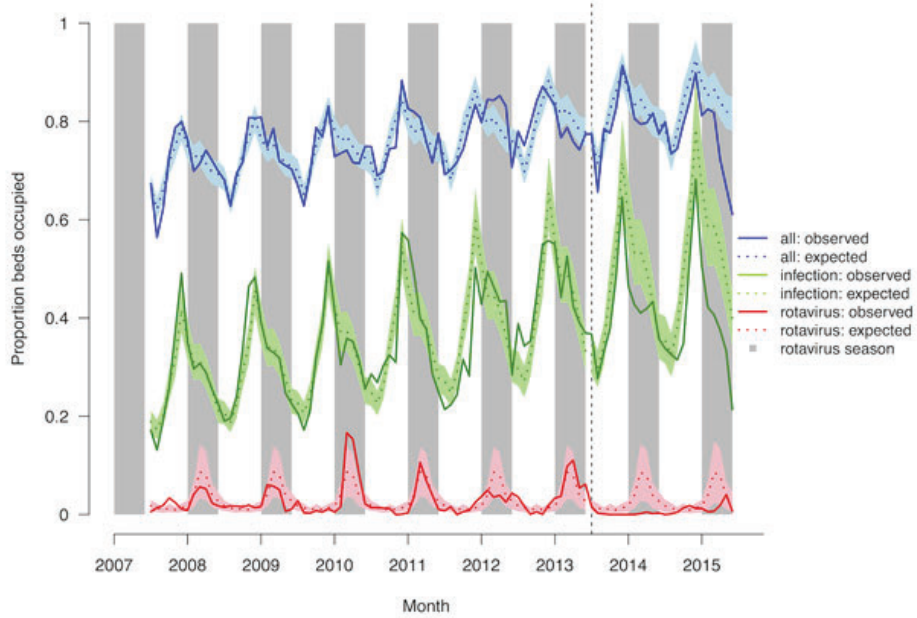


Figure 3. Observed and expected bed occupancy for any admission, any infection and rotavirus gastroenteritis on general medical wards in Alder Hey NHS Foundation Trust, July 2007 – June 2015.

The coloured shading represents the 95% confidence intervals for the expected incidence. Grey shading represents the rotavirus season (January-May). The vertical hashed line represents the introduction of rotavirus vaccine in the UK in July 2013.

NHS: National Health Service.

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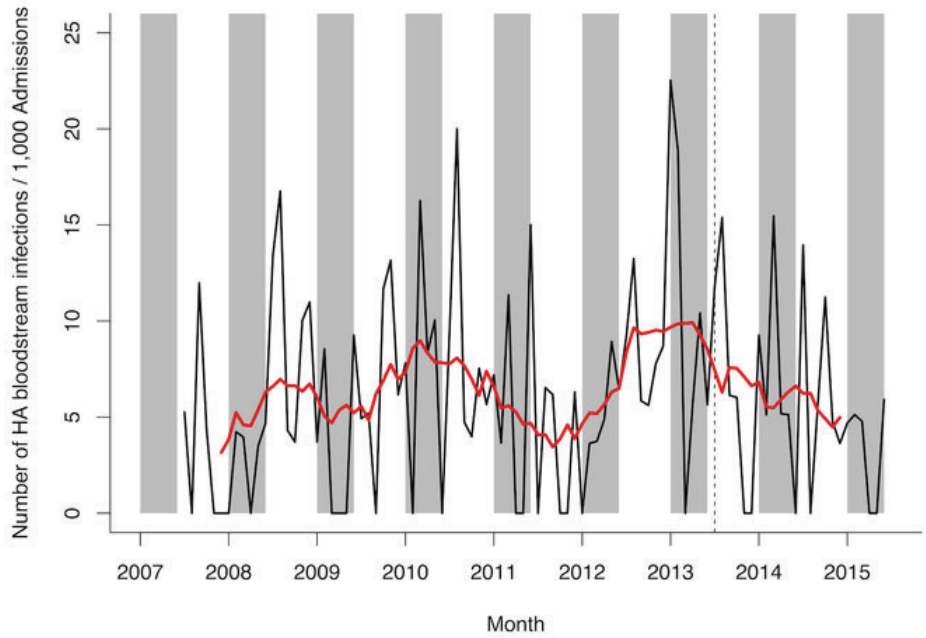


Figure 4. Hospital acquired bloodstream infection rate on general medical wards in Alder Hey NHS Foundation Trust, July 2007 – June 2015.

Black line shows raw data, red line shows smoothed data. Grey shading represents the rotavirus season (January-May). The vertical hashed line represents the introduction of rotavirus vaccine in the UK in July 2013.

HA: hospital-acquired; NHS: National Health Service.

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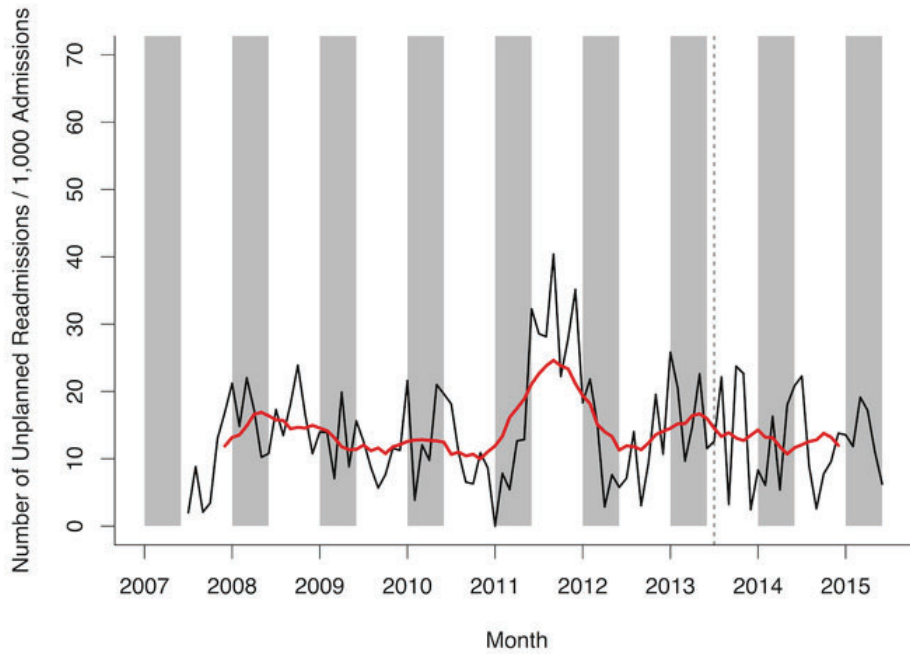


Figure 5. Unplanned readmission rate for any admission on general medical wards in Alder Hey NHS Foundation Trust, July 2007 – June 2015.

Raw data in black, smoothed data in red. Grey shading represents the rotavirus season (January-May). The vertical hashed line represents the introduction of rotavirus vaccine in the UK in July 2013.

NHS: National Health Service.

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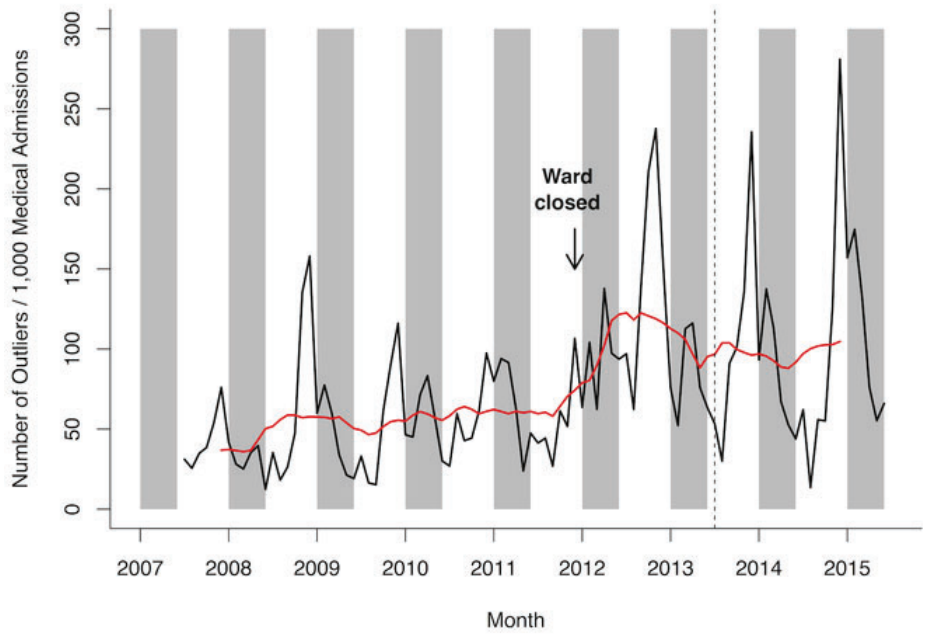
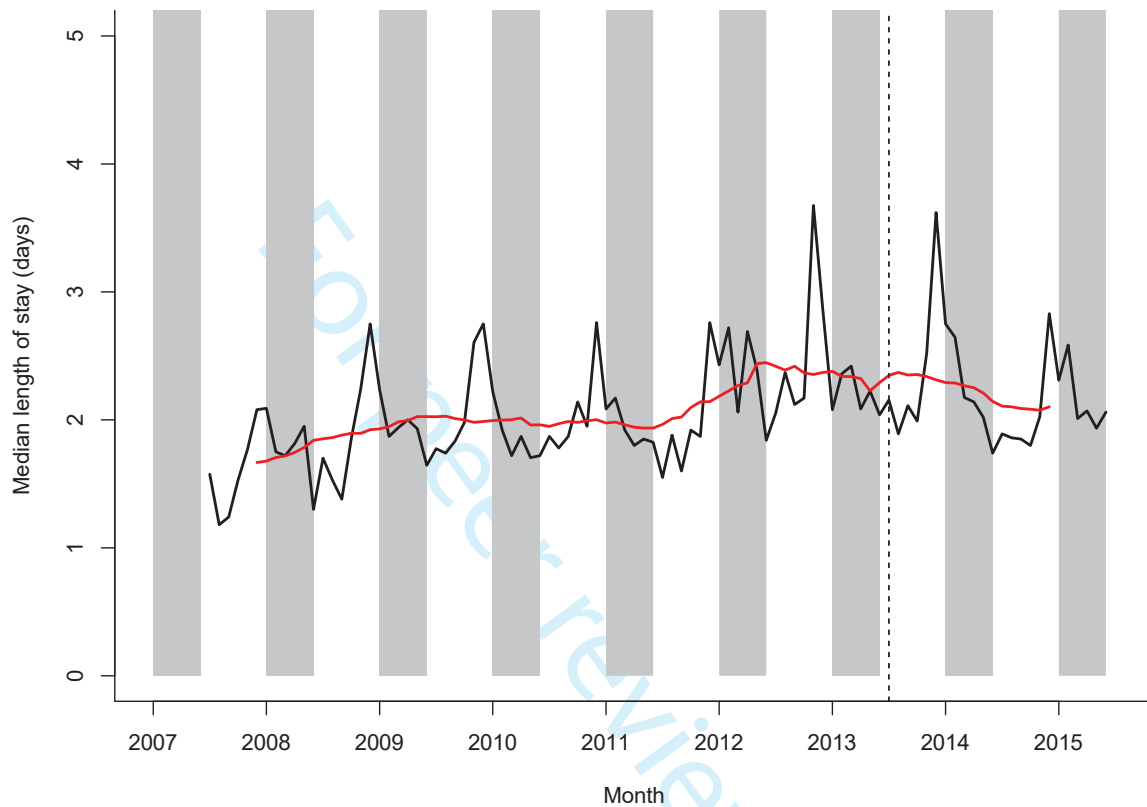


Figure 6. Outlier rate for any admission in Alder Hey NHS Foundation Trust, July 2007 – June 2015.

Raw data in black, smoothed data in red. Grey shading represents the rotavirus season (January-May). The vertical hashed line represents the introduction of rotavirus vaccine in the UK in July 2013.
NHS: National Health Service.

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1 Supplementary Material



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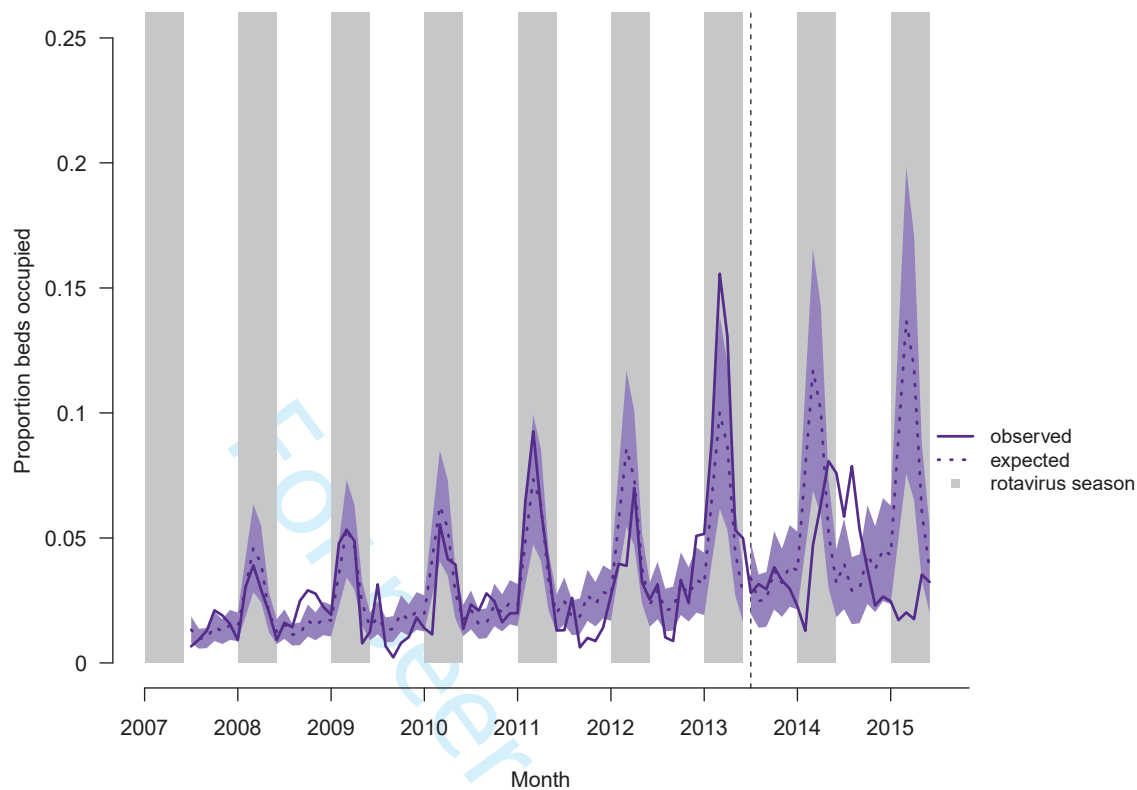
3 **Supplementary Figure 1. Median length of stay (all admissions) on general medical wards in Alder**

4 **Hey Children's NHS Foundation Trust, July 2007 – June 2015.** Raw data in black, smoothed data in

5 red. Grey shading represents the rotavirus season (January-May). The vertical hashed line represents

6 the introduction of rotavirus vaccine in the UK in July 2013.

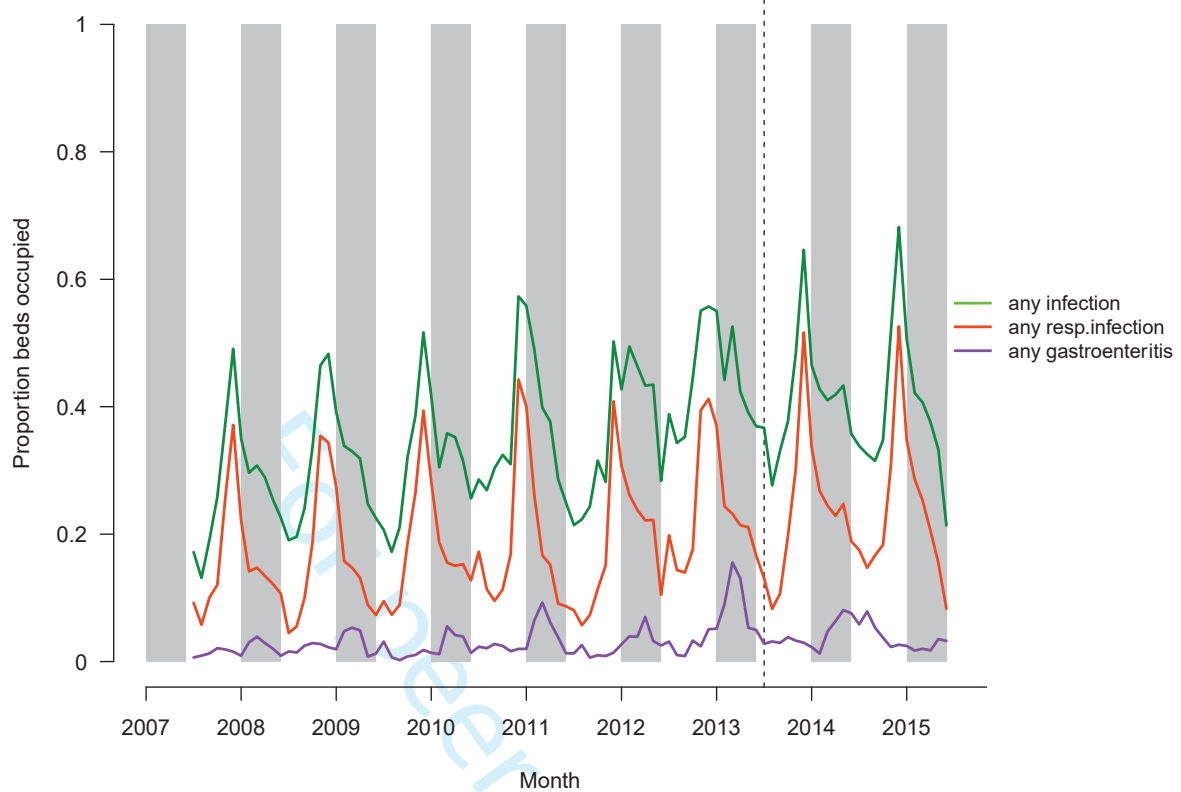
7 *NHS: National Health Service.*



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2 **Supplementary Figure 2. Observed and expected bed occupancy for acute gastroenteritis on**
 3 **general medical wards in Alder Hey NHS Foundation Trust, July 2007 – June 2015.** The coloured
 4 shading represents the 95% confidence intervals for the expected incidence. Grey shading
 5 represents the rotavirus season (January-May). The vertical hashed line represents the introduction
 6 of rotavirus vaccine in the UK in July 2013.

7 *NHS: National Health Service.*



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2 **Supplementary Figure 3. Observed bed occupancy for any infection, any respiratory infection and**
 3 **any gastroenteritis (by clinical coding only) in general medical wards in Alder Hey NHS Foundation**
 4 **Trust, July 2007 – June 2015.** The vertical hashed line represents the introduction of rotavirus
 5 vaccine in the UK in July 2013.

6 *NHS: National Health Service; resp.: respiratory.*