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# Antibiotic Prescribing and Associated Diarrhoea: A Prospective Cohort Study of Care Home Residents

## Abstract:

**Background:** The risk factors for and frequency of antibiotic prescription and antibiotic associated diarrhoea (AAD) among care home residents is unknown.

**Aim:** To prospectively study frequency and risks for antibiotic prescribing and AAD for care home residents.

**Design and setting:** A 12 month prospective cohort study in care homes across South Wales.

**Method:** Antibiotic prescriptions and the development of AAD were recorded on case report forms. We defined AAD as three or more loose stools in a 24 hour period occurring within eight weeks of exposure to an antibiotic.

**Results:** We recruited 279 residents from ten care homes. The incidence of antibiotic prescriptions was 2.16 prescriptions per resident year (95% CI: 1.90 to 2.46). Antibiotics were less likely to be prescribed to residents from dual-registered homes (OR compared to nursing homes: 0.38, 95% CI: 0.18 to 0.79). For those who were prescribed antibiotics, the incidence of AAD was 0.57 episodes per resident year (95% CI: 0.41 to 0.81 episodes). AAD was more likely in residents who were prescribed co-amoxiclav (HR = 2.08, 95% CI: 1.18 to 3.66) or routinely used incontinence pads (HR = 2.54, 95% CI: 1.26 to 5.13) and less likely in residents from residential homes (HR compared to nursing homes: 0.14, 95% CI: 0.06 to 0.32).

**Conclusion:** Residents of care homes, particularly of nursing homes, are frequently prescribed antibiotics and often experience diarrhoea following such prescriptions. Co-amoxiclav is associated with greater risk of AAD.

**Key words**

1. Antibiotic prescribing
2. Antibiotic associated diarrhoea
3. Care home residents
4. *Clostridium difficile*

**Key points**

1. Residents of care homes are frequently prescribed antibiotics and often experience diarrhoea following such prescriptions.
2. Residents in nursing homes are at greater risk of developing AAD than those in residential homes.
3. Co-amoxiclav is associated with greater risk of AAD.

## Introduction:

At least 4% of the UK population aged 65 or over live in care homes.[1, 2] Demand for long-term care in the UK is estimated to rise by up to 150% over the next 50 years.[3]

Although data on infection prevalence in care homes are limited, prevalence studies suggest that between five and ten percent of residents in care homes will be receiving antibiotics for a presumed infection at any one time.[4, 5] Previous research suggests that primary care clinicians tend to view co-morbidity and older age as risk factors for poor clinical outcomes, and would prescribe antibiotics to individuals with these risk factors more quickly than they would to individuals without.[6] This antibiotic use will have consequences for residents quality of life, costs of care, and for subsequent infections that are antibiotic resistant.[7, 9, 10] However, up to 40% of antibiotics prescribed in care homes could be inappropriate. [8, 9, 10] There is limited evidence, particularly in routinely published data, of prescription rates by antibiotic class and indication.

A side effect of antibiotic prescribing that may cause particular problems in care homes is antibiotic associated diarrhoea (AAD),[11, 12] and the incidence of AAD and associated risk factors are not well described for care home residents.

*Clostridium difficile* (*C. difficile*) is a Gram-positive, anaerobic spore-forming bacteria that was identified in the late 1970's and has recently been highlighted as a potential deadly threat to hospitalised patients and residents of care homes.[13, 14] *C. difficile* associated diarrhoea (CDAD) is the most commonly identified cause of AAD, and most cases of pseudomembranous colitis; it typically occurs in care homes among other settings.[15]

Although in the majority of individuals full recovery is usual, elderly and frail individuals in particular may suffer loss of dignity, become seriously ill with dehydration, (as a consequence of the diarrhoea), and some may go on to develop pseudomembranous colitis.

Better knowledge of the incidence and risk factors for antibiotic prescribing and for the development of AAD and CDAD in care home residents is needed to inform interventions for promoting evidence based antibiotic prescribing and for avoiding important adverse effects.

We therefore set out to prospectively study frequency and risks for antibiotic prescribing, AAD and CDAD for care home residents.

## **Methods:**

### *Study design, setting and participants*

This was a prospective cohort study conducted in care homes across South Wales, UK from November 2010 to March 2012. All care homes within South Wales were randomly ordered within three strata (nursing, residential, and dual-registered homes that provided both nursing and residential care). Homes were approached, and those that expressed an interest in participating and could nominate three or more staff in their home to take responsibility for conducting the study were recruited until at least three homes from each stratum had agreed to take part.

Residents were eligible if they had been admitted to the home for more than 24 hours with a planned admission for longer than one month. There were no exclusion criteria. Capacity to provide informed consent was assessed by senior care home staff or nursing staff who had received relevant training. Informed consent was sought from residents with capacity. Where residents lacked capacity, advice was taken from an appropriate personal consultee (typically the next of kin or the person who visited most regularly) about whether the resident would wish to participate in the study.[16] Care home staff and the research team collected data on participating residents using Case Report Forms (CRFs).

### *Data sources*

Baseline characteristics and medical history were collected for each recruited resident. All data were obtained from the care notes kept for each resident in each care home. Frailty status was assessed using the Clinical Frailty Scale (supplementary Box 1).[17] Nutritional risk status was assessed using the Malnutrition Universal Screening Tool.[18] At study entry, we also collected information on whether the resident usually had diarrhoea, a colostomy, a gastrostomy, faecal incontinence with loose stools and if they routinely used incontinence pads, active inflammatory bowel disease, compromised immunity, dysphagia, or compromised gut blood supply. We also asked whether the

resident had tested positive for *C. difficile* in the previous three months, and whether they had been admitted to hospital or prescribed antibiotics in the previous four weeks.

All antibiotics prescribed for the resident after recruitment as part of their routine care were recorded on a CRF by care home staff. This included information on the generic name of the antibiotic, dose, route, frequency, duration, and indication.

Following an antibiotic prescription, care home staff recorded the bowel motions of residents (time of stool and type of stool according to the Bristol Stool Chart[19]) for the period that antibiotics were prescribed, and for an additional eight weeks. We defined antibiotic associated diarrhoea (AAD) as three or more loose stools in a 24 hour period during this follow-up period.[20] Residents whose normal stool habits were three or more loose stools (Bristol Stool Chart type 5-7) in a 24 hour period did not have their diarrhoea attributed to antibiotic treatment. Where stool charts were returned with missing data we have assumed that an AAD episode had not occurred. AAD episodes were considered unique if they were separated by at least three days of no recorded diarrhoea. When loose stools occurred, stool samples were collected and sent to a central laboratory to test for *C. difficile*.

#### *Study size*

A minimum of 270 residents from nine care homes were required to fit a 95% confidence interval around an AAD rate of 25% +/- 10%. We estimated 40% of care home residents would be prescribed antibiotics in a 12 month period and that estimating an AAD rate of 25% would provide sufficient evidence that AAD is an important problem in care homes.

#### *Statistical methods*

Descriptive statistics were calculated for each care home type and overall using means (standard deviations), medians (interquartile ranges) and proportions as appropriate.

All incidence rates were calculated as per care home resident year. Clustering of antibiotic prescriptions and AAD by resident was explored and estimates were appropriately inflated.

The risk of residents being prescribed antibiotics was estimated by fitting a logistic regression model, with results presented as odds ratios, 95% CIs, and p-values.

The time from antibiotic prescription to first episode of AAD was estimated by fitting a two-level Cox proportional hazards model. Results are presented as hazard ratios with associated 95% CIs, and p-values.

In all regression models, variables were entered in the following blocks: stool monitoring characteristics (AAD models only), resident characteristics and care home characteristics. Explanatory variables were included if they were associated with their outcome at the 20% level in a univariable analysis, with variables removed from the final multivariable regression models if they were not significant at the 5% level and were of marginal significance (p-value > 0.1) in the univariable analysis. All relevant modelling assumptions were checked prior to reporting. Estimates from the regression models are presented from each stage of the multivariable model, with corresponding univariable estimates. Clustering by care home was investigated via multilevel analysis. However, owing to the small number of care homes, the models would not converge. Therefore the estimates presented are not adjusted for clustering at the care home level.

The two-level Cox proportional hazards model was implemented using Stata version 10.0. All other analyses were performed using IBM SPSS Statistics 20.



## **Results:**

### *Care homes*

Eleven care homes were recruited in the study. However, one withdrew before any residents were recruited. Residents were therefore recruited from ten care homes; four nursing, four residential, and two dual-registered homes. Nine homes were privately managed and one managed by a Local Authority. The median number of beds was 39.5 (IQR: 31.0 to 50.0) and the median number of residents at the time of recruitment was 33.0 (IQR: 28.0 to 50.0). The median number of staff working in a care home over a typical 24 hour period was 16.0 (IQR: 14.0 to 25.0), with 20.5% (41) categorised as short term staff members (i.e. employed for less than 12 months).

### *Participants*

Three of the 389 residents (or consultees) approached were ineligible and 107 declined participation. A total of 279 residents were therefore recruited (71.7%). 19 withdrew, 16 (84.2%) due to residents being moved to a non-participating care home. Five of the 19 residents who withdrew from the study also withdrew permission for data already collected to be used; therefore, our analyses are based on a maximum of 274 residents (Figure 1). There were 81 hospitalisations reported during the study period, with at least one hospitalisation reported for 58 (21.2%) residents (incidence rate of 0.14 hospitalisations per resident year, 95% CI: 0.09 to 0.20 hospitalisations). In total, 64 residents died during the study period. No deaths were deemed study related. Residents were observed for a median of 310 days (IQR: 230 to 364 days).

### *Descriptive data*

Residents had a median age of 86 years (IQR: 82 to 90), with 20.4% (56) less than 80 years, 57.7% (158) between 80 and 90 years, and 21.9% (60) older than 90 years. 75.9% (208) were female. Overall, 28.5% (78) had capacity to provide informed consent for themselves. Few residents had any of the pre-specified relevant serious medical conditions. 7.7% (21) had faecal incontinence with

loose stools and 1.8% (5) had diarrhoea at baseline. 66.8% routinely used incontinence pads (183). 13.5% (37) were classed by the clinical frailty score as 'very fit to managing well', 51.1% (140) as 'vulnerable to moderately frail', and 35.4% (97) as 'severely frail to terminally ill'. Nursing homes had more frail residents than residential homes. At baseline, 63.0% (172) were classified as having a low nutritional risk status, 14.3% (39) as medium risk, and 22.7% (62) as high risk. In the four weeks prior to recruitment, 6.9% (19) had been admitted to hospital and 20.8% (57) of residents were prescribed antibiotics (Table 1).

### *Antibiotic prescriptions*

There were 609 antibiotic prescriptions recorded over the study period, with 73.7% of residents being prescribed at least one antibiotic course (202). We found an incidence of 2.16 antibiotic prescriptions per care home resident year (95% CI: 1.90 to 2.46 prescriptions).

Antibiotics were prescribed for a median of 7.0 days (IQR: 6.0 to 7.0), with 14.7% (88) prescribed for less than five days, 74.9% (447) prescribed for between five and seven days, 6.7% (40) prescribed for between eight and ten days, and 3.7% (21) prescribed for more than ten days (we were unable to determine the length of course for 12 prescriptions due to transcribing errors). The proportion of antibiotics prescribed for each indication varied by care home type (Supplementary Figure 1, accessible on the journal website <http://www.ageing.oxfordjournals.org/>). There was also a wide range of antibiotics prescribed for each indication (Supplementary Figure 2, accessible on the journal website <http://www.ageing.oxfordjournals.org/>). While the total number of antibiotic prescriptions each month varied considerably (range 0.09 to 0.29 and average 0.21 prescriptions per resident), there was no obvious marked seasonal variation.

Compared to nursing home residents, those from dual-registered care homes had a significantly lower chance of being prescribed antibiotics during the study period (OR = 0.38, 95% CI from 0.18 to 0.79,  $p = 0.009$ ). The odds of being prescribed an antibiotic during the study period were 2.64 times

higher for residents who had been prescribed antibiotics in the four weeks before study entry (95% CI from 1.17 to 5.99,  $p = 0.020$ ). Exposure to antibiotics was similar in residents who were vulnerable to moderately frail or severely frail to terminally ill as in those who were very fit to managing well (Supplementary Table 1, accessible on the journal website <http://www.ageing.oxfordjournals.org/>).

#### *Antibiotic associated diarrhoea*

Three antibiotic prescriptions from two residents provided no corresponding stool monitoring data. From the remaining 606 antibiotic prescriptions there were 571 stool monitoring periods, ranging between one and 11 weeks. The discrepancy between the number of prescriptions and monitoring periods arose because residents could be prescribed multiple antibiotics in the same week (hence there was only one, ongoing monitoring period). There were 447 unique episodes of AAD reported, with 43.5% (87) of residents who were prescribed antibiotics experiencing at least one episode of AAD during the study period. There were 0.57 episodes of AAD per care home resident year for those prescribed antibiotics, 95% CI: 0.41 to 0.81 episodes.

The rate of AAD was more than twice as high in residents who were prescribed co-amoxiclav (HR = 2.08, 95% CI: 1.18 to 3.66,  $p = 0.011$ ). Residents who routinely used incontinence pads also had a higher rate of AAD (HR = 2.54, 95% CI: 1.26 to 5.13,  $p = 0.009$ ). Compared to residents in nursing homes, those in residential homes were significantly less likely to develop AAD during the study period (HR = 0.14, 95% CI: 0.06 to 0.32,  $p < 0.001$ ) (Table 3).

#### *C. difficile associated diarrhoea*

Of the 447 unique episodes of AAD, only 55 had corresponding microbiological data from stool samples. Eight of the samples cultured *C. difficile*. *C. difficile* was also detected in a further five stool samples taken after residents experienced loose stools (i.e. BSC type 5 – 7 stools where the frequency of stools did not meet our definition of AAD). The 13 samples were obtained from nine residents in the same care home. In total, 12 samples were toxin B positive and there were nine

different ribotypes (005, 010, 014, 020, 026, 027, 106, 160 and 193). No ribotype was found in more than one resident.

## **Discussion:**

### *Summary*

This study found that antibiotics were prescribed at a rate of 2.16 per resident year, with almost three quarters of residents prescribed at least one antibiotic course during the 16 month study period (310 day median length of follow-up). Residents were over two and a half times more likely to be prescribed antibiotics during the study period if they had been prescribed antibiotics in the four weeks prior to study entry. Residents were prescribed a wide range of antibiotics for each indication. The incidence of AAD in those prescribed antibiotics was 0.57 episodes per resident year, with 43.5% of residents prescribed antibiotics experiencing at least one episode of AAD. *C. difficile* associated diarrhoea (CDAD) occurred in less than 15% of residents who developed AAD and for whom a stool sample was sent for microbiological analysis. While all CDAD episodes were found in residents from the same care home, the unique ribotypes suggest that the episodes were not associated with an outbreak. Residents in nursing homes were more likely to be prescribed antibiotics and experience AAD. Residents were more likely to experience AAD if they had been prescribed co-amoxiclav or if they routinely used incontinence pads.

### *Strengths and Limitations*

We conducted this study in a population and setting difficult to research,[21, 22] but we were able to estimate the rates of participation, antibiotic prescription and AAD. Despite needing to obtain advice about resident participation from consultees for the majority of participants in care homes, the recruitment target was achieved. Our study can be considered to have a low risk of bias because of relatively high inclusion rates in each care home and relatively complete follow up data.[23] Despite most residents lacking capacity to consent to inclusion in the study, a majority in each of the ten homes were included and the population is representative of those now living in care homes in the UK.[24, 25] While every effort was made to maintain the validity of the antibiotic and stool data, it is possible that this was not always achieved. Prescriptions during periods of hospitalisation were

not transcribed onto study CRFs; therefore the number of antibiotic prescriptions may have been under-reported. Antibiotic prescriptions that were not recorded for the purpose of the study may also have resulted in a lack of stool data for the defined follow-up period. It is therefore possible that we have underestimated the incidence of AAD. Residents who were recorded as routinely experiencing three or more loose stools in a 24 hour period before observations were started were not classed as experiencing AAD during the study. We assumed that if stool data were missing, AAD was unlikely to have occurred, but there may have been some episodes of AAD that were not recorded. Our approach has therefore provided a conservative lower-bound of estimated AAD in care homes. However given the observational nature of this study with no control group, and that we did not record episodes of diarrhoea in participants who were not prescribed antibiotics, it is not possible to state the direct cause of the diarrhoea. We are also unable to determine from this study whether diarrhoea was related to the illness itself rather than its management (i.e. the antibiotic prescription). While we found that residents in residential homes are significantly less likely to experience AAD than those in nursing homes, this may be in part due to the increased mobility, with associated less intense monitoring, of residents' stools. We also found that residents were more likely to experience AAD if they routinely used incontinence pads. This may be a real effect, but could reflect easier observation and reporting of loose stool types, or be an artefact as a result of stool and urine mixing in an incontinence pad. That we only obtained microbiological data from 12% of diarrhoeal episodes limited the reliability of our estimation of CDAD.

#### *Comparison with existing literature*

Residents were predominantly aged 80 years and above, frail and at high nutritional risk. Levels of nutritional risk were similar to levels found in care homes in the 2011 Nutritional Screening Survey.[26] Residential, nursing and dual-registered homes were included, nearly all were privately managed, and some specialised in looking after the elderly mentally infirm. We found little seasonal

variation in antibiotic prescribing and AAD, consistent with the mandatory and voluntary surveillance data.[27]

Our estimate of antibiotic prescribing is consistent with an estimate obtained from a study conducted in North Wales,[28] where 203 antibiotic prescriptions were recorded over a nine-week period in 15 nursing homes (giving an incidence rate of 2.3 antibiotic prescriptions per resident year). A study conducted in nursing homes in Sweden[29] found a rate of 0.51 antibiotic prescriptions per resident year.

Estimates of AAD range from virtually zero in low risk groups to over 40% in those at higher risk, but these estimates are derived from control groups in trials of interventions for AAD, and not prospective observational studies such as ours.[30] A recently published trial of probiotics to prevent AAD in elderly hospitalised patients found that AAD occurred in 10.4% of patients randomised to placebo.[31]

#### *Implications for future research and practice*

Care home staff should weigh up the potential benefit a resident may receive from an antibiotic against the potential risk of side effects, such as diarrhoea and its consequences, from that antibiotic. When diarrhoea does occur, staff should more routinely send a sample for microbiological testing. Clinicians should ensure that their antibiotic prescribing is evidence based in this setting wherever possible. However, there is a paucity of evidence to support antibiotic prescribing in care home residents. Further research is needed to investigate the benefits of antibiotic treatment, and the development and evaluation of preventative strategies for AAD in this setting.

**Additional information:**

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The funding sources had no roles in data collection, analysis, or interpretation; report writing; or submission. All authors had full access to all the data in the study and take responsibility for the integrity and the accuracy of the data analysis. All authors had responsibility for the final decision to submit for publication. The manuscript is an honest, accurate and transparent account of the study being reported. No important aspects of the study have been omitted.

**Ethical approval:** This study was approved by the South East Wales Research Ethics Committee Panel C (reference 10/WSE03/31).

**Competing interests:** All authors declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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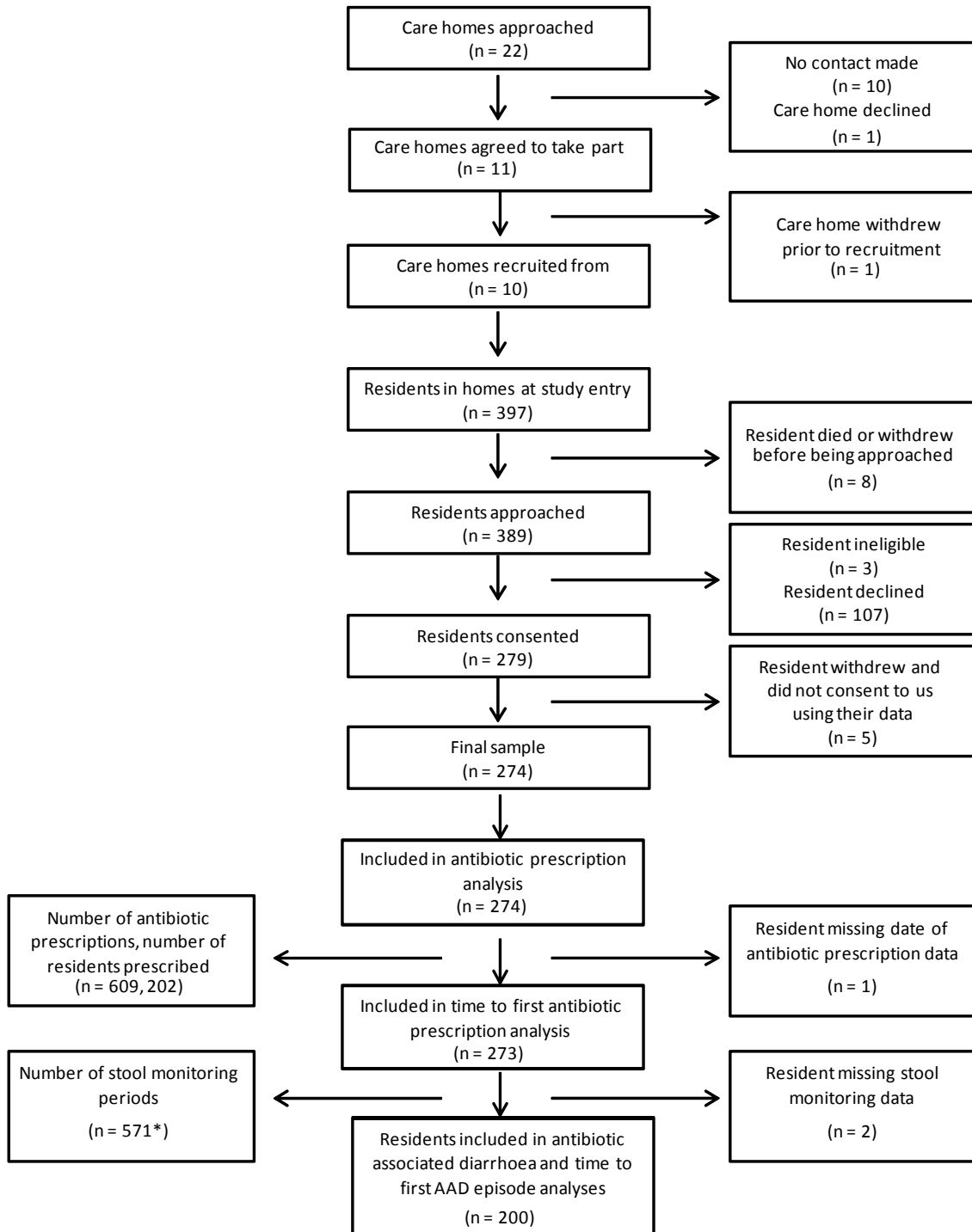
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## Tables and Figures

**Figure 1:** STROBE flow diagram



\*Some prescriptions overlapped in time and so did stool monitoring periods in these instances.

**Table 1:** Resident characteristics at study entry by care home type

Care home type (no. residents)	Age*	Gender (male) <sup>†</sup>	Capacity to provide informed consent for study <sup>†</sup>	Admitted to hospital in last 4 weeks <sup>†</sup>	Prescribed antibiotics in last 4 weeks <sup>†</sup>	Routinely wear incontinence pads <sup>‡</sup>	MUST : Low risk <sup>§</sup>	MUST: Medium risk <sup>§</sup>	MUST: High risk <sup>§</sup>	Clinical frailty score of 1-3 <sup>  </sup>	Clinical frailty score of 4-6 <sup>  </sup>	Clinical frailty score of 7-9 <sup>  </sup>
Nursing (n = 87)	87.0 (83.0, 91.5)	26 (29.9)	25 (28.7)	11 (12.6)	17 (19.5)	66 (75.9)	55 (64.0)	9 (10.5)	22 (25.6)	2 (2.3)	42 (48.3)	43 (49.4)
Residential (n = 87)	85.0 (76.5, 89.0)	19 (21.8)	33 (37.9)	6 (6.9)	18 (20.7)	39 (44.8)	58 (66.7)	14 (16.1)	15 (17.2)	22 (25.3)	47 (54.0)	18 (20.7)
Dual-registered (n = 100)	85.0 (82.0, 90.0)	21 (21.0)	20 (20.0)	2 (2.0)	22 (22.0)	78 (78.0)	59 (59.0)	16 (16.0)	25 (25.0)	13 (13.0)	51 (51.0)	36 (36.0)
<b>Overall (n = 274)</b>	<b>86.0</b> (82.0, 90.0)	<b>66</b> (24.1)	<b>78</b> (28.5)	<b>19</b> (6.9)	<b>57</b> (20.8)	<b>183</b> (66.8)	<b>172</b> (63.0)	<b>39</b> (14.3)	<b>62</b> (22.7)	<b>37</b> (13.5)	<b>140</b> (51.1)	<b>97</b> (35.4)

\*Median (IQR)

<sup>†</sup>Number (% of residents)

<sup>‡</sup>Wears incontinence pads for more than half the week

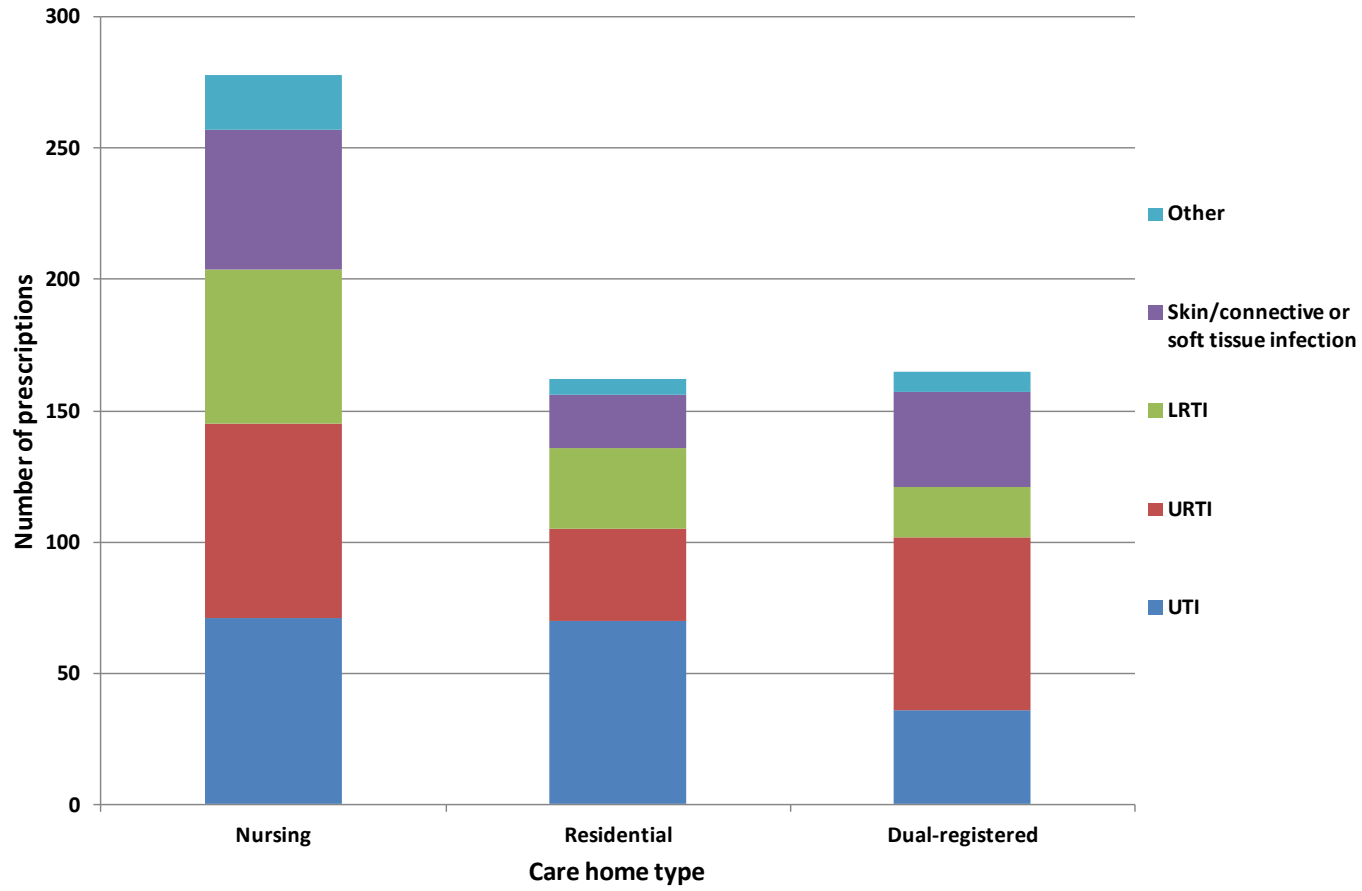
<sup>§</sup>Malnutrition Universal Screening Tool (MUST). Calculated using BMI (weight(kg)/height(m)<sup>2</sup>), unplanned weight loss (% of total body weight) in past 3-6 months, and noting if the resident is acutely ill and there has been / is likely to be no nutritional intake for > 5 days. Scores summed to give total MUST score. 0 = low risk; 1 = medium risk; 2+ = high risk.

<sup>||</sup> Clinical Frailty Score: 1 – very fit; 2 – well; 3 – managing well; 4 – vulnerable; 5 – mildly frail; 6 – moderately frail; 7 – severely frail; 8 – very severely frail; 9 – terminally ill

**Table 2:** Factors associated with time to first antibiotic associated diarrhoea episode (based on 571 stool monitoring periods nested within 200 care home residents)

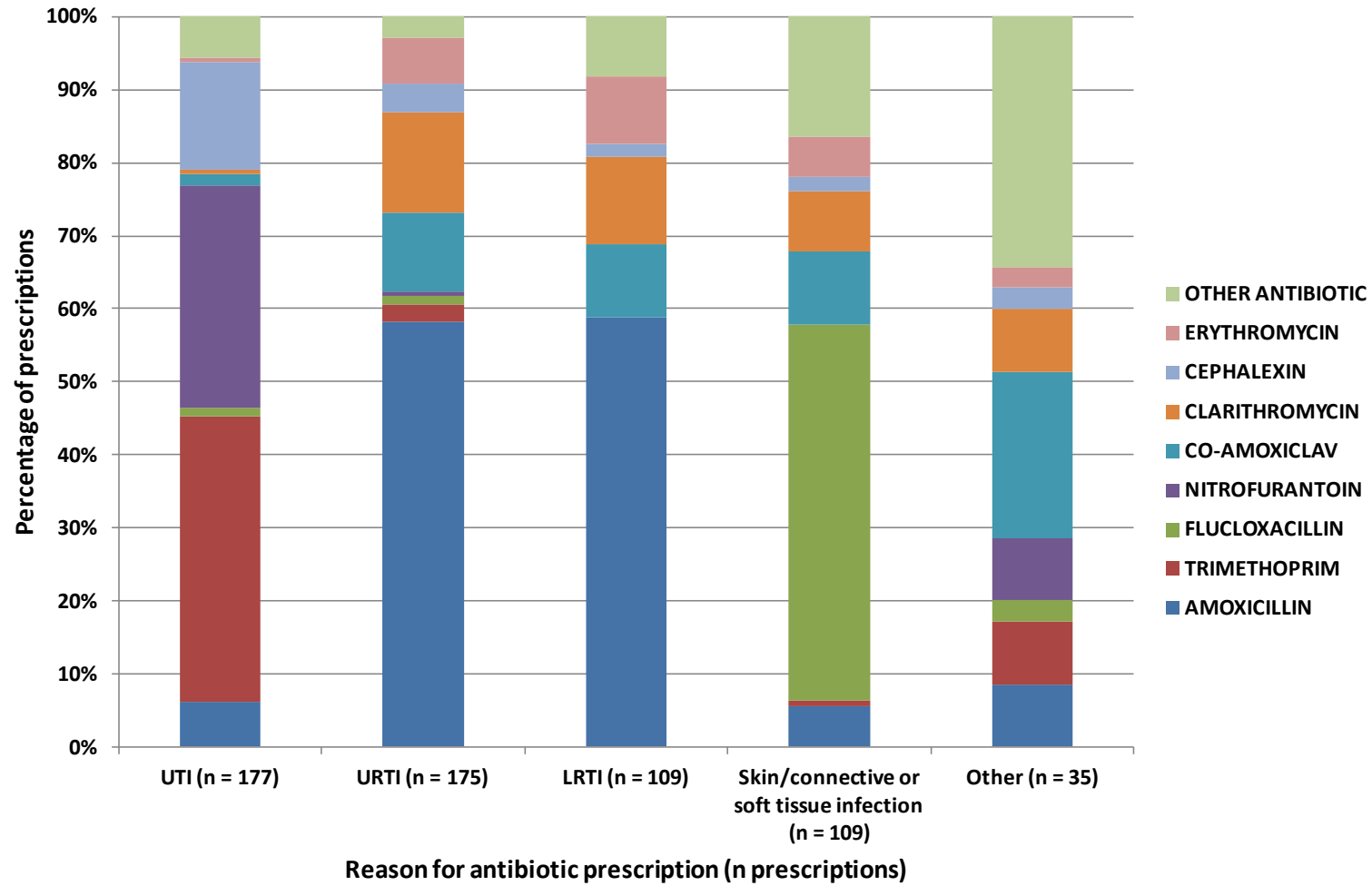
Variable	Univariable		Multivariable					
			Stool monitoring period characteristics		With resident characteristics		With care home characteristics	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Prescribed Co-Amoxiclav during stool monitoring period	2.13 (1.20-3.78)	0.010	2.13 (1.20-3.78)	0.010	1.96 (1.11-3.47)	0.020	2.08 (1.18-3.66)	0.011
Resident frequently used incontinence pads at study entry	4.04 (2.04-7.99)	<0.001			3.80 (1.87-7.70)	<0.001	2.54 (1.26-5.13)	0.009
Clinical frailty: very fit to managing well	Reference category for clinical frailty							
Clinical frailty: vulnerable to moderately frail	4.60 (1.50-14.07)	0.007			3.76 (1.19-11.85)	0.024	2.49 (0.78-7.94)	0.124
Clinical frailty: severely frail to terminally ill	4.58 (1.44-14.50)	0.010			2.98 (0.91-9.78)	0.071	1.75 (0.50-6.09)	0.381
Care home type: nursing	Reference category for care home type							
Care home type: residential	0.10 (0.05-0.23)	<0.001					0.14 (0.06-0.32)	<0.001
Care home type: dual-registered	0.80 (0.44-1.47)	0.476					0.82 (0.43-1.57)	0.547

Supplementary Figure 1: Reason for antibiotic prescriptions by care home type





Supplementary Figure 2: Type of antibiotic prescribed by indication



**Supplementary Table 1: Factors associated with being prescribed antibiotics during the study period**

(based on 274 care home residents)

Variable	Univariable		Multivariable			
			Resident characteristics		With care home characteristics	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Clinical frailty: very fit to managing well	Reference category for clinical frailty					
Clinical frailty: vulnerable to moderately frail	2.14 (0.99-4.65)	0.054	2.15 (0.98-4.71)	0.057	1.88 (0.84-4.23)	0.127
Clinical frailty: severely frail to terminally ill	1.58 (0.71-3.51)	0.263	1.67 (0.74-3.75)	0.218	1.33 (0.56-3.16)	0.525
Prescribed antibiotics four weeks prior to study entry	2.56 (1.15-5.72)	0.022	2.55 (1.14-5.72)	0.023	2.64 (1.17-5.99)	0.020
Care home type: nursing	Reference category for care home type					
Care home type: residential	0.48 (0.23-0.99)	0.048			0.49 (0.22-1.09)	0.080
Care home type: dual-registered	0.39 (0.19-0.79)	0.009			0.38 (0.18-0.79)	0.009

**Supplementary Box 1:** Description of scores on the Clinical Frailty Scale

**1 – Very fit:** People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

**2 - Well:** People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally.

**3 – Managing well:** People whose medical problems are well controlled, but are not regularly active beyond routine walking.

**4 - Vulnerable:** While not dependent on others for daily help, often symptoms limit activities. A common complaint is being “slowed up”, and/or being tired during the day.

**5 – Mildly frail:** These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

**6 – Moderately frail:** People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.

**7 – Severely frail:** Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

**8 – Very severely frail:** Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

**9 – Terminally ill:** Approaching the end of life. This category applies to people with a life expectancy <6 months, who are not otherwise evidently frail.