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Prospective cohort study to investigate the burden and transmission of acute gastroenteritis in care homes: epidemiological results

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Complete List of Authors:	Inns, Thomas; University of Liverpool, Institute of Psychology, Health and Society Pulawska-Czub, Anna; University of Liverpool, Institute of Infection and Global Health Harris, John; University of Liverpool, Institute of Psychology, Health and Society Vivancos, Roberto; Public Health England, Field Epidemiology Services, Health Protection Beeching, Nicholas; Royal Liverpool and Broadgreen University Hospitals NHS Trust, Tropical and Infectious Disease Unit Iturriza-Gomara, Miren; University of Liverpool, 1. Department of Clinical Infection, Microbiology & Immunology, Institute of Infection and Global Health O'Brien, Sarah; University of Liverpool, Institute of Psychology, Health and Society
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TITLE

Prospective cohort study to investigate the burden and transmission of acute gastroenteritis in care homes: epidemiological results

AUTHOR INFORMATION

Thomas Inns^{1,2}, Anna Pulawska-Czub^{2,3}, John P Harris^{1,2}, Roberto Vivancos^{2,4}, Nicholas J Beeching^{2,5,6}, Miren Iturriza-Gomara^{2,3}, Sarah J O'Brien^{2,7}

1. Institute of Population Health Sciences, University of Liverpool, Liverpool, UK
2. NIHR Health Protection Research Unit in Gastrointestinal Infections, University of Liverpool, Liverpool, UK
3. Institute of Infection and Global Health, University of Liverpool, Liverpool, UK
4. Field Epidemiology, Field Service, National Infection Service, Public Health England, UK
5. Tropical and Infectious Disease Unit, Royal Liverpool and Broadgreen University Hospitals NHS Trust, Liverpool, UK
6. Clinical Sciences Group, Liverpool School of Tropical Medicine, Liverpool, UK
7. School of Natural and Environmental Science, Newcastle University, Newcastle upon Tyne, UK

Corresponding author: Thomas Inns

Telephone number: +44 151 794 9871

Postal address: The University of Liverpool
The Farr Institute@HeRC
Waterhouse Building (2nd Floor, Block F)
1-5 Brownlow Street
Liverpool
L69 3GL

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ABSTRACT

Objectives To estimate the incidence of gastroenteritis in individuals in care homes.

Design Prospective cohort study.

Setting Five participating care homes in North West England, United Kingdom.

Participants Residents and staff present at the five study care homes between 15 August 2017 and 30 May 2019 (n = 268).

Outcome measures We calculated incidence rates for all gastroenteritis cases per 1000 person-years at risk and per 1000 bed-days at risk. We also calculated the incidence rate of gastroenteritis outbreaks per 100 care homes per year.

Results In total 45 cases were reported during the surveillance period, equating to 133.7 cases per 1000 person-years at risk. In residents the incidence rate was 0.69 cases per 1000 bed-days. We observed 7 outbreaks in study participants, a rate of 76.4 outbreaks per 100 care homes per year. 15 stool samples were tested; three were positive for norovirus, no other pathogens were detected.

Conclusions The current general approach to surveillance of infectious gastroenteritis in care homes, focussing on outbreaks, is detecting a majority of cases of gastroenteritis. However, if policymakers are to estimate the burden of infectious gastroenteritis in this setting using only outbreak surveillance data, this study implies that the total burden will be underestimated by around 25%.

Keywords

Gastroenteritis; Viral gastroenteritis; Norovirus; Outbreaks; Surveillance; Epidemiology; Infection Control

Strengths and limitations of this study

- To our knowledge the first systematic active surveillance study of gastroenteritis in care home residents in the UK
- Prospective cohort design with active follow-up of individual care home residents by fully trained research nurses
- Small number of care homes included and so results might not be generalisable
- Challenges in obtaining stool samples in a timely manner
- Study period coincided with a low incidence of norovirus in the community

1 INTRODUCTION

2 Gastrointestinal infections are an important issue in care homes for the elderly (also known as long-
3 term care facilities). Care home residents are more susceptible to infectious gastroenteritis and the
4 environment is ideal for transmission of gastroenteritis.¹ Because infection control measures are
5 challenging to implement, further infections and outbreaks frequently occur based on a single index
6 case.² In this population, gastrointestinal infections can cause more severe morbidity,
7 hospitalisation, and are associated with greater mortality.^{3,4}

8
9 Surveillance of infectious gastroenteritis in care homes varies in presence and scope in different
10 countries, and where it exists it is focussed on the detection of outbreaks. These outbreak
11 surveillance systems exist in countries such as France, Australia and England.⁵⁻⁷ Using these
12 surveillance data, it is possible to estimate the burden of care home gastroenteritis outbreaks.⁸
13 However this does not account for any sporadic (non-outbreak-related) disease.

14
15 The incidence of gastroenteritis in care homes is poorly researched, with few studies published over
16 the last 40 years, the majority originating in the United States.^{9,10} The objective of this study was to
17 estimate the incidence of gastroenteritis in individuals in care homes in north west England;
18 therefore, addressing this gap in the evidence base, and providing data to understand the burden of
19 infectious gastroenteritis in this setting.

21 METHODS

22 The study protocol has been published and the methods are fully described there.¹¹ Briefly, we
23 conducted a prospective cohort study in residents of five care homes in North West England. The
24 study took place from 15 August 2017 to 30 May 2019.

26 Study population

27 The sampling frame was the total number of residential care homes for the elderly in the local
28 authorities of Liverpool and Sefton, registered with the Care Quality Commission. The five care
29 homes selected were a convenience sample of care homes in this sampling frame that were
30 approached and agreed to participate. The locations of the study care homes are shown in Figure 1.
31 All residents and staff members who were present at study care homes during the study period were
32 eligible to participate. Eligible participants with capacity to consent were consented by study
33 research nurses; for those without capacity to consent a nominated person who met the criteria
34 described in Section 32 of the Mental Capacity Act 2005 was asked to provide consent.

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Figure 1 – Location of study sites, England, 2017-2019

Surveillance system

The number of residents and staffing levels at each care home were collected using a questionnaire, administered to each care home manager. Data including: age, sex, general practitioner, date of arrival at the home and position in the home was collected in person by trained research nurses. Study research nurses employed active surveillance by visiting each study care home on a weekly basis to ascertain new participants, episodes of illness meeting the case definition and details about participants withdrawing from the study. For each case, information including onset date, medical history, duration of symptoms, complications and hospitalisation were collected using a questionnaire. Case report questionnaires were completed by a study research nurse.

Case definitions

The primary outcome was a case of gastroenteritis. Gastroenteritis cases were defined as persons in the study population with vomiting (two or more episodes of vomiting in a 24-hour period) OR diarrhoea (three or more loose stools in a 24-hour period), OR Vomiting AND diarrhoea (one or more episodes of both symptoms in a 24-hour period). Confirmed cases were defined as cases with a positive laboratory diagnosis of an infectious cause. Non-infectious causes such as long-standing diarrhoea associated with disability or incontinence and ingestion of laxative drugs were excluded from the study case definition. Outbreaks were defined as two or more cases occurring in an institution, with onset of illness being within 5 days.

Study size

As described in the CHANGE study protocol, the target study sample size was for 268 participants to be included.¹¹

Microbiological analysis

For each case, participants were asked to provide a faecal sample to determine the cause of symptoms; these samples were collected as soon as possible after onset of illness. Samples were sent to Liverpool Clinical Laboratories, based in the Royal Liverpool University Hospital. Diagnostic tests were conducted in real time and results reported to the study team. Samples were tested for 16 pathogens using Luminex xTAG Gastrointestinal Pathogen Panel (Luminex Molecular Diagnostics, Austin, Texas, USA). Results were reported to the study team and copied to the participant's general

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3 69 practitioner. The operation of this study was designed so that it did not interfere with public health
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5 70 action.

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8 72 **Statistical methods**

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10 73 We characterised the demographics of study participants and described differences between
11 74 residents and staff. We described the distribution of gastroenteritis case onset date over time, along
12 75 with the number and incidence rate of outbreaks. We calculated incidence rates for all
13 76 gastroenteritis cases, and for norovirus cases only. Participants could contribute multiple illness
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15 77 episodes. The denominator was the person-time at risk (PTAR) in study participants; incidence rates
16 78 are expressed per 1000 person-years at risk. PTAR commenced when participants were recruited
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18 79 into the study and was censored when they left the study care home; otherwise it was censored
19
20 80 when the surveillance period ended on 30 May 2019.
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22 81

23 24 25 82 **Ethical approval**

26 83 The study was approved by the North West–Greater Manchester South NHS Research Ethics
27 84 Committee (REC Reference: 16/NW/0541).
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29 85

30 31 32 86 **Patient and Public Involvement**

33 87 Patients, carers, or members of the public were not actively involved in the design of this research
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35 88

36 37 38 90 **RESULTS**

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40 91 In total 268 participants (159 residents and 109 staff) were recruited into the study from five care
41 92 homes. Seventy nine participants (59 residents and 20 staff) withdrew from the study before the end
42 93 of the surveillance period. None of these withdrawals were due to serious adverse events. The
43 94 participants contributed a total of 122,898 days PTAR (66,489 days PTAR for residents; 56,409 days
44 95 PTAR for staff). The median contribution of PTAR was 504 days (range 2 – 837 days). A summary of
45 96 participant demographics is shown in Table 1. The median age of participants was 71 years (range
46 97 19-99); the median age of residents was 82 and the median age of staff was 44. In total, 190
47 98 participants were female (70.9%); 62.9% of residents and 82.6% of staff were female.
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103 Table 1 – Demographics of study participants, by care home and role in the home

Care home	<i>Total</i>			<i>Residents</i>			<i>Staff</i>		
	N	Median age	% Female	N	Median age	% Female	N	Median age	% Female
1	88	79	59	69	82	58	19	37	63
2	45	79	62	34	85	62	11	55	64
3	80	55	83	33	78	70	47	44	92
4	29	59	79	13	86	69	16	43	88
5	26	59	81	10	88	70	16	49	88
Total	268	70	71	159	82	63	109	44	83

104

105 In total 45 cases of gastroenteritis were reported during the surveillance period, equating to 133.7
 106 cases per 1000 person-years at risk. The incidence rate of illness in residents was 252.5 cases per
 107 1000 person-years at risk and the incidence rate of illness in staff was 25.9 cases per 1000 person-
 108 years at risk. For residents, the incidence rate was 0.69 cases per 1000 bed-days. Two participants
 109 became a case twice during the study.

110

111 Table 2 – Case incidence rates, by care home and role in the home

Care home	<i>Total</i>			<i>Residents</i>			<i>Staff</i>		
	PTAR (days)	Cases	Incidence rate	PTAR (days)	Cases	Incidence rate	PTAR (days)	Cases	Incidence rate
1	40259	15	136.1	29519	14	173.2	10740	0	0
2	20423	6	107.3	13759	6	159.3	6664	0	0
3	39550	16	147.8	14151	12	309.7	25399	3	43.1
4	13115	6	167.1	5413	5	337.4	7702	1	47.4
5	9551	2	76.5	3647	2	200.3	5904	0	0
Total	82358	45	133.7	66489	41	252.5	56409	4	25.9

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113

114 The distribution of case onset dates is shown in Figure 2. A majority of cases were reported in
 115 September and October during both winters. We observed seven outbreaks in study participants in
 116 these care homes, an incidence rate of 76.4 outbreaks per 100 care homes per year. The most
 117 frequently reported symptoms were: diarrhoea (62%), vomiting (47%), nausea (22%) and abdominal
 118 pain (6%). No cases reported bloody stool, fever or headache. Seven cases (16%) reported both
 119 diarrhoea and vomiting. Duration of illness for cases was not available.

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3 1204
5 121 Figure 2 – Epidemic curve showing distribution of cases by month and study care home

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8 123 At least one faecal sample was collected for 15 cases (33.3%) of the 45 reported cases. No samples
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10 124 were collected for any of the three cases in staff. The 15 samples were tested for multiple
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12 125 pathogens. Norovirus was detected in three samples. No pathogen was detected in 12 samples.

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15 127 For the 15 stool specimens which were received, the median time between onset of symptoms and
16
17 128 the sample being taken was 3 days (range 0 – 18 days). The median time difference for samples
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19 129 positive for norovirus was 0 days (range 0-1 days). This was significantly shorter (Wilcoxon rank sum
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21 130 test, p-value = 0.016) than the difference for samples which were negative (median 4 days, range 1-
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23 131 18 days)

24 132

25 133 **DISCUSSION**26 134 **Main findings**27
28 135 In this active surveillance study using a prospective cohort design we recorded gastroenteritis cases
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30 136 in care homes over a 22 month period and observed 7 outbreaks in study participants, a rate of 76.4
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32 137 outbreaks per 100 care homes per year. This is substantially higher than the incidence rate of 37.1
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34 138 outbreaks per 100 care homes per year reported during routine, passive surveillance in the same
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36 139 geographical area between 2012 and 2016. ⁷ This difference may reflect increased reporting of
37
38 140 illness due to regular contact with the care homes as part of the study, which is likely to have
39
40 141 improved ascertainment of outbreaks.

41 142

42 143 We found that the incident rate of illness in participants was 133.7 per 1000 person-years at risk,
43
44 144 and that the rate was far higher in residents (252.5 per 1000 person years) than in staff (25.9 per
45
46 145 1000 person years). This difference could be caused by a number of factors: it may reflect trends in
47
48 146 the wider community where norovirus incidence is higher in older people than those of working age,
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50 147 ¹² good hygiene and infection control practices by staff, the increased susceptibility of elderly
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52 148 residents who are physically debilitated, ¹³ and illness not being reported by staff, some of whom do
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54 149 not receive sick pay. The incidence rate of illness in residents can also be expressed as 0.78 cases per
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56 150 1000 bed-days; this study is the first time this metric has been estimated for care homes in the UK
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58 151 and as such will provide data to inform any modelling of the economic burden of gastroenteritis in
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60 152 this setting.

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3 154 In this study, we observed that 89% of cases were defined as part of an outbreak. This comparatively
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5 155 low level of individual cases may be due to factors such as; the susceptible nature of residents, the
6
7 156 high degree of potential contacts and the difficulty of maintaining hygiene. These factors could
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9 157 explain why people in a care home who acquire a GI infection are likely to infect another and
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11 158 therefore GI illness in these settings frequently causes outbreaks. This finding therefore supports the
12
13 159 continued surveillance of GI disease in care homes being focussed on outbreaks as this constitutes
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15 160 the majority of disease burden.

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16
17 162 The study protocol was for a stool sample to be submitted for each case; in practice this only
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19 163 occurred for 33% cases. Of the 15 samples tested, norovirus was the only pathogen identified, being
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21 164 found in 3 cases. Despite being tested for, no other pathogens were identified. Due to the small
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23 165 number of stool samples in this study, caution should be exercised if these results are to be used to
24
25 166 infer the proportion of gastroenteritis in care homes caused by norovirus.

167

168 **Strengths**

28
29 169 One of the key strengths of this study was its active surveillance design, whereby a research nurse
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31 170 visited each study site each week to check on the status of study participants. During the 22-month
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33 171 duration of the study, this was a resource-intensive approach and meant that care homes involved in
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35 172 the study were constantly aware of the need to report illness in study participants. This active
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37 173 surveillance design meant that our study is likely to have recorded a higher proportion of cases than
38
39 174 an alternative passive surveillance design, an assertion supported by the incidence rate being higher
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41 175 than that reported from the same area during routine surveillance.

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43 177 This is the first active surveillance study to follow up individuals in a care home setting for
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45 178 gastrointestinal illness. The advantage of this study design is that the individual level of participation
46
47 179 and surveillance allowed the calculation of person-time at risk and the recording of sporadic cases of
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49 180 illness, in addition to outbreaks. This is a valuable addition to the literature as the description of
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51 181 individual cases, including sporadic illness, is not covered in other studies that mainly focus on the
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53 182 burden of gastroenteritis outbreaks. These findings are key to understanding the burden of sporadic
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55 183 gastroenteritis in care homes, which is important when calculating the total burden of illness in this
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57 184 setting.

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57 186 An additional strength of this study was the capacity to test each of the cases for a wide variety of
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59 187 pathogens. In contrast to other studies which focus on testing for norovirus or other viral pathogens

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3 188 in care home settings, we used a multiplex PCR test which was capable of detecting 15 pathogens.
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5 189 By using the Luminex GPP, we were confident that we had coverage for the most likely known
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7 190 pathogens and would be able to detect them in any cases that arose during the study.
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10 192 **Limitations**

11 193 A key limitation of this study was that it included a small convenience sample of care homes in one
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13 194 area of England. Due to the nature of the study, it was only possible to include those care homes
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15 195 which were approached and agreed to participate. It may have been that the five care homes
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17 196 included in the study varied systematically from the others in the sampling frame in aspects such as:
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19 197 the level of care provided, the vulnerability of residents to infection, the socio-economic status of
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21 198 residents and infection prevention and control practices. However, it was not possible to obtain such
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23 199 information on all homes in the sampling frame and therefore it is not possible to make a formal
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25 200 comparison. Due to the resource-intensive active surveillance design it was only possibly to include a
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27 201 maximum of five sites in this study. It may be that the small number of geographically clustered care
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29 202 homes in this study limits the generalisability of these findings to other areas of the country and
30
31 203 internationally. The inferences that can be made from this study may also be affected by the
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33 204 duration of the surveillance period; although the 22 months of the study include two winters, it may
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35 205 have been that the circulating viruses during these seasons was atypical.
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38 207 Another potential limitation may have been that the participants in our study care homes who
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40 208 consented to take part were systematically different from those in the care homes who did not take
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42 209 part. The consenting process to enrol participants in this study was agreed with the relevant ethics
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44 210 committee and meant that the study team did not have access to the personal information of staff
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46 211 or residents at the home who did not consent to take part. Therefore, it was not possible to
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48 212 compare the characteristics of those who took part to those who did not. Furthermore, by following
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50 213 the agreed consenting process, because we could not record departures and arrivals of persons at
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52 214 the home who were not participants, although we knew the capacity of each home, we could not
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54 215 calculate the percentage coverage in each home. Although it was not possible to formally calculate
55
56 216 the percentage coverage, it is possible to note that participation could have been higher. One reason
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58 217 for this was the consenting process for those (mainly elderly) residents without capacity to consent.
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60 218 Safeguarding the rights of such people is very important, but the process we were asked to follow
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62 219 made it very difficult to identify and contact the correct person to represent the interests of that
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64 220 person. Therefore, fewer residents without capacity were enrolled in the study than would have
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66 221 otherwise been the case.

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223 One issue that has previously been identified when studying gastroenteritis illness in care homes is
224 the difficulty in obtaining stool samples for pathogen testing.⁷ Even with weekly visits to the care
225 homes, we only obtained stool samples from 33% of the cases. For the samples we received, we
226 found that frequently these were taken several days after the onset of symptoms and this may
227 account for the 80% of samples where no pathogen was identified. During the study we
228 acknowledged this difficulty in obtaining stool samples and implemented a £5 voucher scheme on 28
229 June 2018 to incentivise stool collection. Unfortunately, this was not particularly effective as 30% of
230 cases submitted a stool sample before this point, compared to 36% afterwards. This low proportion
231 of stool samples shows one of the challenges of operating the study in very busy care home
232 environments with staff working at a level where they do not have much excess capacity.

233

234 **Results in the context of the international literature**

235 In this study, the incidence rate of infectious gastroenteritis in care home residents was estimated to
236 be 0.78 cases per 1000 bed-days. This finding is almost double than the mean global incidence
237 estimate in a systematic review of published surveillance; the pooled estimate of incidence from this
238 meta-analysis was 0.40 (95% confidence interval 0.27–0.56) episodes per 1000 bed-days.⁹ However
239 there was considerable heterogeneity between the 15 studies, with the highest incidence (1.9
240 episodes per 1000 bed-days) being reported from a German study using electronic health records.¹⁴
241 The authors of this systematic review were surprised with the low rate of gastroenteritis in the
242 meta-analysis and the results of our study support this observation, being a substantially higher
243 incidence. This higher incidence is likely to reflect enhanced case-finding in our study due to the
244 active surveillance design. However, the incidence rate from our study was still lower than that
245 reported in persons aged over 65 years living in the community.¹⁵

246

247 **CONCLUSION**

248 The key implication for policymakers to be drawn from this study is that the current general
249 approach to surveillance of infectious gastroenteritis in care homes, focussing on outbreaks, is
250 detecting a majority of cases of gastroenteritis. However, if policymakers are to estimate the burden
251 of infectious gastroenteritis in this setting using only outbreak surveillance data, this study implies
252 that the total burden will be underestimated by around 25%. Combining findings from this study
253 with data on the distribution of outbreaks in care homes would be a way for future research to fully
254 estimate the burden of infectious gastroenteritis in this setting.

255

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260 each of the study care homes for their engagement in participate in this study. The authors would
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269 Public Health England.

271 **Competing interests statement**

272 The authors declare no competing interests

274 **Author contributions**

275 TI, APC, JPH, RV, NJB, MIG and SOB conceived and designed the study. TI and APC co-ordinated data
276 collection. TI undertook the analysis, wrote the first draft and revised the manuscript. TI, APC, JPH,
277 RV, NJB, MIG and SOB provided input to the manuscript drafting process. All authors reviewed and
278 approved the final manuscript.

280 **Data sharing statement**

281 The datasets used and/or analysed during the current study are available from the corresponding
282 author on reasonable request.

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Figure 1

203x127mm (96 x 96 DPI)

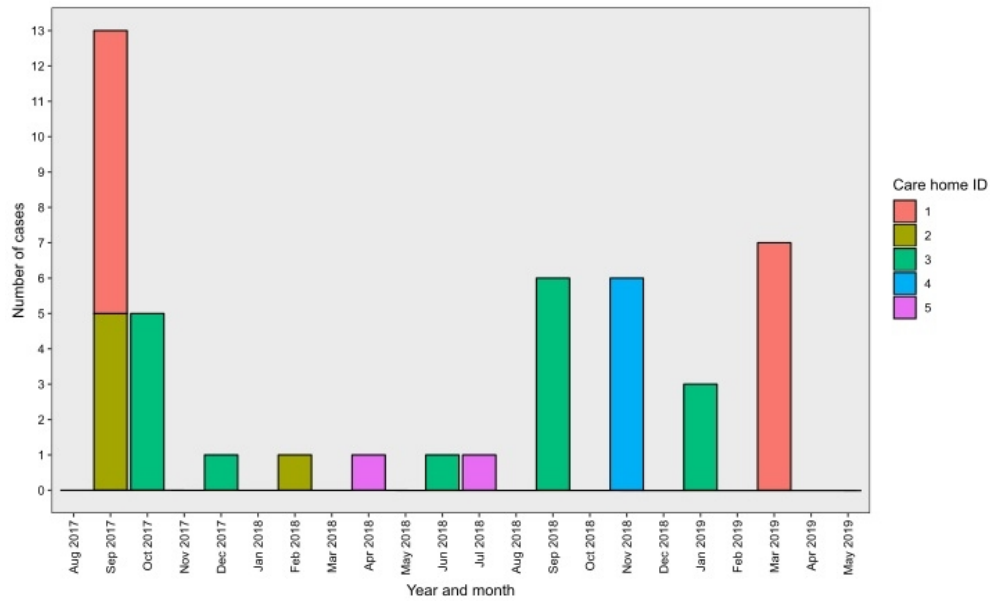


Figure 2

190x114mm (96 x 96 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	3
		(b) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5
		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data were addressed	5
		(d) If applicable, explain how loss to follow-up was addressed	5
		(e) Describe any sensitivity analyses	n/a
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) Summarise follow-up time (eg, average and total amount)	5
Outcome data	15*	Report numbers of outcome events or summary measures over time	6
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6
		(b) Report category boundaries when continuous variables were categorized	n/a
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Prospective cohort study to investigate the burden and transmission of acute gastroenteritis in care homes: epidemiological results

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Manuscripts

TITLE

Prospective cohort study to investigate the burden and transmission of acute gastroenteritis in care homes: epidemiological results

AUTHOR INFORMATION

Thomas Inns^{1,2}, Anna Pulawska-Czub^{2,3}, John P Harris^{1,2}, Roberto Vivancos^{2,4}, Nicholas J Beeching^{2,5,6}, Miren Iturriza-Gomara^{2,3}, Sarah J O'Brien^{2,7}

1. Institute of Population Health Sciences, University of Liverpool, Liverpool, UK
2. NIHR Health Protection Research Unit in Gastrointestinal Infections, University of Liverpool, Liverpool, UK
3. Institute of Infection and Global Health, University of Liverpool, Liverpool, UK
4. Field Epidemiology, Field Service, National Infection Service, Public Health England, UK
5. Tropical and Infectious Disease Unit, Royal Liverpool University Hospital, Liverpool, UK
6. Clinical Sciences Group, Liverpool School of Tropical Medicine, Liverpool, UK
7. School of Natural and Environmental Science, Newcastle University, Newcastle upon Tyne, UK

Corresponding author: Thomas Inns

Corresponding author's email address: thomas.inns@liverpool.ac.uk

Telephone number: +44 151 794 9871

Postal address: The University of Liverpool
The Farr Institute@HeRC
Waterhouse Building (2nd Floor, Block F)
1-5 Brownlow Street
Liverpool
L69 3GL

Word count: 3288

ABSTRACT

Objectives To estimate the incidence of gastroenteritis in individuals in care homes.

Design Prospective cohort study.

Setting Five participating care homes in North West England, United Kingdom.

Participants Residents and staff present at the five study care homes between 15 August 2017 and 30 May 2019 (n = 268).

Outcome measures We calculated incidence rates for all gastroenteritis cases per 1000 person-years at risk and per 1000 bed-days at risk. We also calculated the incidence rate of gastroenteritis outbreaks per 100 care homes per year.

Results In total 45 cases were reported during the surveillance period, equating to 133.7 cases per 1000 person-years at risk. In residents the incidence rate was 0.62 cases per 1000 bed-days. We observed 7 outbreaks in all care homes included in surveillance, a rate of 76.4 outbreaks per 100 care homes per year. 15 stool samples were tested; three were positive for norovirus, no other pathogens were detected.

Conclusions We found that surveillance of infectious gastroenteritis disease in care homes based on outbreaks, the current general approach, detected a majority of cases of gastroenteritis. However, if policymakers are to estimate the burden of infectious gastroenteritis in this setting using only routine outbreak surveillance data and not accounting for non-outbreak cases, this study implies that the total burden will be underestimated.

Keywords

Gastroenteritis; Viral gastroenteritis; Norovirus; Outbreaks; Surveillance; Epidemiology; Infection Control

Strengths and limitations of this study

- To our knowledge this is the first systematic active surveillance study of gastroenteritis in care home residents in the UK
- Prospective cohort design with active follow-up of individual care home residents by fully trained research nurses
- Small number of care homes included and so results might not be generalisable
- Challenges in obtaining stool samples in a timely manner
- Study period coincided with a low incidence of norovirus in the community

1 INTRODUCTION

2 Gastrointestinal infections are an important issue in care homes for the elderly (also known as long-
3 term care facilities). Care home residents are more susceptible to infectious gastroenteritis and the
4 environment is ideal for transmission of gastroenteritis.¹ Because infection control measures are
5 challenging to implement, further infections and outbreaks frequently occur based on a single index
6 case.² In this population, gastrointestinal infections can cause more severe morbidity,
7 hospitalisation, and are associated with greater mortality.^{3,4}

8
9 Surveillance of infectious gastroenteritis in care homes varies in presence and scope in different
10 countries, and where it exists it is focussed on the detection of outbreaks. These outbreak
11 surveillance systems exist in countries such as France, Australia and England.⁵⁻⁷ Using these
12 surveillance data, it is possible to estimate the burden of care home gastroenteritis outbreaks.⁸
13 However this does not account for any sporadic (non-outbreak-related) disease.

14
15 The incidence of gastroenteritis in care homes is poorly researched, with few studies published over
16 the last 40 years, the majority originating in the United States.⁹⁻¹² The objective of this study was to
17 estimate the incidence of gastroenteritis in individuals in care homes in north west England;
18 therefore, addressing this gap in the evidence base, and providing data to understand the burden of
19 infectious gastroenteritis in this setting.

21 METHODS

22 The study protocol has been published and the methods are fully described there.¹³ Briefly, we
23 conducted a prospective cohort study in residents of five care homes in North West England. The
24 study took place from 15 August 2017 to 30 May 2019.

26 Study population

27 The sampling frame was the total number of residential care homes for the elderly in the local
28 authorities of Liverpool and Sefton, registered with the Care Quality Commission. The five care
29 homes selected were a convenience sample of care homes in this sampling frame that were
30 approached and agreed to participate. The locations of the study care homes are shown in Figure 1.
31 All study care homes were recruited prospectively at the same time; no other care homes were
32 invited to participate and declined. All residents and staff members who were present at study care
33 homes during the study period were eligible to participate. Eligible participants with capacity to
34 consent were consented by study research nurses; for those without capacity to consent a

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3 35 nominated person who met the criteria described in Section 32 of the Mental Capacity Act 2005 was
4 36 asked to provide consent.
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8 38 Figure 1 – Location of study sites, England, 2017-2019
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11 40 **Surveillance system**

12 41 The number of residents and staffing levels at each care home were collected at the start of the
13 42 study period using a questionnaire, administered to each care home manager. Data including: age,
14 43 sex, general practitioner, date of arrival at the home and position in the home was collected in
15 44 person by trained research nurses. Participants were recruited between 15 August 2017 and 08
16 45 November 2018. Participants were recruited from the start of the study period, with new residents
17 46 and staff being recruited when entering the care home. No participants were ill with gastroenteritis
18 47 at the point of recruitment or recruited as a result of such illness. Study research nurses employed
19 48 active surveillance by visiting each study care home on a weekly basis to ascertain new participants,
20 49 episodes of illness meeting the case definition and details about participants withdrawing from the
21 50 study. During these visits, study research nurses met with key leadership staff to understand any
22 51 changes at the home in the preceding week. For each case, information including onset date,
23 52 medical history, duration of symptoms, complications and hospitalisation were collected using a
24 53 questionnaire. Case report questionnaires were completed by a study research nurse.
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38 55 **Case definitions**

39 56 The primary outcome was a case of gastroenteritis. Gastroenteritis cases were defined as persons in
40 57 the study population with vomiting (two or more episodes of vomiting in a 24-hour period) OR
41 58 diarrhoea (three or more loose stools in a 24-hour period), OR vomiting AND diarrhoea (one or more
42 59 episodes of both symptoms in a 24-hour period). Confirmed cases were defined as cases with a
43 60 positive laboratory diagnosis of an infectious cause. Non-infectious causes such as long-standing
44 61 diarrhoea associated with disability or incontinence and ingestion of laxative drugs were excluded
45 62 from the study case definition based on the clinical judgement of a study research nurse. Outbreaks
46 63 were defined as two or more cases occurring in an institution, with onset of illness being within 5
47 64 days.
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57 66 **Study size**

58 67 As described in the CHANGE study protocol, the target study sample size was for 268 participants to
59 68 be included.¹³
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45 70 **Microbiological analysis**

6 71 For each case, participants were asked to provide a faecal sample to determine the cause of
7
8 72 symptoms; these samples were collected as soon as possible after onset of illness. Samples were
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10 73 sent to Liverpool Clinical Laboratories, based in the Royal Liverpool University Hospital. Diagnostic
11
12 74 tests were conducted in real time and results reported to the study team. Samples were tested for
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14 75 16 pathogens using Luminex xTAG Gastrointestinal Pathogen Panel (Luminex Molecular Diagnostics,
15
16 76 Austin, Texas, USA). Results were reported to the study team and copied to the participant's general
17
18 77 practitioner. The operation of this study was designed so that it did not interfere with public health
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20 78 action.
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22 79

23 80 **Statistical methods**

24 81 We characterised the demographics of study participants and described differences between
25
26 82 residents and staff. We described the distribution of gastroenteritis case onset date over time, along
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28 83 with the number and incidence rate of outbreaks (with binomial 95% Confidence Interval). We
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30 84 calculated incidence rates for all gastroenteritis cases. Participants could contribute multiple illness
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32 85 episodes. The denominator was the person-time at risk (PTAR) in study participants; incidence rates
33
34 86 are expressed per 1000 person-years at risk for all groups and per 1000 bed-days for residents. Bed-
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36 87 days were defined as days that the resident was present in the care home; participant PTAR was
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38 88 censored if they left the care home. PTAR was calculated in the same way for residents and staff and
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40 89 commenced when participants were recruited into the study and was censored when they left the
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42 90 study care home; otherwise it was censored when the surveillance period ended on 30 May 2019.
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45 92 **Ethical approval**

46 93 The study was approved by the North West–Greater Manchester South NHS Research Ethics
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48 94 Committee (REC Reference: 16/NW/0541).
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50 95

51 96 **Patient and Public Involvement**

52 97 Patients, carers, or members of the public were not actively involved in the design of this research.
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56 100 **RESULTS**

57 101 In total 268 participants (159 residents and 109 staff) were recruited into the study from five care
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59 102 homes. Seventy nine participants (59 residents and 20 staff) withdrew from the study before the end
60

103 of the surveillance period. None of these withdrawals were due to serious adverse events. Fifty five
 104 (93%) of resident withdrawals were due to death from an unrelated cause, with four residents
 105 leaving the care home to return to live independently. All 20 staff withdrawals were due to the
 106 participant leaving employment at the study care home. The participants contributed a total of
 107 122,898 days PTAR (66,489 days PTAR for residents; 56,409 days PTAR for staff). The median
 108 contribution of PTAR was 504 days (range 2 – 837 days). A summary of participant demographics is
 109 shown in Table 1. The median age of participants was 71 years (range 19-99); the median age of
 110 residents was 82 and the median age of staff was 44. In total, 190 participants were female (70.9%);
 111 62.9% of residents and 82.6% of staff were female. It was not possible to calculate the participation
 112 rate as the denominator of staff and residents in each home was not available.

113

114 Table 1 – Demographics of study participants, by care home and role in the home

Care home	<i>Total</i>			<i>Residents</i>			<i>Staff</i>		
	N	Median age	% Female	N	Median age	% Female	N	Median age	% Female
1	88	79	59	69	82	58	19	37	63
2	45	79	62	34	85	62	11	55	64
3	80	55	83	33	78	70	47	44	92
4	29	59	79	13	86	69	16	43	88
5	26	59	81	10	88	70	16	49	88
Total	268	70	71	159	82	63	109	44	83

115

116 In total 45 cases of gastroenteritis were reported during the surveillance period, equating to 133.7
 117 cases per 1000 person-years at risk. The incidence rate of illness in residents was 225.2 cases per
 118 1000 person-years at risk and the incidence rate of illness in staff was 25.9 cases per 1000 person-
 119 years at risk (Table 2). For residents, the incidence rate was 0.62 cases per 1000 bed-days. Two
 120 participants became a case twice during the study. No cases were excluded based on a non-
 121 infectious cause of diarrhoea.

122

123 Table 2 – Case incidence rates, by care home and role in the home

Care home	<i>Total</i>			<i>Residents</i>			<i>Staff</i>		
	PTAR (years)	Cases	Incidence rate (1000)	PTAR (years)	Cases	Incidence rate (1000)	PTAR (years)	Cases	Incidence rate (1000)

		person – years)		person- years			person- years)		
1	110.2	15	136.1	80.8	15	185.6	29.4	0	0
2	55.9	6	107.3	37.7	6	159.3	18.3	0	0
3	108.3	16	147.8	38.7	13	335.5	69.5	3	43.1
4	35.9	6	167.1	14.8	5	337.4	21.1	1	47.4
5	26.2	2	76.5	10.0	2	200.3	16.2	0	0
Total	336.5	45	133.7	182.0	41	225.2	154.4	4	25.9

124

125

126 The distribution of case onset dates is shown in Figure 2. A majority of cases were reported in
 127 September and October during both winters. We observed seven outbreaks in study participants in
 128 these care homes, an incidence rate of 76.4 outbreaks per 100 care homes per year (95% Confidence
 129 Interval: 44.2 – 92.9 outbreaks per 100 care homes per year). Three outbreaks were observed in care
 130 home 3 (5, 6 and 3 cases, respectively), two outbreaks were observed in care home 1 (8 cases and 7
 131 cases) and one outbreak was observed in both care homes 2 (5 cases) and 4 (6 cases). No outbreaks
 132 occurred in care home 5 during the study. In total, 40 (89%) cases were defined as part of an
 133 outbreak. The most frequently reported symptoms were: diarrhoea (62%), vomiting (47%), nausea
 134 (22%) and abdominal pain (6%). No cases reported bloody stool, fever or headache. Seven cases
 135 (16%) reported both diarrhoea and vomiting. Duration of illness for cases was not available.

136

137 Figure 2 – Epidemic curve showing distribution of cases by month and study care home

138

139 At least one faecal sample was collected for 15 cases (33.3%) of the 45 reported cases. No samples
 140 were collected for any of the four cases in staff. The 15 samples were tested for multiple pathogens.
 141 Norovirus was detected in three samples. No pathogen was detected in 12 samples.

142

143 For the 15 stool specimens which were received, the median time delay between onset of symptoms
 144 and the sample being taken was 3 days (range 0 – 18 days). The median delay for samples positive
 145 for norovirus was 0 days (range 0-1 days). This was significantly shorter (Wilcoxon rank sum test, p-
 146 value = 0.016) than the delay for samples which were negative (median 4 days, range 1-18 days).

147

148 DISCUSSION

149 Main findings

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3 150 In this active surveillance study using a prospective cohort design we recorded gastroenteritis cases
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5 151 in care homes over a 22 month period and observed 7 outbreaks in study participants, a rate of 76.4
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7 152 outbreaks per 100 care homes per year. Both this point estimate and the lower bound of the 95%
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9 153 Confidence Interval are greater than the incidence rate of 37.1 outbreaks per 100 care homes per
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11 154 year reported during routine, passive surveillance in the same geographical area between 2012 and
12
13 155 2016.⁷ This difference may reflect increased reporting of illness due to regular contact with the care
14
15 156 homes as part of the study, which is likely to have improved ascertainment of outbreaks.

157

16
17 158 We found that the incident rate of illness in participants was 133.7 per 1000 person-years at risk,
18
19 159 and that the rate was far higher in residents (225.2 per 1000 person-years) than in staff (25.9 per
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21 160 1000 person-years). This difference could be caused by a number of factors: it may reflect trends in
22
23 161 the wider community where norovirus incidence is higher in older people than those of working age,
24
25 162 ¹⁴ good hygiene and infection control practices by staff, reduced exposure in staff who go home
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27 163 when not on shift, the increased susceptibility of elderly residents who are physically debilitated,¹⁵
28
29 164 and illness not being reported by staff, some of whom do not receive sick pay. The incidence rate of
30
31 165 illness in residents can also be expressed as 0.62 cases per 1000 bed-days; this study is the first time
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33 166 this metric has been estimated for care homes in the UK and as such will provide data to inform any
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35 167 modelling of the economic burden of gastroenteritis in this setting.

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36
37 169 In this study, we observed that 89% of cases were defined as part of an outbreak. This comparatively
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39 170 low level of individual cases may be due to factors such as; the susceptible nature of residents, the
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41 171 high degree of potential contacts and the difficulty of maintaining hygiene. These factors could
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43 172 explain why people in a care home who acquire a GI infection are likely to infect another and
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45 173 therefore GI illness in these settings frequently causes outbreaks. This finding therefore supports the
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47 174 continued surveillance of GI disease in care homes being focussed on outbreaks as this constitutes
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49 175 the majority of disease burden.

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51 177 The study protocol was for a stool sample to be submitted for each case; in practice this only
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53 178 occurred for 33% cases. Of the 15 samples tested, norovirus was the only pathogen identified, being
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55 179 found in 3 cases. Despite being tested for, no other pathogens were identified, which may have been
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57 180 associated with delay between symptom onset and stool submission. Due to the small number of
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59 181 stool samples in this study, caution should be exercised if these results are to be used to infer the
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182 proportion of gastroenteritis in care homes caused by norovirus.

183

184 **Strengths**

185 One of the key strengths of this study was its active surveillance design, whereby a research nurse
186 visited each study site each week to check on the status of study participants. During the 22-month
187 duration of the study, this was a resource-intensive approach and meant that care homes involved in
188 the study were constantly aware of the need to report illness in study participants. This active
189 surveillance design meant that our study is likely to have recorded a higher proportion of cases than
190 an alternative passive surveillance design, an assertion supported by the incidence rate being higher
191 than that reported from the same area during routine surveillance.

192
193 This is the first active surveillance study to follow up individuals in a care home setting for
194 gastrointestinal illness. The advantage of this study design is that the individual level of participation
195 and surveillance allowed the calculation of person-time at risk and the recording of sporadic cases of
196 illness, in addition to outbreaks. This is a valuable addition to the literature as the description of
197 individual cases, including sporadic illness, is not covered in other studies that mainly focus on the
198 burden of gastroenteritis outbreaks. These findings are key to understanding the burden of sporadic
199 gastroenteritis in care homes, which is important when calculating the total burden of illness in this
200 setting.

201
202 An additional strength of this study was the capacity to test each of the cases for a wide variety of
203 pathogens. In contrast to other studies which focus on testing for norovirus or other viral pathogens
204 in care home settings, we used a multiplex PCR test which was capable of detecting 15 pathogens.
205 By using the Luminex GPP, we were confident that we had coverage for the most likely known
206 pathogens and would be able to detect them in any cases that arose during the study.

208 **Limitations**

209 A key limitation of this study was that it included a small convenience sample of care homes in one
210 area of England. Due to the nature of the study, it was only possible to include those care homes
211 which were approached and agreed to participate. It may have been that the five care homes
212 included in the study varied systematically from the others in the sampling frame in aspects such as:
213 the level of care provided, the vulnerability of residents to infection, the socio-economic status of
214 residents and infection prevention and control practices. However, it was not possible to obtain such
215 information on all homes in the sampling frame and therefore it is not possible to make a formal
216 comparison. Due to the resource-intensive active surveillance design it was only possibly to include a
217 maximum of five sites in this study. It may be that the small number of geographically clustered care

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3 218 homes in this study limits the generalisability of these findings to other areas of the country and
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5 219 internationally. The inferences that can be made from this study may also be affected by the
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7 220 duration of the surveillance period; although the 22 months of the study include two winters, it may
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9 221 have been that the circulating viruses during these seasons was atypical.

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11 223 Another potential limitation may have been that the participants in our study care homes who
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13 224 consented to take part were systematically different from those in the care homes who did not take
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15 225 part. The consenting process to enrol participants in this study was agreed with the relevant ethics
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17 226 committee and meant that the study team did not have access to the personal information of staff
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19 227 or residents at the home who did not consent to take part. Therefore, it was not possible to
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21 228 compare the characteristics of those who took part to those who did not. Furthermore, by following
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23 229 the agreed consenting process, because we could not record departures and arrivals of persons at
24
25 230 the home who were not participants, although we knew the capacity of each home, we could not
26
27 231 calculate the participation rate in each home. Although it was not possible to formally calculate the
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29 232 participation rate, it is possible to note that participation could have been higher. One reason for
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31 233 this was the consenting process for those (mainly elderly) residents without capacity to consent.
32
33 234 Safeguarding the rights of such people is very important, but the process we were asked to follow
34
35 235 made it very difficult to identify and contact the correct person to represent the interests of that
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37 236 person. Therefore, fewer residents without capacity were enrolled in the study than would have
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39 237 otherwise been the case.

36 238

38 239 One issue that has previously been identified when studying gastroenteritis illness in care homes is
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40 240 the difficulty in obtaining stool samples for pathogen testing.⁷ Even with weekly visits to the care
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42 241 homes, we only obtained stool samples from 33% of the cases. For the samples we received, we
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44 242 found that frequently these were taken several days after the onset of symptoms and this may
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46 243 account for the 80% of samples where no pathogen was identified. During the study we
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48 244 acknowledged this difficulty in obtaining stool samples and implemented a £5 voucher scheme on 28
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50 245 June 2018 to incentivise stool collection. Unfortunately, this was not particularly effective as 30% of
51
52 246 cases submitted a stool sample before this point, compared to 36% afterwards. This low proportion
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54 247 of stool samples shows one of the challenges of operating the study in very busy care home
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56 248 environments with staff working at a level where they do not have much excess capacity.

55 249

57 250 **Results in the context of the international literature**

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3 251 In this study, the incidence rate of infectious gastroenteritis in care home residents was estimated to
4
5 252 be 0.62 cases per 1000 bed-days. This finding is substantially higher than the mean global incidence
6
7 253 estimate in a systematic review of published surveillance; the pooled estimate of incidence from this
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9 254 meta-analysis was 0.40 (95% confidence interval 0.27–0.56) episodes per 1000 bed-days.⁹ However
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11 255 there was considerable heterogeneity between the 15 studies, with the highest incidence (1.9
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13 256 episodes per 1000 bed-days) being reported from a German study using electronic health records.¹⁶
14
15 257 The authors of this systematic review were surprised with the low rate of gastroenteritis in the
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17 258 meta-analysis and the results of our study support this observation, being a substantially higher
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19 259 incidence. This higher incidence is likely to reflect enhanced case-finding in our study due to the
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21 260 active surveillance design. However, the incidence rate from our study was still lower than that
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23 261 reported in persons aged over 65 years living in the community.¹⁷
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25 262

263 **CONCLUSION**

264 The key implication for policymakers to be drawn from this study is that we found that surveillance
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266 of infectious gastroenteritis disease based on outbreaks in care homes, the current general
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268 approach, detected a majority of cases of gastroenteritis. However, if policymakers are to estimate
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270 the burden of infectious gastroenteritis in this setting using only routine outbreak surveillance data
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272 and not accounting for non-outbreak cases, this study implies that the total burden will be
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274 underestimated. Combining findings from this study with data on the distribution of outbreaks in
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276 care homes would be a way for future research to fully estimate the burden of infectious
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278 gastroenteritis in this setting.
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3 285 those of the author(s) and not necessarily those of the NHS, the NIHR, the Department of Health or
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5 286 Public Health England.
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8 288 **Competing interests statement**

9
10 289 The authors declare no competing interests
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12 290

13 291 **Author contributions**

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15 292 TI, APC, JPH, RV, NJB, MIG and SOB conceived and designed the study. TI and APC co-ordinated data
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17 293 collection. TI undertook the analysis, wrote the first draft and revised the manuscript. TI, APC, JPH,
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19 294 RV, NJB, MIG and SOB provided input to the manuscript drafting process. All authors reviewed and
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21 295 approved the final manuscript.
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24 297 **Data sharing statement**

25 298 The datasets used and/or analysed during the current study are available from the corresponding
26
27 299 author on reasonable request.
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30 301 **REFERENCES**

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Figure 1

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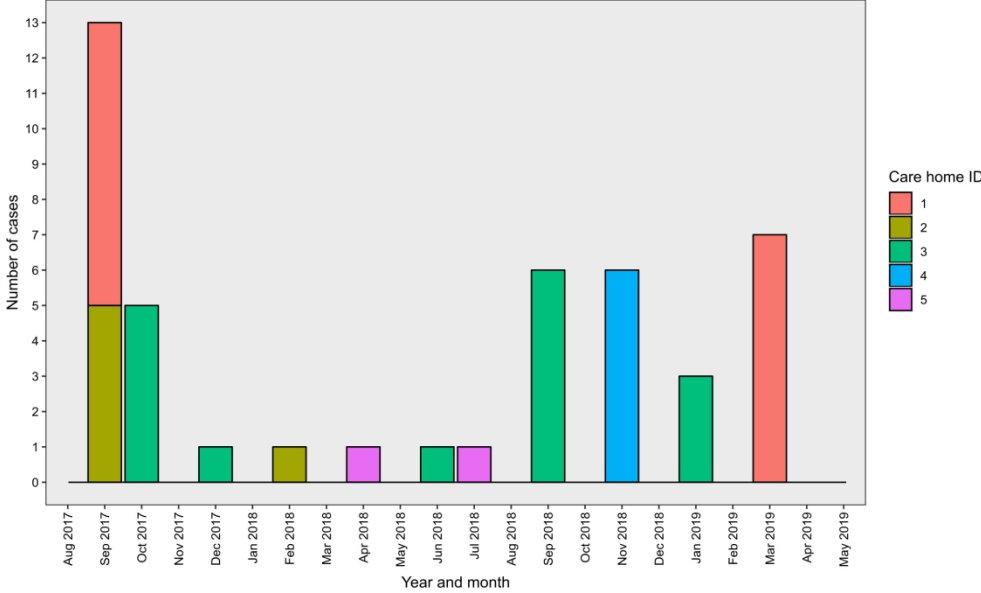


Figure 2

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	3
		(b) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5
		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data were addressed	5
		(d) If applicable, explain how loss to follow-up was addressed	5
		(e) Describe any sensitivity analyses	n/a
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) Summarise follow-up time (eg, average and total amount)	5
Outcome data	15*	Report numbers of outcome events or summary measures over time	6
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6
		(b) Report category boundaries when continuous variables were categorized	n/a
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.