Food Standards Scotland

For safe food and healthy eating

CAMPYLOBACTER

Estimating the burden of gastrointestinal infection in Scotland using data linkage

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Summary

This report produced by Health Protection Scotland (HPS) on behalf of FSS outlines the results of analysis of linked data for laboratory confirmed *Campylobacter* cases in Scotland during the 5-year period 2013-2017. ECOSS laboratory data was linked to deprivation, hospitalisation, cancer, prescribing and mortality data to determine the demographic characteristics of confirmed *Campylobacter* cases, rates of hospitalisation, mortality, and the incidence of complications and sequelae. Results are presented in tabular and graphical form, and discussed in the context of findings of a literature review on *Campylobacter* infections and associated outcomes.

Terminology

ANOVA- Analysis of Variance

ALD-Alcoholic liver disease

BNF- British National Formulary

CD-Crohn's disease

CCI- Charlson Comorbidity Index

CI- Confidence Interval

CLD- Chronic liver disease

Data zone- small geographical area system used in Scotland.

ECOSS- The Electronic Communication of Surveillance in Scotland

GBS-Guillain-Barré Syndrome

HDU- High Dependency Unit

IBS- Irritable Bowel Syndrome

IBD-Inflammatory Bowel Disease

ICD-10- International Statistical Classification of Diseases and Related Health Problems 10th revision

ICU- Intensive Care Unit

ISD- Information Services Division, NHS National Services Scotland

PPI- Protein Pump Inhibitor

PRISMS- Prescribing Information System for Scotland

ReA- Reactive Arthritis

RUK- Rest of UK, excluding Scotland

SD- Standard Deviation

SIMD- Scottish Index of Multiple Deprivation

SMR01- General/Acute Inpatient and Day Case

SMR06- Scottish Cancer Registry

UC- Ulcerative colitis

Introduction

Campylobacter is recognised as being responsible for a significant disease burden in the Scottish population with around 6000 laboratory confirmed cases per year. While ECOSS laboratory data is available for all confirmed cases of *Campylobacter* in Scotland, little is known about how the demographic characteristics of confirmed cases relate to their clinical outcomes. The availability of individual-level hospitalisation, mortality and prescribing datasets in Scotland enables linkage with laboratory data, thus providing information on relevant health events before and after the episode of infection for each individual. Through analysis of this linked data, this project sought to estimate the disease burden of *Campylobacter* in Scotland, identify risk factors associated with hospitalisation, and gather information on the proportion of cases developing complications and sequelae.

A systematic literature review was undertaken to determine a list of conditions reported as being associated with *Campylobacter*, either as predisposing conditions, presenting symptoms, complications or sequelae, and the time periods for their development. The review also sought to obtain estimates of the *Campylobacter* disease burden calculated by other authors, and identify risk factors associated with infection, hospitalisation, and the development of sequelae.

Search strategies used are outlined in the 'Methods' section. A table outlining the conditions of interest and their corresponding ICD-10 codes is included in the appendices.

In summary, the literature review revealed:

- the percentage of confirmed cases hospitalised across a range of settings.
- reports of risk factors associated with infection, hospitalisation and the development of sequelae.
- number of descriptive case studies reporting rare complications, often in the presence of specific underlying conditions.
- estimates of the percentage of cases developing sequelae vary greatly in the literature with studies exhibiting considerable heterogeneity with inconsistent methods of reporting sequelae, with different follow-up times.

A limited number of studies have used analysis of linked data to estimate mortality resulting from *Campylobacter* infection [1] or to estimate the incidence of infection in a cohort with a specific underlying risk factor [2].

Estimates of the percentage of cases hospitalised for their infection varied from 2.3% [3] to 15% [4] and confirmed cases requiring hospital treatment in England and Wales being reported as 10% between 1990 and 2007 [5] and as 10% of cases consulting their GP in 2000 [6]. A case control study in the Grampian Health Board area conducted by Health Protection Scotland in 2010 (https://www.foodstandards.gov.scot/downloads/Final_Report_2.pdf) recorded a 10.7% overnight hospitalisation rate. As this was based on voluntary questionnaires returned by cases this may have been biased towards those who were more severely ill rather than those with mild illness who may

have been less inclined to submit their questionnaire, but nevertheless is consistent with the two reports from England and Wales.

Higher rates of hospitalisation were reported for cases in the ≥60 age group [7;8]and the very young, with length of hospitalisation being associated with the presence of underlying conditions and increased age [9]. Slightly higher rates of hospitalisation were seen among female cases [10].

Risk factors, besides the usual association with poultry and poultry products, reported in the literature as being associated with illness from *Campylobacter* infection included being less deprived[11] and living in an urban area [12;13] and protein pump inhibitor use [14-16].

Risk factors reported as being associated with greater severity of symptoms included the presence of underlying conditions requiring treatment with immunosuppressant medications [17].

A number of underlying conditions were reported as being associated with both acquiring *Campylobacter* infection and a greater severity of symptoms than for cases without underlying conditions, namely inflammatory bowel disease [18], ulcerative colitis [19] and coeliac disease [20].

Complications commonly reported in the literature included bacteraemia, Guillan Barré Syndrome, peritonitis, and intestinal obstruction [21-24]. Several authors also reported complications developing in the presence of specific underlying conditions responsible for immunosuppression e.g. bacteraemia in the presence of HIV [25] or alcoholic liver disease [26].

While previous studies have attempted to estimate the incidence of sequelae or prevalence of predisposing conditions, many of these studies used data from self-reported questionnaires rather than linkage of routine datasets, therefore it is challenging to quantify the true burden of sequelae, especially as participation bias may favour those with more severe outcome and sequelae was self-reported rather than clinically diagnosed. Mangen et al., estimated sequelae (reactive arthritis, irritable bowel syndrome, and GBS) to be responsible for 82% of the total *Campylobacter* disease burden [27] when using the Daily Adjusted Life Years (DALY) method to quantify health losses in years.

A 2014 systematic review by Keithlin et al.[21] outlined estimates of the incidence of sequelae and complications commonly reported in the literature. The estimated incidence of GBS was 0.07% (95% CI 0.03 - 0.15), of reactive arthritis was 2.86% (95% CI 1.40 - 5.61), and of irritable bowel syndrome was 4.01% (95% CI 1.41 - 10.88). These estimates were derived by a systematic literature review using 20 studies from nine countries, 8 of which were European.

Sequelae associated with *Campylobacter* infection were ulcerative colitis [19;28], coeliac disease [29], inflammatory bowel disease [30-32] irritable bowel syndrome (IBS), Crohn's disease, and reactive arthritis (Ternhag et al., 2008). It is of note that IBS, ulcerative colitis and coeliac disease have also been associated with acquiring infection and the severity of infection [19]. Notably, severity of initial illness, female gender and antibiotic use during infection were associated with IBS development in children [33].

The majority of studies reporting the incidence of sequelae focused on the year following infection, while a few investigated cases of sequelae up to ten years following infection. The incidence of sequelae reported generally increased with the length of follow-up time of the study, however as

the time from initial infection increases so does the potential for other factors to have contributed to the development of the sequelae.

While some *Campylobacter* subtypes are reported in the literature as being associated with particularly severe outcomes or high rates of sequelae development e.g. *Campylobacter* concisus [34] *Campylobacter* jejuni [35], *Campylobacter* lari and *Campylobacter* fetus [36] the analysis undertaken for this report considered all confirmed *Campylobacter* cases, as the typing of *Campylobacter* is not routinely performed by diagnostic laboratories in Scotland. Furthermore, where typing has been conducted in the UK approximately 90% of isolates are C. jejuni[37].

Mortality rates reported in the literature were from 0.03% [38] and 0.04% [39].

Datasets used

ECOSS data: 5 years (2013-2017) containing all laboratory confirmed cases of *Campylobacter* in Scotland.

National Records of Scotland Death Records: mortality records dating from 2012-2018, detailing the date of death and the underlying cause of death.

National Records of Scotland Mid-Year population estimates for 2017

SIMD 2012: The 2012 release of Scottish Index of Multiple Deprivation data, based on 2001 Data zones.

SMR01: Acute and inpatient records dating from 2012-2018.

SMR04: Cancer register records dating from 2012-2017.

PRISMS: Prescribing data records dating from 2012-2018.

Urban/rural locality data: Scottish Government 6-fold Urban Rural classification 2013-2014.

Methods

Literature review and clinical coding

Medical databases PubMed and MedLine were interrogated systematically using combinations of search terms. A table outlining these terms and how they were combined is included in Appendix 1 of this document. Lists of search terms were expanded based on the results of preliminary searches.

The time periods reported in the literature for the development of symptoms and sequelae, and those relating to underlying medical conditions or use of medication being associated as underlying risk factors for infection were recorded. These time periods were used as a basis for defining the time periods over which to link the ECOSS data to SMR01 and prescribing data. Once a list of conditions had been compiled, their corresponding ICD-10 codes were identified.

Data request and cleaning

ECOSS laboratory data for all human cases of *Campylobacter* during the five-year period 2013-2017, to include all relevant variables were obtained. Data were sorted by CHI number and checked for quality and completeness. Where information was missing from the age field, this was completed using the date of birth field. Where postcodes were missing but an address was available, the postcode field was seeded using the address information. Where multiple rows existed for one individual, and information was missing from the first row but available in subsequent rows, variable fields in the first row were seeded as appropriate. Data were restricted to rows describing 'episode 1' cases, a term used to the describe the first time a case tested positive for *Campylobacter* within a 4 week period, 4 weeks being the time period defined as being the length of one episode of illness. Checks on whether the correct health board was recorded for each case were undertaken.

Data linkage

The cleaned ECOSS dataset was sent to ISD colleagues for linkage.

Demographic data

Where available, postcodes listed in the file of all confirmed cases were used to obtain the Data zone corresponding to the location of each case. This information was then linked to a look-up file containing Scottish Index of Multiple Deprivation (SIMD) data to obtain the deprivation status of each case.

The Scottish Index of Multiple Deprivation (SIMD) identifies small area concentrations of multiple deprivation across all of Scotland in a consistent way. It allows effective targeting of policies and funding where the aim is to wholly or partly tackle or take account of area concentrations of multiple deprivation.

SIMD ranks small areas (called data zones) from most deprived (ranked 1) to least deprived (ranked 6,976). Further information is available here: https://www2.gov.scot/Topics/Statistics/SIMD

Where a postcode was missing for a case, and therefore deprivation and urban/rural locality information could not be obtained, the case was retained in the dataset for inclusion in the analysis, but excluded from specific analysis using deprivation and locality variables.

Hospitalisation data

Cases were linked via CHI number to corresponding records in SMR01, mortality and prescribing data. Where possible, where CHI numbers were missing from the ECOSS records, these were seeded from the CHI register, based on matching to date of birth and name. Cases for whom a CHI number was missing and could not be seeded from the CHI register were excluded from the linkage and subsequent analysis.

All cases who were recorded as having an admission or discharge date within the time period ± 14 days of their laboratory sample date were flagged as having being hospitalised. In the absence of information on a disease onset date, the laboratory sample date was used as a time point with which to compare the timing of hospital stays and prescriptions. A second variable, 'hospitalised for *Campylobacter*', was added to identify those cases that were hospitalised specifically as a result of *Campylobacter* infection, associated symptoms or related complications as specified by the ICD-10 code recorded for the main condition on admission, or one of the six diagnostic codes recorded for the episode of care. It was this second variable that was subsequently used in the analysis to indicate cases hospitalised for *Campylobacter*. The conditions, symptoms and complications of interest and their corresponding diagnostic codes are outlined in the appendix.

Where hospitalisation was present, length of stay was calculated and indicated in the linked data file. Time between laboratory confirmation and hospitalisation was also indicated. Flags to indicate admission to intensive care (ICU), high-dependency unit (HDU), renal and care of the elderly specialisms were created. The number of subsequent stays during the 30 days following the episode of infection, and the total length of stay over the 12 months following infection were also calculated. A flag was added to indicate where the case was admitted as an emergency, either via A&E, emergency transfer or other urgent admission.

A definition of emergency admission as used by ISD can be found at: http://www.ndc.scot.nhs.uk/Data-Dictionary/SMR-Datasets/Episode-Management/Admission-Type/index.asp

For all cases, SMR01 data was searched over the 12 months prior to laboratory confirmation and the presence of conditions identified as either predisposing an individual to *Campylobacter*, or chronic conditions which may increase length of hospitalisation were flagged. SMR01 data was also searched during the 12 months following laboratory confirmation of infection in order to identify where sequelae occurred.

Mortality data

A field denoting the Charlson Comorbidity Index (CCI) was included, which predicts the one-year mortality for a patient who may have a range of comorbid conditions such as heart disease, AIDS, or cancer (a total of 22 conditions). Each condition is assigned a score of 1, 2, 3, or 6, depending on the risk of dying associated with each one [37;40;41]. This index is often to referred to as the Charlson Score.

Where death occurred, time between laboratory confirmation and death was indicated. This variable was then used to identify cases who died within 365 days of their laboratory confirmation date. The ICD-10 code representing the main underlying cause of death reported in the death records was included as a variable in the linked data. This variable was used to identify those cases

who had *Campylobacter* enteritis recorded as their main cause of death, and cases with a complication associated with *Campylobacter* infection recorded as the main cause of death.

Prescribing data

Linkage with prescribing data was used to identify use of the following medication groups in the 12 months prior to, and following, the laboratory sample date: immuno-suppressants, and drugs for use in arthritis, diabetes and bowel conditions. The BNF classification codes (https://www.bnf.org/about/) flagged in the linked data in order to ascertain the presence of the above conditions are outlined as follows:

Immunosuppression and cancer treatment: 8

Chronic bowel conditions: 1.5

Diabetes: 6.1

Arthritis: 10.1

Use of antibiotics and anti-diarrhoeal drugs in the 30 days either side of the *Campylobacter* laboratory date, and protein pump inhibitor (PPI) use in the 12 and 3 month periods preceding the laboratory sample date were flagged. In addition, a field was added to include antibiotic prescribing in the seven days after laboratory sample date along with the names of the antibiotics prescribed within those seven days.

An additional measure was used to help determine comorbidity using prescribing data. A field was included in the dataset to denote the number of unique drug classes of the British National Formulary that a case had been prescribed in the 12 months preceding their laboratory specimen date. These were grouped in the datasets as 0, 1-5, 6-10 and 11-15 chapters.

Predisposing conditions

The presence of the following predisposing and chronic conditions were flagged in the linked data file: immunosuppression, cancer, diabetes, ulcerative colitis (UC), Crohn's disease (CD), inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), HIV, rheumatoid arthritis, coeliac disease, liver disease and chronic gastritis. The presence of predisposing conditions was flagged in the data using the following method:

One variable was created to indicate the presence of predisposing conditions, comprised of the following categories: individuals with none of the predisposing conditions listed above, individuals with predisposing conditions identified by linkage with prescribing data, but not requiring hospital treatment in the 12 months prior to the *Campylobacter* diagnosis date, and individuals with predisposing conditions that required hospital treatment in the 12 months prior to the *Campylobacter* diagnosis date.

In a separate analysis, variables were created to indicate the presence of specific predisposing or long-term health conditions (diabetes, arthritis), or groups of related conditions (bowel conditions, cancer and immunodeficiencies, liver disease), as defined by their presence in either SMR01 or prescribing data.

The term 'predisposing conditions' is used in this report to refer to the conditions listed above, as identified by the methods used in the linkage and analysis.

Sequelae

The presence of the following conditions in the SMR01 data in the 12 months following infection were flagged: reactive arthritis (ReA), irritable bowel syndrome (IBS), inflammatory bowel disease, ulcerative colitis, Crohn's disease, coeliac disease, and chronic gastritis. The creation of flags to identify the presence of sequelae used the same methods as those used to identify the presence of predisposing conditions. Where a condition was recorded in the SMR01 data both before and after the episode of infection, or the prescribing data indicated that prescriptions for a class of drugs (e.g. drugs used in bowel conditions or immunosuppressants) were used, then the condition appearing in the SMR01 data following the infection was not flagged as a sequelae.

For each condition, two variables indicating its presence as a sequelae were created: one using only hospitalisation data (e.g. presence of hospitalisation for a condition in the 12 months following infection when it was absent in the hospitalisation data in the 12 months before), and the other using hospitalisation and prescribing data (presence of a condition in the hospitalisation data in the 12 months following infection where it was absent in the hospitalisation data for the 12 months before, and its absence was also indicated by the classes of drugs prescribed in the 12 months prior to infection).

Severe outcomes

A variable indicating the presence of one the following outcomes was created: death within 30 days (of any cause) of *Campylobacter* diagnosis, or among those cases hospitalised for *Campylobacter*, admission to ICU or HDU. This allowed the calculation of the proportion of cases for whom a severe outcome was recorded and to determine their characteristics and compare those characteristics to cases for whom outcomes were not severe.

Data confidentiality

Approval for the linkage of the datasets was obtained via the NSS generic PAC and linkage registration form.

Personally identifiable information (e.g. names and addresses) were removed from the dataset during the linkage process, and the final data file for use in analysis was kept in a restricted area within the Gastrointestinal and Zoonoses team's folder.

Analysis

SPSS version 24 and Tableau 10.4 was used for the analysis.

Descriptive and inferential analysis

Summary statistics on the demographic characteristics (age, sex, deprivation and locality) of all confirmed cases were derived.

For those cases hospitalised as a result of their *Campylobacter* infection, summary statistics on length of stay, the prevalence of predisposing conditions, and the incidence of complications and sequelae were derived.

For continuous variables, summary statistics were calculated (mean and standard deviation, and median), and where appropriate, t-tests or analysis of variance were used to determine whether differences between means were significant. For categorical variables cross-tabulations were used to obtain frequencies and percentages, and where appropriate the Chi^2 test of association was used to test whether the differences between groups in the proportions of cases with a particular characteristic was significant. For all statistical tests used to obtain a p value, 0.05 was used as the level of significance. For the occurrence of rare complications and sequelae, frequencies were listed in results tables and incidences calculated.

Trends over time

Trends over time were analysed in terms of demographic characteristics of cases and the main outcomes of interest (hospitalisation, length of hospitalisation and incidence of sequelae). Where differences in proportions were calculated, Chi^2 tests were used to test for statistical significance.

Results

ECOSS data was available for 30,196 confirmed cases of *Campylobacter* over the period 2013-2017.

Of the ECOSS totals, 30,032 (99.5%) had a CHI number assigned in the dataset and could therefore be linked to SMR01, mortality and prescribing data. Those cases not assigned a CHI number were either overseas or rest of UK (RUK) cases who had not received medical treatment in Scotland either prior to their infection or as a result of it.

Laboratory reports of *Campylobacter* in Scotland decreased in 2016 then slightly increased in 2017 (Table 1).

Table 1: Laboratory Reports of *Campylobacter* 2013-2017

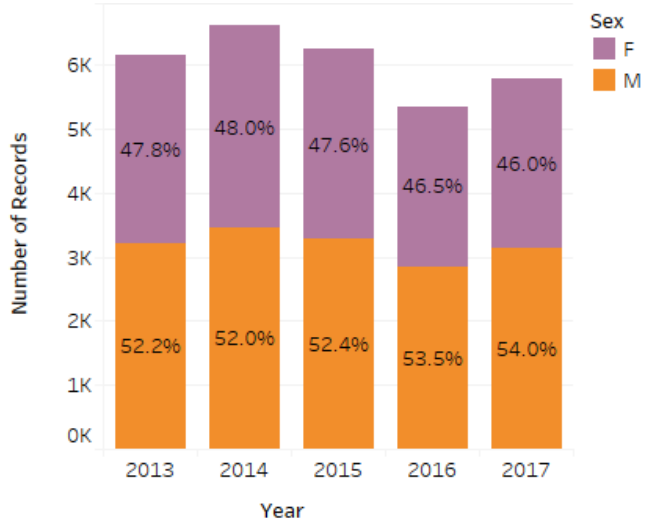
Year				
2013	2014	2015	2016	2017
6,161	6,637	6,264	5,338	5,796

Using the 2017 mid-year population estimate for Scotland of 5,424,800 this gives an average annual incidence rate of 111.3 confirmed cases of *Campylobacter* per 100,000.

Demographic characteristics of cases

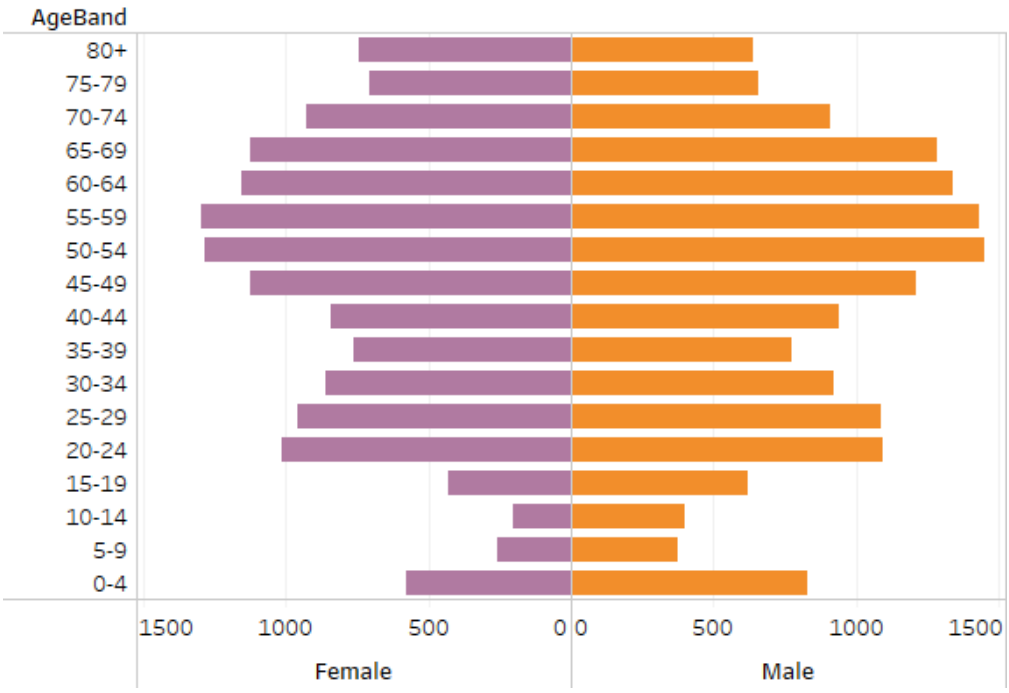
More males had a positive *Campylobacter* report than females in each of the years (Figure 1), and overall males accounted for 52.8% of laboratory confirmed cases.

Figure 1: Laboratory Reports of *Campylobacter* 2013-2017 by Sex



In each age group up to age 70 there were more male than female cases, while after age 70, females outnumbered males (Figure 2).

Figure 2: Laboratory Reports 2013 - 2017 by Age Band and Sex



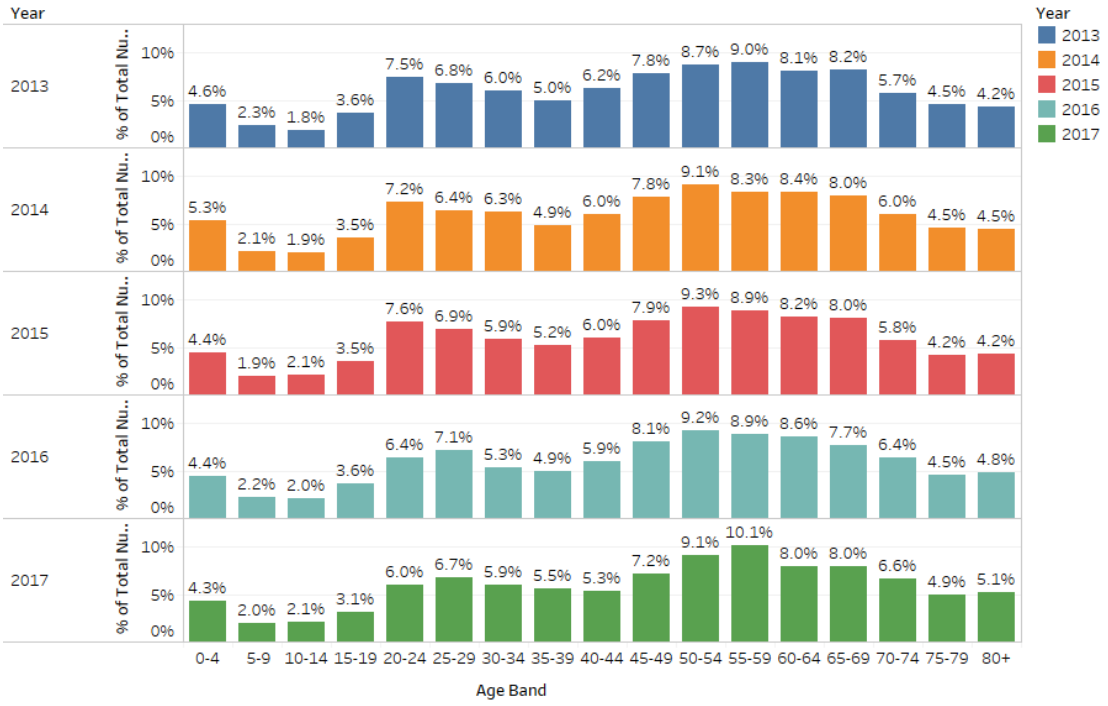
The highest percentage of cases was in the 50-54 and 55-59 age groups (Table 2).

Table 2: Percentage of Laboratory Reports of *Campylobacter* 2013 -2017 by Age Band

AgeBand	Cases	% of Total
0-4	1,402	4.6%
5-9	633	2.1%
10-14	600	2.0%
15-19	1,044	3.5%
20-24	2,109	7.0%
25-29	2,044	6.8%
30-34	1,781	5.9%
35-39	1,537	5.1%
40-44	1,781	5.9%
45-49	2,334	7.7%
50-54	2,732	9.0%
55-59	2,724	9.0%
60-64	2,489	8.2%
65-69	2,410	8.0%
70-74	1,831	6.1%
75-79	1,366	4.5%
80+	1,379	4.6%

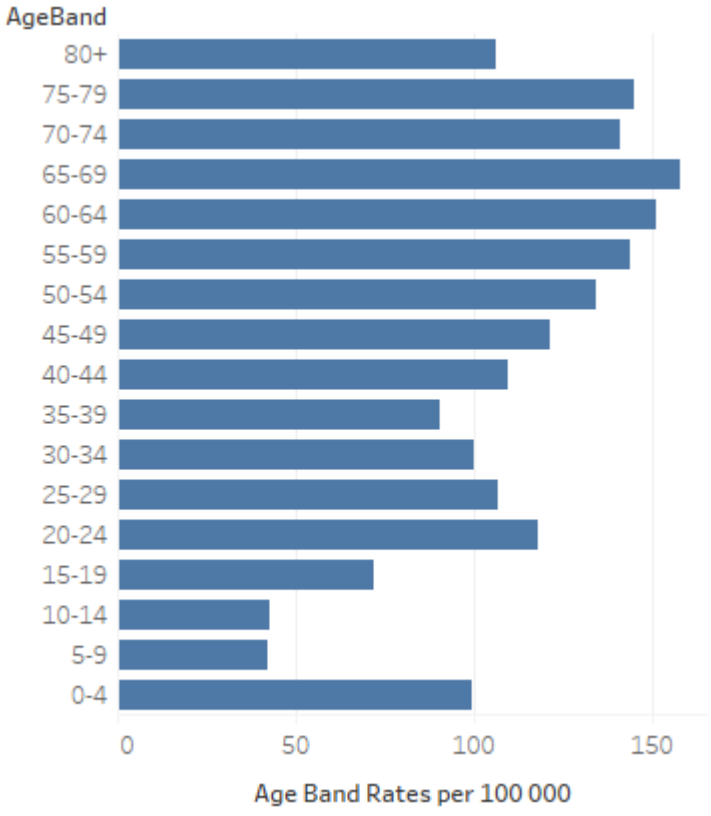
There was little variation in the proportions in each age band over the five-year period (Figure 3).

Figure 3: Laboratory Reports of *Campylobacter* by Age Band Percentage, 2013-2017



While the highest percentage of cases were in the 50-54 and 55-59 age groups, the highest incidence was in individuals in the 65-69 age group (Figure 4).

Figure 4: Laboratory Reports of *Campylobacter* per 100,000 by Age Band, 5 Year Average



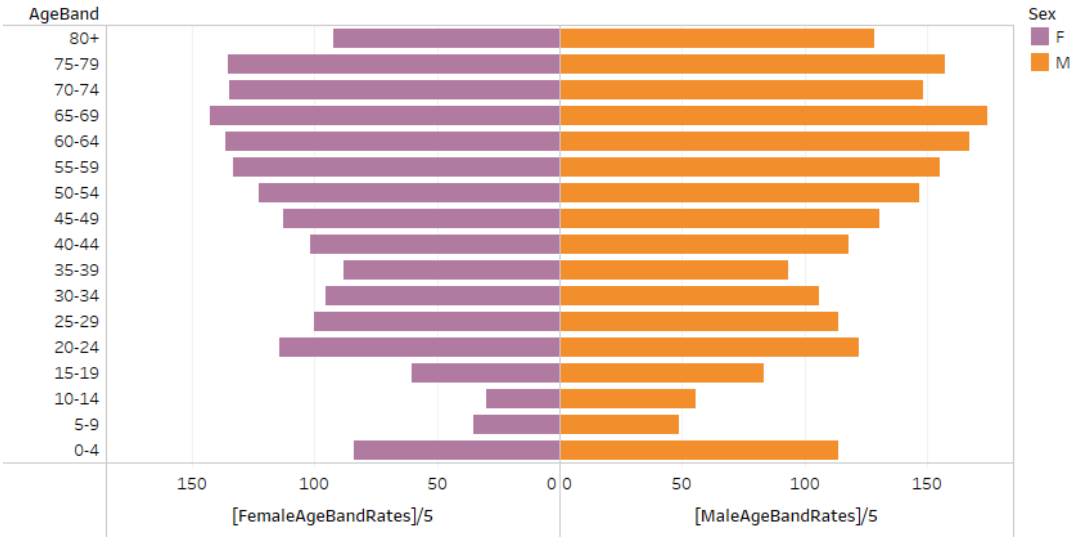
The incidence rate per 100,000 was higher in males than females.

Table 3: Rates of *Campylobacter* per 100,000 by Sex, 5 Year Average

FemaleRate	102.4
MaleRate	120.7

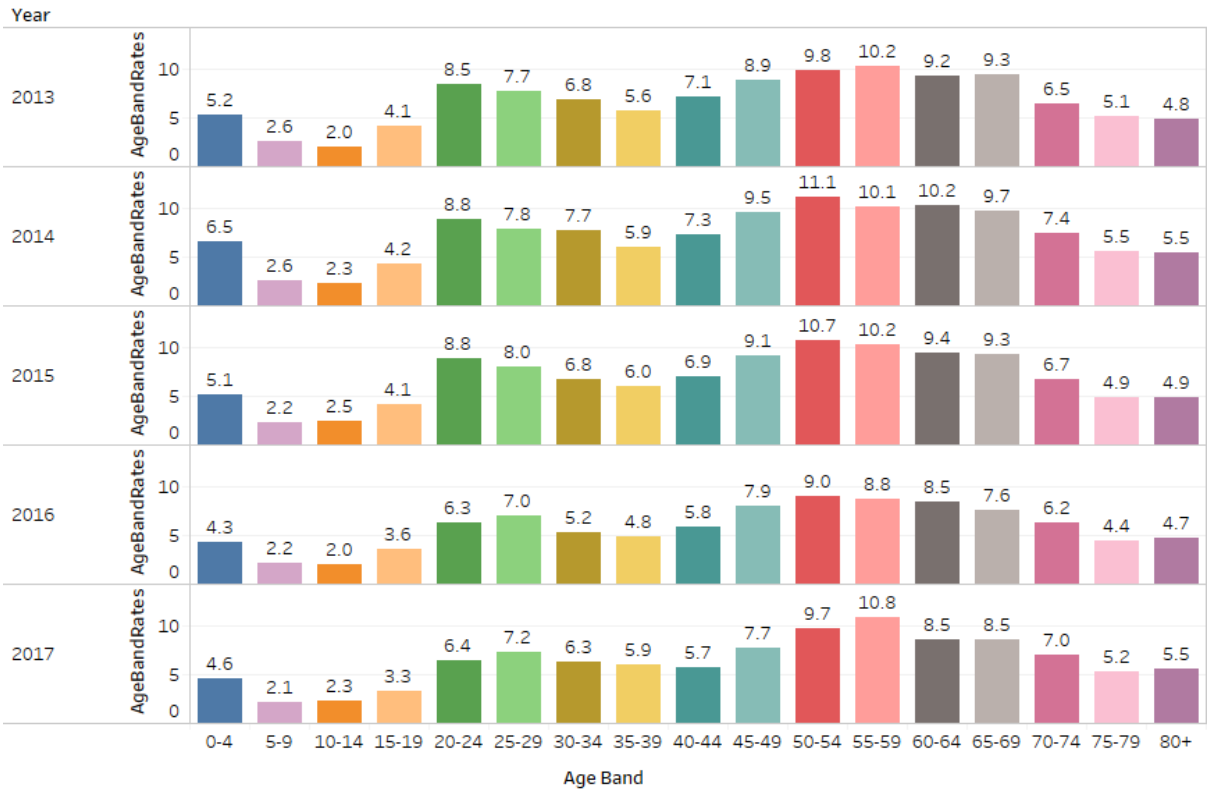
In every age group the incidence rate was also higher in males than in females (Figure 5), despite actual number of laboratory reports being greater among female than males in some of the older age bands.

Figure 5: Rates of *Campylobacter* per 100,000 by Age Band and Sex, 5 Year Average



There was little variation in the rates in each age band over the five-year period (Figure 6).

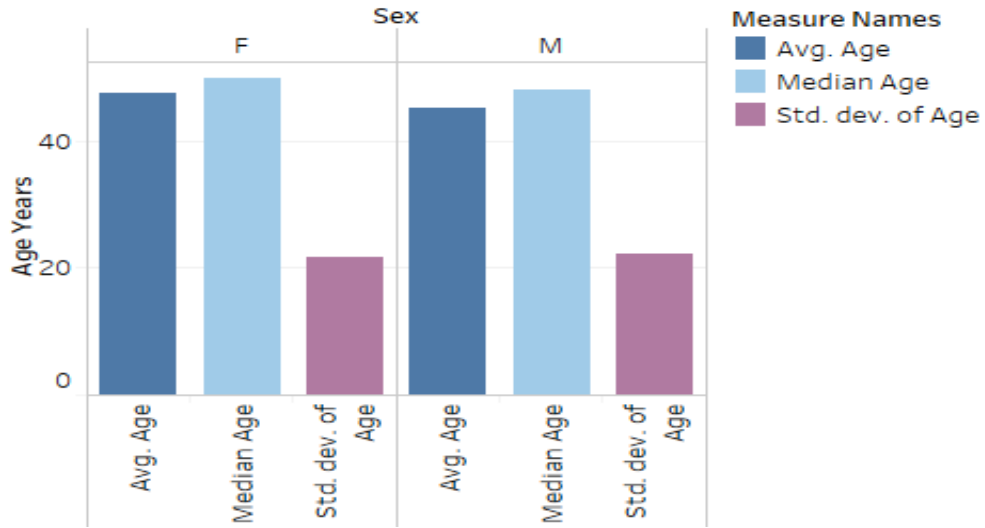
Figure 6: Rates per 100,000 by Year and Age Band



The mean age was 46.2 years, median age 49 with a range of 0-100 (Figure 7). When the dataset was stratified by sex, the mean age for male cases was 45.3 (SD 22), with a median of 48. For female cases, the mean age was slightly higher at 47.4 (SD 21.6), with a median age of 50.

A t-test showed the difference in mean age by sex was significant ($p < 0.001$).

Figure 7: Laboratory Reports of *Campylobacter*, Mean and Median Age by Sex



The distribution of *Campylobacter* cases by locality (Table 4) was roughly the same as the Scottish population as a whole (data from National Records Scotland).

Locality information was missing for 205 (0.7%) cases.

Percentages are valid for the number of cases for whom deprivation and locality information was available.

Table 4: Laboratory Reports of *Campylobacter* by Locality

UrbanRural	Cases	% of Total Records	Scottish population % resident in locality
LargeUrbanAreas	10,072	33.6%	34.6%
OtherUrbanAreas	10,409	34.7%	34.5%
AccessibleSmallTowns	2,811	9.4%	9.1%
RemoteSmallTowns	978	3.3%	3.3%
AccessibleRuralAreas	3,875	12.9%	12.3%
RemoteRuralAreas	1,826	6.1%	6.1%

When stratified by deprivation category (Table 5) the less deprived categories reported a higher proportion of *Campylobacter* laboratory reports than more deprived areas (Quintile 1 is most deprived and 5 is least).

Table 5: Laboratory Reports of *Campylobacter* by Deprivation Category, 2013-2017

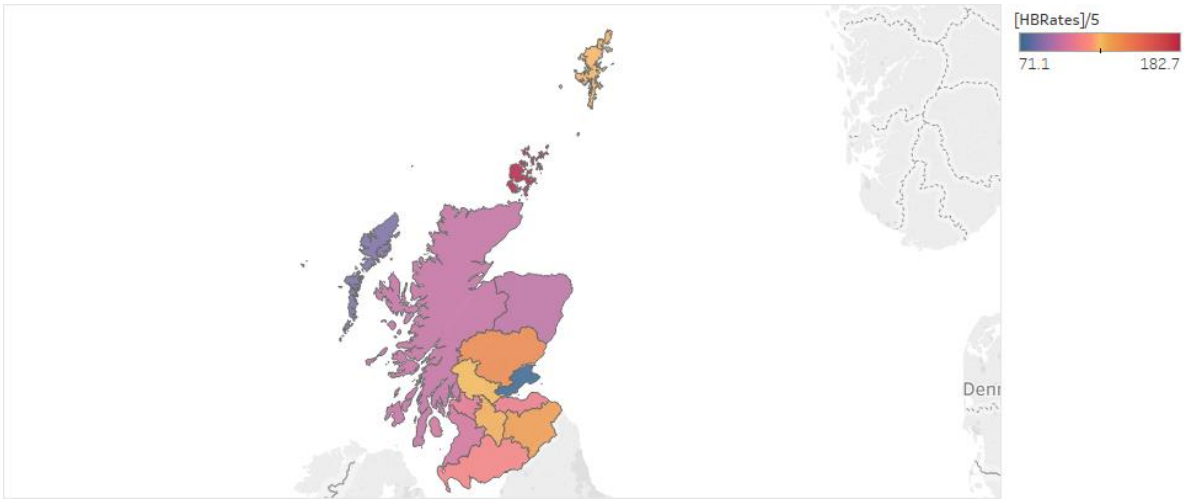
SIMDQuintile	Cases	%
1	5,086	17.0%
2	5,828	19.4%
3	6,037	20.1%
4	6,553	21.9%
5	6,467	21.6%

There is year on year variation in the rates across the mainland NHS Boards (Table 6), but it is of note that in some boards in particular Fife (FF) rates were consistently well below the average, while in others including Tayside (TY) rates were consistently above the average. The yearly rates for the Island NHS boards should be viewed with caution due to the small population size.

Table 6: *Campylobacter* Rates per 100,000 by Health Board and Year, 2013-2017

	Year				
Health Board	2013	2014	2015	2016	2017
AA	131.5	106.6	102.3	83.2	87.5
BR	106.1	124.3	137.4	135.6	173.9
DG	113.9	144.1	122.7	94.5	97.2
FF	80.2	75.1	69.5	70.3	60.6
FV	134.5	142.7	132.2	98.5	132.5
GC	100.5	116.3	115.6	96.8	110.5
GR	134.6	112.7	81.3	76.9	79.0
HG	103.7	103.7	93.8	87.3	104.0
LN	112.6	144.8	139.9	123.4	132.5
LO	112.5	121.3	124.0	97.6	98.4
OR	140.9	240.9	240.9	86.4	204.5
SH	73.7	151.6	199.3	86.7	117.0
TY	134.6	160.8	147.3	134.3	136.5
WI	89.1	92.8	55.7	107.6	74.2
Scotland	113.6	122.3	115.5	98.4	106.8

Figure 8: *Campylobacter* Rates per 100,000 by Health Board, 5 Year Average Map



Hospitalisation

The proportion of confirmed *Campylobacter* cases hospitalised for their infection was 14.0% (4193 individuals over the 5-year period). These figures refer to hospitalisations attributable to the *Campylobacter* infection, using ICD 10 codes, in the 14 days before or after the laboratory sample date, not to cases hospitalised around the time period but for reasons other than infection and where symptoms of infection were not recorded. This includes cases hospitalised and discharged on same day.

The proportion of cases admitted to hospital and discharged on same day was 9.8%, and 12.6% for those admitted and kept in for at least one overnight stay.

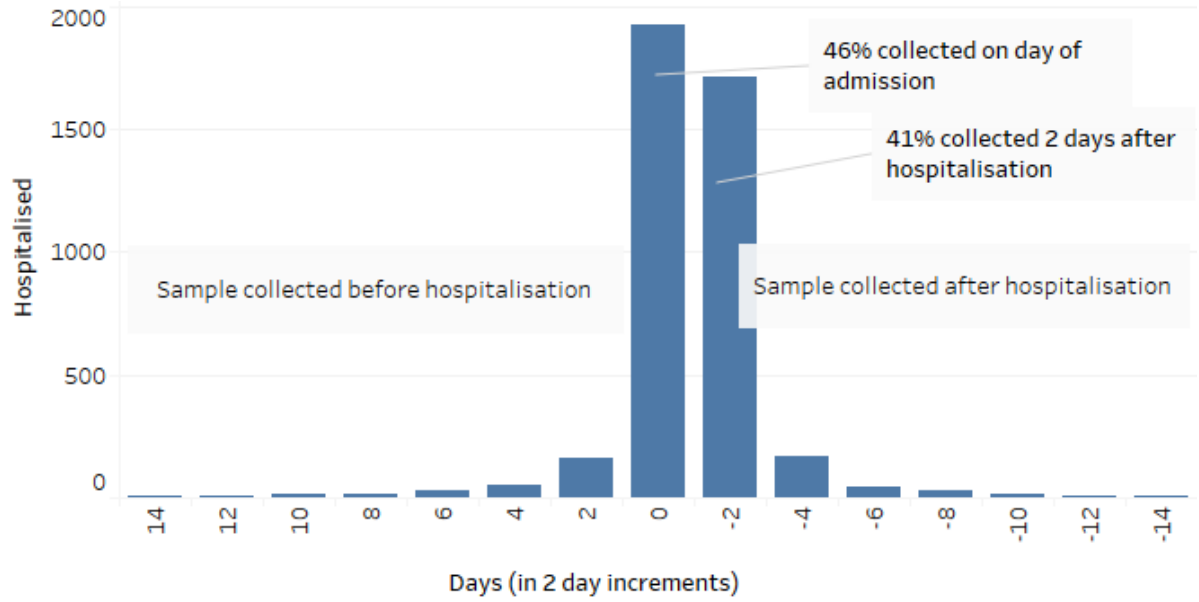
There was some annual variation in the percentage of cases hospitalised, with a low of 13.3% in 2013 to 14.9% in 2017 (Table 7). Each successive year the percentage hospitalised either stayed the same or increased, but never decreased.

Table 7: Percentage of *Campylobacter* Cases Hospitalised, 2013-2017

Year	Cases	Hospitalisations	Hosp%
2013	6,116	816	13.3
2014	6,576	897	13.6
2015	6,216	847	13.6
2016	5,306	779	14.7
2017	5,750	854	14.9
Grand Total	29,964	4,193	14.0

Nearly 90% of cases admitted to hospital had a positive laboratory specimen for *Campylobacter* taken within two days of admission (Figure 9).

Figure 9: Time Difference from Specimen Date to Hospitalisation



The proportion of females hospitalised was slightly higher than the proportion of males (Table 8). The difference in proportion of males and females hospitalised was not significantly different.

Table 8: Percentage of *Campylobacter* Cases Hospitalised by Sex

Sex	Cases	Hospitalisations	Hosp%
F	14,180	2,008	14.2
M	15,784	2,185	13.8
Grand Total	29,964	4,193	14.0

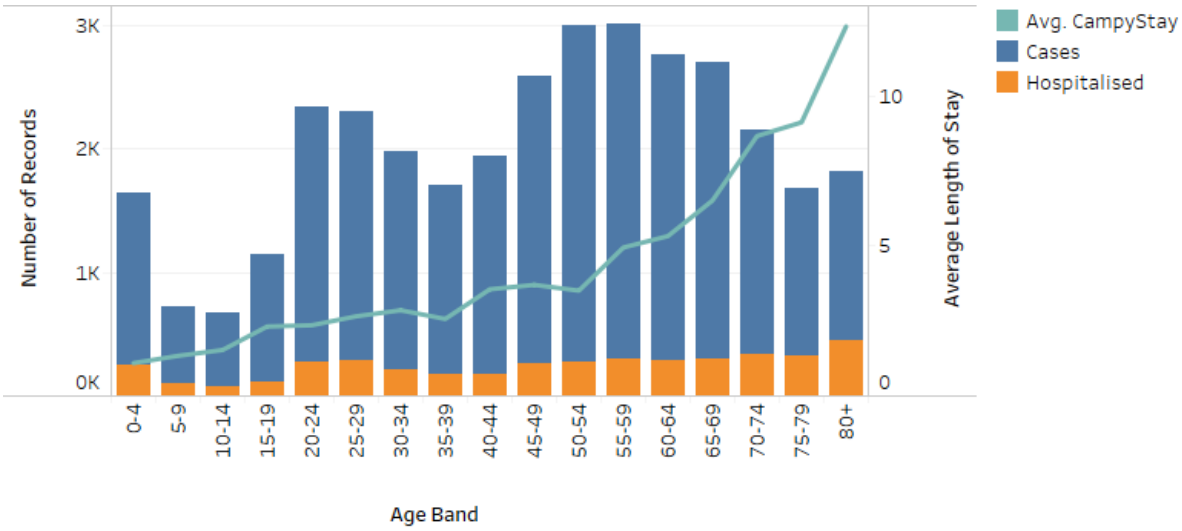
Table 9 shows that the highest hospitalisation rates were observed in young children and those 70 years and over. The hospitalisation rate among cases aged 80 years and over was more than twice that of middle- aged adults.

Table 9: Percentage of *Campylobacter* Cases Hospitalised by Age Band

AgeBand	Cases	Hosp	Hosp%
0-4	1,390	252	18.1
5-9	628	94	15.0
10-14	596	71	11.9
15-19	1,031	113	11.0
20-24	2,061	278	13.5
25-29	2,015	290	14.4
30-34	1,758	215	12.2
35-39	1,530	177	11.6
40-44	1,772	168	9.5
45-49	2,324	266	11.4
50-54	2,723	274	10.1
55-59	2,711	298	11.0
60-64	2,475	288	11.6
65-69	2,400	304	12.7
70-74	1,819	336	18.5
75-79	1,359	320	23.5
80+	1,372	449	32.7
Grand Total	29,964	4,193	14.0

Among those cases that were hospitalised, the mean length of stay increased with age.

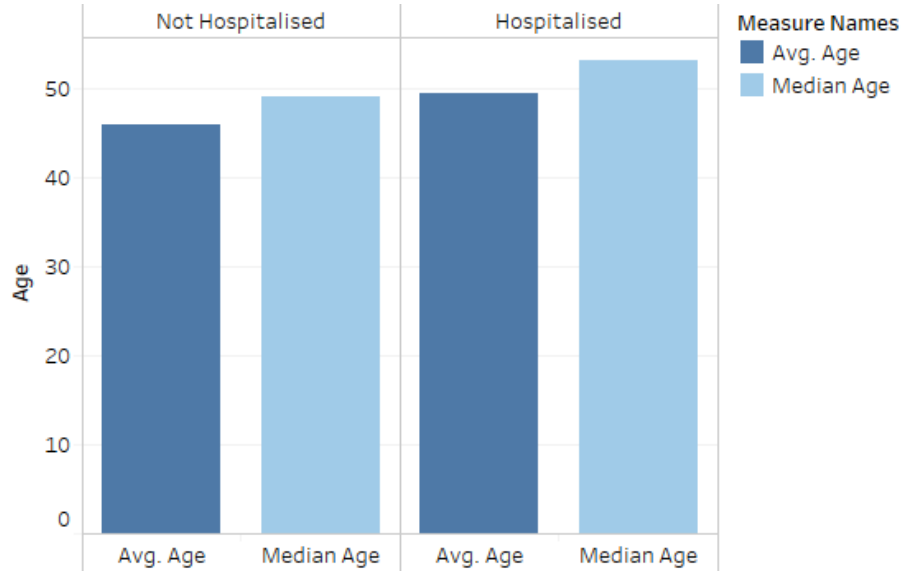
Figure 10: *Campylobacter* Laboratory Results and Hospitalisation by Age Band and Mean Length of Stay, 2013-2017



The mean age for cases hospitalised (49.4 years) was higher than the mean age for cases not hospitalised (45.9 years) (Figure 11).

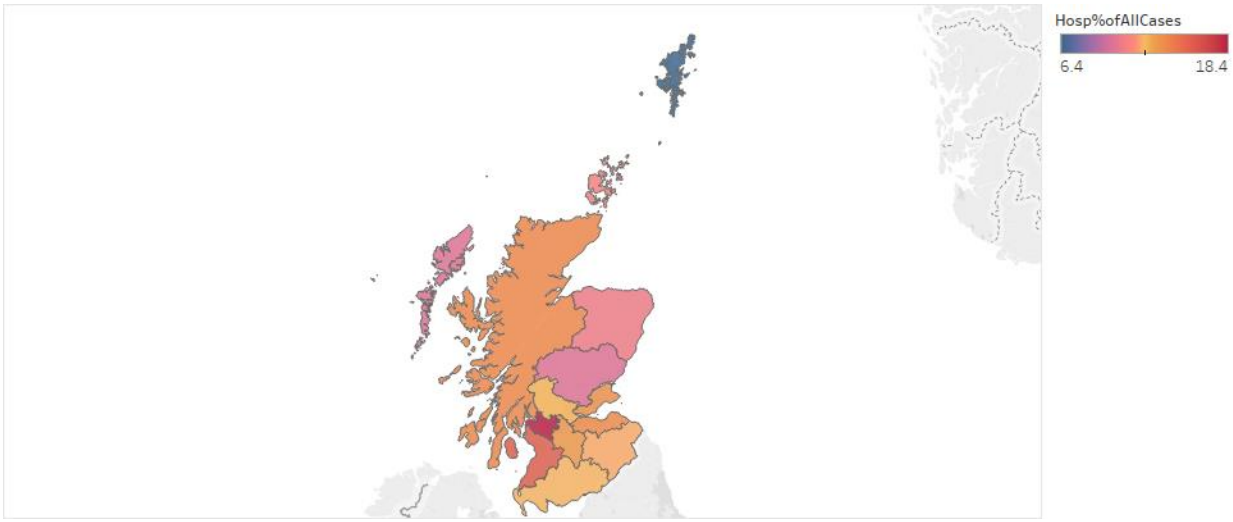
A t-test on the difference in mean age for those hospitalised and not hospitalised showed that the difference was significant (P<0.001).

Figure 11: Mean and Median Age of Hospitalised and Non-Hospitalised Cases of *Campylobacter*, 2013-2017



The difference in proportion hospitalised by Health Board was significant (p<0.001), with a substantially higher proportion of cases hospitalised in Greater Glasgow and Clyde (18.4%) than the lowest mainland board of Tayside (10.1%) (Table 10).

Figure 12: Percentage of Health Board Cases Hospitalised



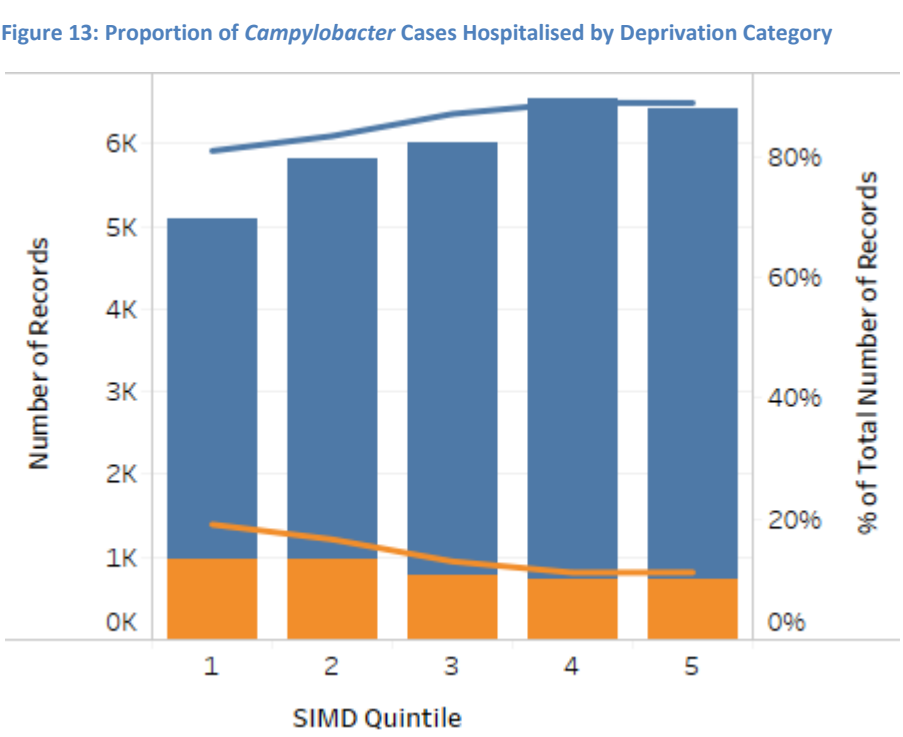
Hospitalisation rates in the mainland NHS Board ranged from 19.9 per 100,000 in Greater Glasgow and Clyde to 9.7 per 100,000 in Fife. Due to relatively small numbers the hospitalisation rate for the Island boards should be viewed with caution.

Table 10: Hospitalisation Rates per 100 000 by Health Board, 5 Year Average

Health Board	Rate
AA	16.1
BR	16.3
DG	13.9
FF	9.7
FV	16.1
GC	19.9
GR	10.4
HG	13.4
LN	17.4
LO	15.2
OR	20.0
SH	7.8
TY	14.4
WI	8.2

The proportion of cases hospitalised due to their *Campylobacter* infection increased with deprivation.

Figure 13: Proportion of *Campylobacter* Cases Hospitalised by Deprivation Category



Proportion of laboratory reports (blue line) greater in less deprived category but proportions hospitalised (orange line) greater in more deprived categories.

The Odds Ratios for deprivation categories and hospitalisation (1 is most deprived and 5 is least deprived), shows decreasing risk of hospitalisation among laboratory confirmed cases with decreasing deprivation. SIMD1 was used as the reference.

It is of note that whilst the incidence of *Campylobacter* is higher in the least deprived areas compared to the most deprived (Figure 13) among those who are confirmed with *Campylobacter*,

the risk of hospitalisation is significantly less in the least deprived areas compared to the most deprived (Figure 14).

Figure 14: Odds Ratio for Hospitalisation and Deprivation

Analysis For Linear Trends In Proportions

SIMD	Hospitalised	Not Hospitalised	Odds Ratio
1	907	4179	1.000
2	898	4930	0.839
3	727	5310	0.631
4	674	5879	0.528
5	685	5782	0.546

Chi Square for linear trend (Extended Mantel-Haenszel)	191.23100
p value	0

A higher proportion of urban cases were hospitalised than those in rural localities (Table 11).

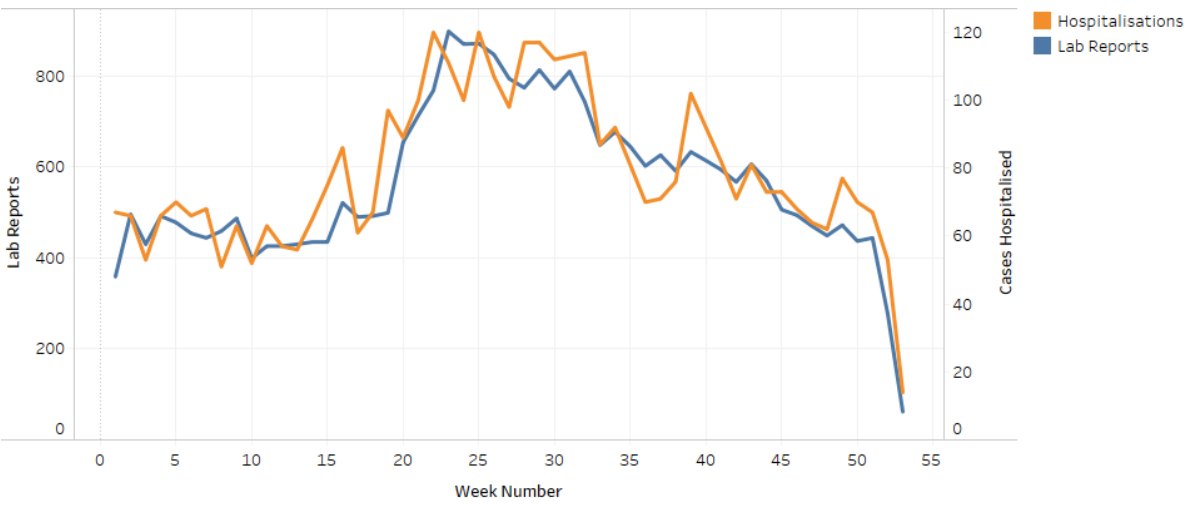
A Chi^2 test showed the difference in proportions hospitalised between urban/rural localities was significant (P value <0.001).

Table 11: Hospitalisation Percentage by Locality

UrbanRural	Cases	Hospitalisation..	Hosp%
LargeUrbanAreas	10,029	1,623	16.2
OtherUrbanAreas	10,390	1,435	13.8
AccessibleSmallTowns	2,805	353	12.6
RemoteSmallTowns	971	119	12.3
AccessibleRuralAreas	3,864	427	11.1
RemoteRuralAreas	1,808	201	11.1

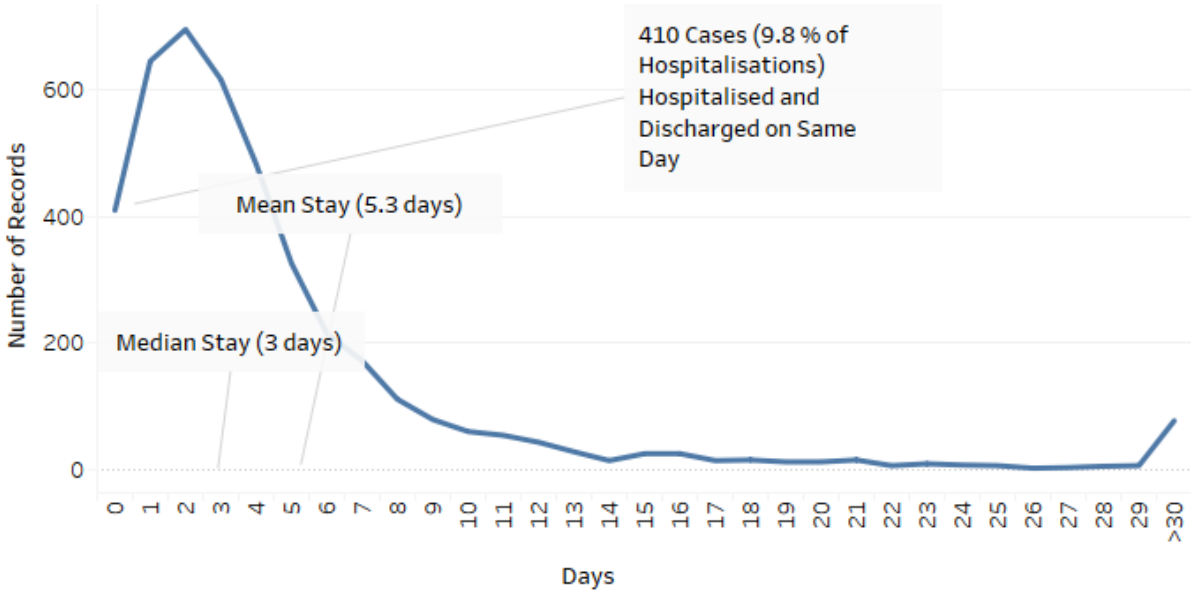
Laboratory reports and hospitalisations generally follow the same seasonal pattern (Figure 15), with a small spike in hospitalisations around week 40 that is not seen in the number of laboratory reports. Some years have a reporting week 53 which is shown in Figure 15.

Figure 15: Laboratory Reports and Cases Hospitalised by Week Number, 2013-2017



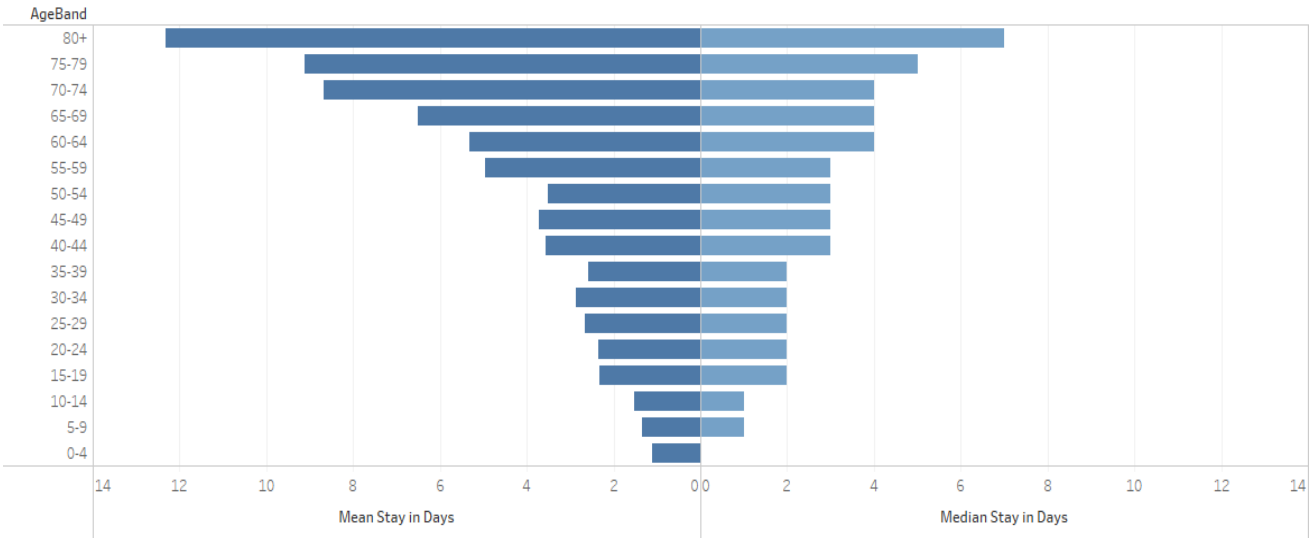
Just under 10% of hospitalised cases were admitted to hospital then discharged on the same day (Figure 16). The characteristics of these cases are described in the Same Day Discharge Characteristics chapter on page 36.

Figure 16: Length of Stay for Hospitalisations for a *Campylobacter* Related Condition



Among those cases hospitalised, mean length of stay increased with age (Figure 17).

Figure 17: Mean and Median Length of Stay by Age Band



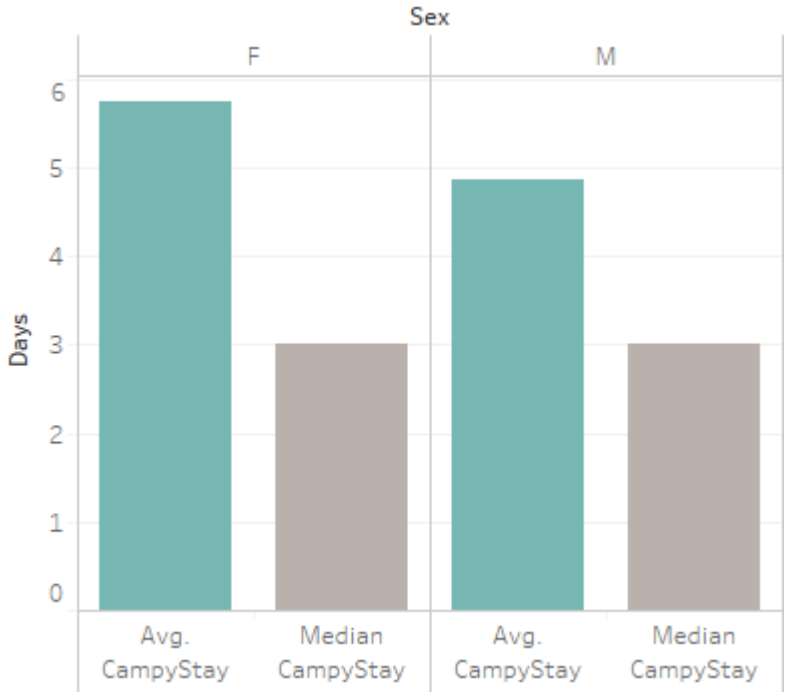
Mean duration of hospitalisation (Figure 18) was longer for females (5.7) than for males (4.9), although the median was the same for both sexes (Range 0 to 275).

The mean duration of stay was greatly influenced by 136 cases who had a hospital stay in excess of 20 days. Of these 136 cases 121 were in the 65 and over broad age group.

Whilst it is likely that conditions other than *Campylobacter* were contributing to these extended stays and therefore overestimating the hospitalisation burden due to *Campylobacter*, they have not been excluded from the outputs other than a couple of alternative analytical outputs in this chapter which are clearly labelled, to show the impact of including and excluding hospital stays of longer than 20 days.

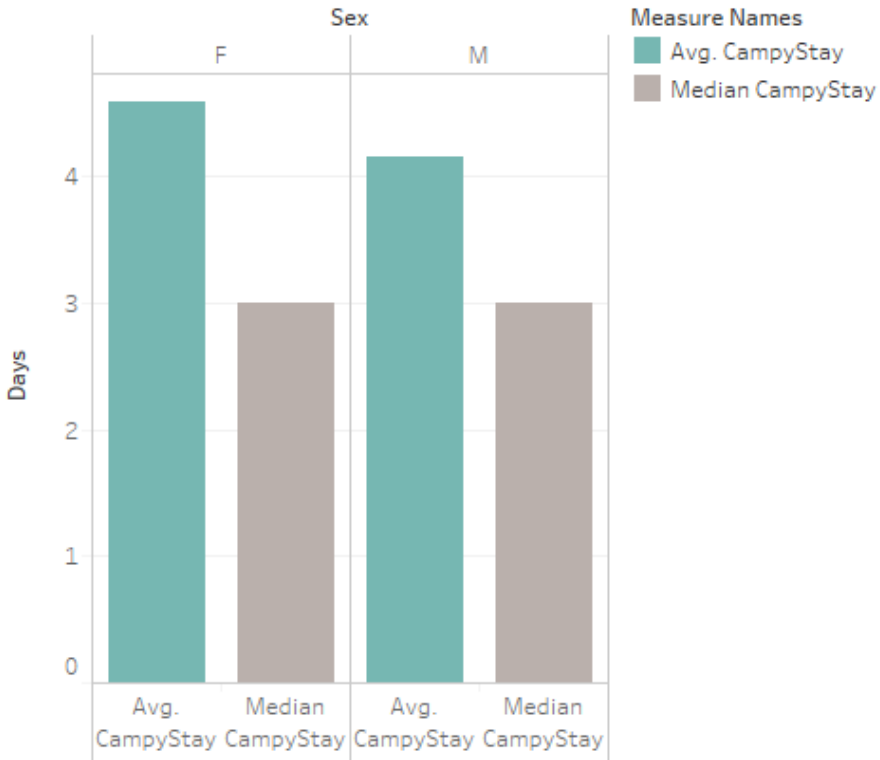
The results of a t-test on all hospitalisations for a *Campylobacter* related condition showed that the difference in mean duration of stay by sex was significant, with a p value=0.038

Figure 18: Mean & Median Length of Stay by Sex



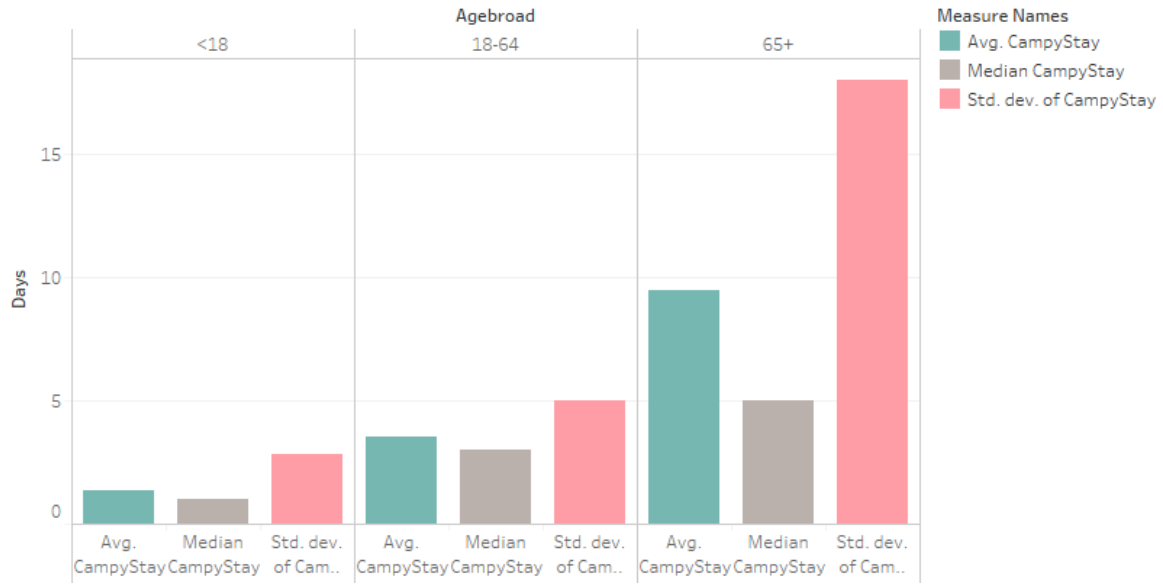
When the t-test was repeated excluding hospitalisations for a *Campylobacter* related condition of greater than 20 days (Figure 19), it showed that the difference in mean duration of stay by sex was not significant.

Figure 19: Mean & Median Length of Stay by Sex, Excluding Stay of >20 Days



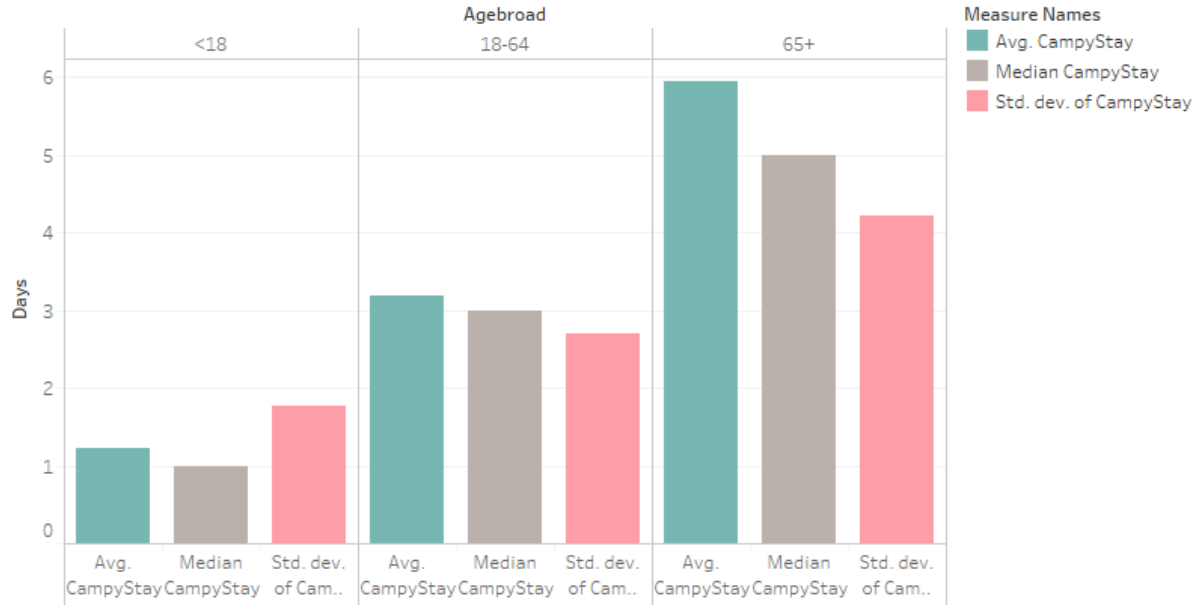
The difference in increasing mean stay from youngest to oldest broad age band (Figure 20) is significant (p value <0.001).

Figure 20: Mean and Median Stay by Broad Age Band



When the ANOVA test was repeated excluding stays of greater than 20 days, the difference in increasing mean stay between broad age bands (Figure 21) remained significant (p value <0.001).

Figure 21: Mean and Median Stay by Broad Age Band, Excluding Stay >20 Days



There was very little difference in mean stay length between SIMD quintiles, with no overall trend (Table 12), whilst the median stay of 3 days is consistent across all quintiles.

The difference in mean length of stay between SIMD quintiles was not significant. Therefore, whilst there was as previously noted (Figure 13) a significant trend for hospitalisation by SIMD, among the cases who were admitted to hospital there was no significant difference in duration of stay.

Table 12: Mean and Median Length of Stay by Deprivation Category

SIMDQuintile	Avg. CampyStay	Median CampyStay	Std. dev. of CampyStay
1	5.4	3.0	12.2
2	5.7	3.0	13.2
3	4.8	3.0	9.5
4	5.7	3.0	13.6
5	4.9	3.0	7.7

The difference in mean length of stay between urban/rural localities was not significant and the median stay of 3 days remained constant.

Table 13: Mean and Median Length of Stay by Locality

UrbanRural	Avg. CampyStay	Median CampyStay
LargeUrbanAreas	5.8	3.0
OtherUrbanAreas	4.8	3.0
AccessibleSmallTowns	5.2	3.0
RemoteSmallTowns	4.4	3.0
AccessibleRuralAreas	5.1	3.0
RemoteRuralAreas	5.8	3.0

The hospitalisation rate for cases with no underlying condition detected in SMR01 or prescribing data was 11.2%. For those with an underlying condition identified in prescribing data but which did not require a hospital admission in the 12 months prior to the *Campylobacter* infection the rate was 14.2%. Among cases who had one or more of the pre-defined underlying medical conditions requiring hospitalisation in the previous 12 months the hospitalisation rate was 43.2%.

Table 14 categorises those with no predisposing conditions, those with predisposing conditions indicated in prescribing data only and those where predisposing conditions were indicated in hospital admissions.

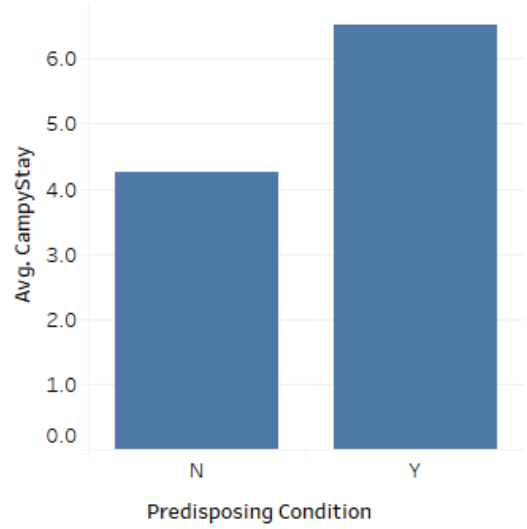
Table 14: Percentage of Hospitalised *Campylobacter* Cases by Underlying Condition Status

Predisposing	Cases	Hospitalisations	Hosp%
NoPredis	20,183	2,258	11.2
PredisMedOnly	7,897	1,121	14.2
PredisHosp	1,884	814	43.2

The following outputs were based on a combined indicator of underlying conditions using both prescribing and SMR01 data.

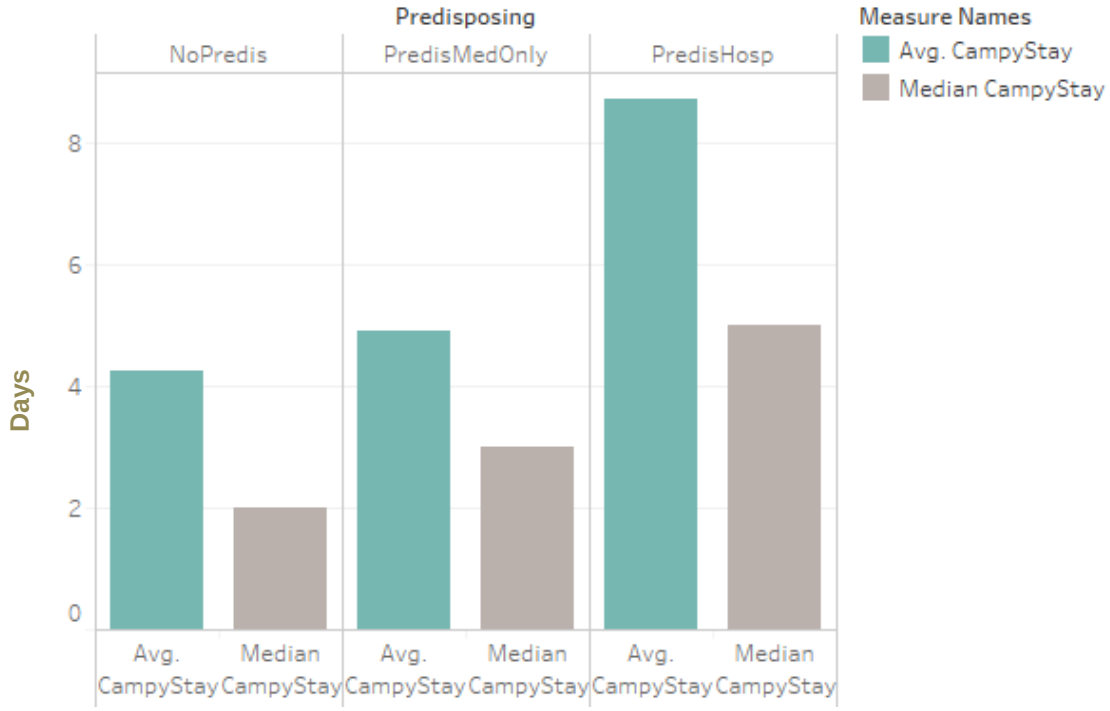
The average stay was higher (6.5 days) for those with a predisposing condition than those who did not have a predisposing condition (4.2 days).

Figure 22: Mean Stay for Those With and Without an Underlying Condition



When broken down by category of predisposing condition (Figure 23), those with a predisposing condition requiring hospitalisation had a mean stay of 8.7 days, which is much longer than the 4.9 day mean stay for those with a predisposing condition requiring medication only. This, in turn, is much closer to the mean stay of 4.2 days for those where no predisposing condition was recorded in either SMR01 or prescribing data.

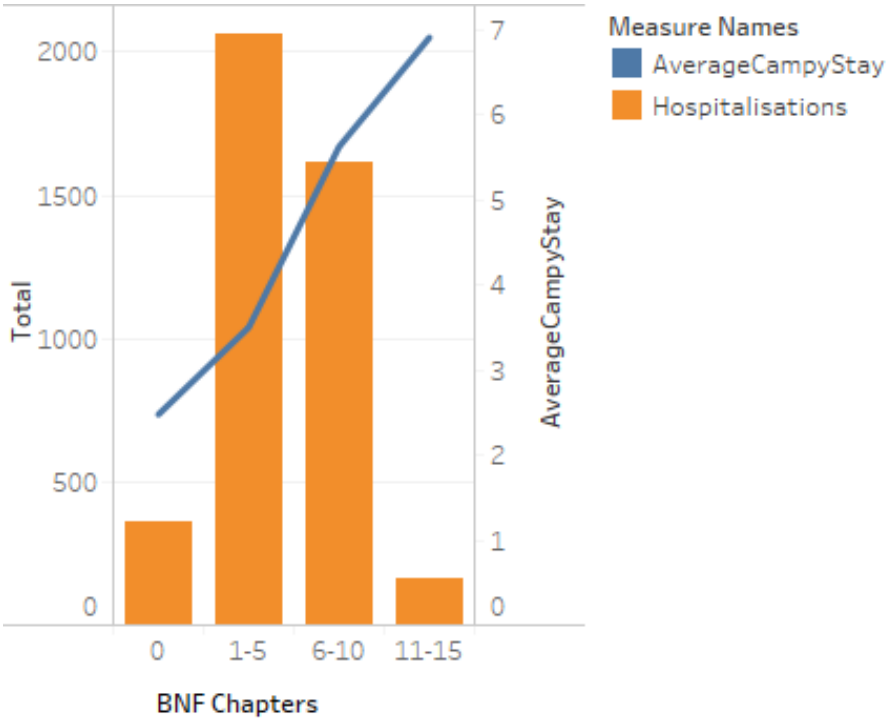
Figure 23: Mean Stay for Those With and Without Underlying Conditions by Category



The number of unique BNF chapters prescribed in the 12 months prior to infection were categorised and used as an indication of comorbidity (each chapter was only counted once, although there may have been multiple prescriptions within individual chapters).

Among the hospitalised cases the mean length of stay increased with number of BNF chapters from which prescriptions were recorded over the 12 months prior to infection. Those with no prescriptions in the 12 months prior to their *Campylobacter* specimen date had a mean hospital stay of 2.6 days (Figure 24) compared with 10.5 days for those with prescriptions from 11 or more BNF chapters.

Figure 24: BNF Chapters Prescribed and Mean Stay

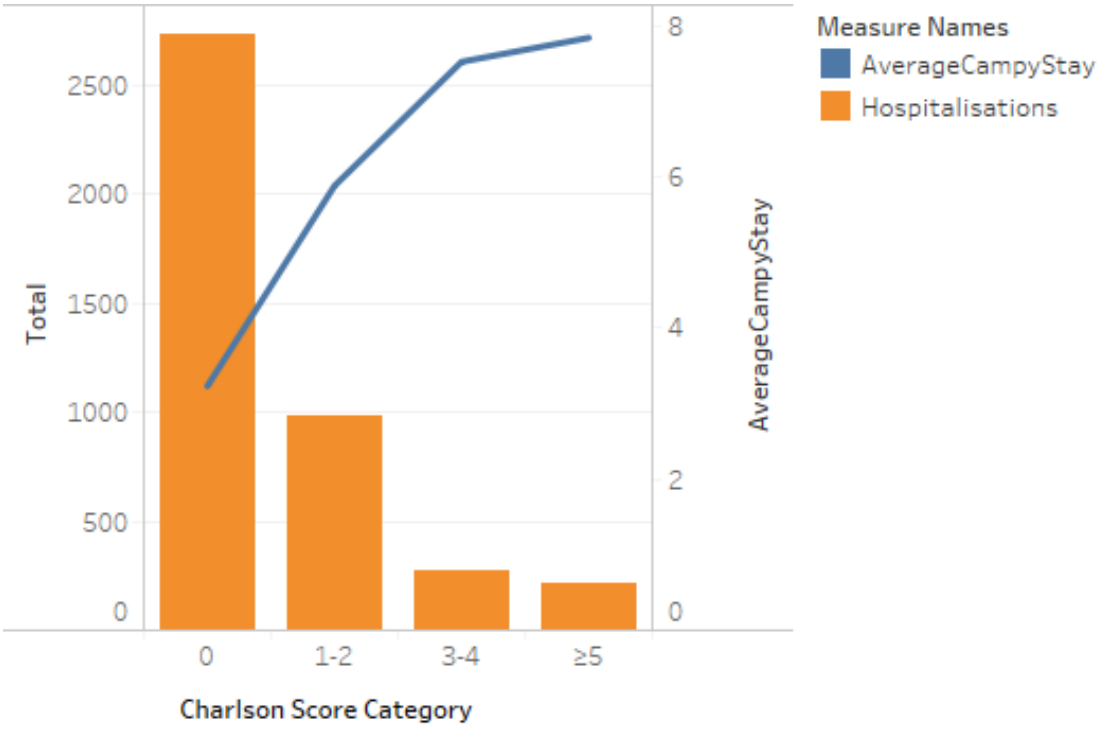


The Charlson Comorbidity Index (CCI) predicts the one-year mortality for a patient who may have a range of comorbid conditions, such as heart disease, AIDS, or cancer (a total of 22 conditions).

Each condition is assigned a score. The higher the score the greater comorbidity.

As with the trends seen with the BNF chapters (Figure 24) a similar trend is seen among hospitalised cases by Charlson score (Figure 25). Those with a Charlson score of 0 had a mean hospital stay of 3.6 days, whilst those with a score of 1-2 had a mean stay of 7.7 days, compared with 9.4 days for those with a score or 3-4 and 10.9 days for those with a score of 5 or higher.

Figure 25: Charlson Score and Mean Stay



When looking at hospitalisations and Charlson score (Table 15) the proportion being admitted to hospital for their *Campylobacter* infection rose from 10.7% in those with no score to 46.3% in those with a score of 5 or more.

Table 15: Hospitalisation Status and Charlson Score

Hospcamp T	CharlsonScore..	Cases	% of Total Number of..
Not Hospitalised	0	22,742	89.3%
	1-2	2,352	70.6%
	3-4	433	61.4%
	≥5	244	53.7%
Hospitalised	0	2,733	10.7%
	1-2	978	29.4%
	3-4	272	38.6%
	≥5	210	46.3%

Same Day Discharge Characteristics

The 410 (1.4% of confirmed cases and 9.8% of those hospitalised) cases who were not kept in hospital overnight were considerably younger on average than those who were kept in, with a mean age of 24.3 (SD 23.6) compared to 52.4 (SD 23.3) for those hospitalised for at least one night (p value <0.001). This compares with a mean age of 45.9 for *Campylobacter* cases who were not hospitalised for a *Campylobacter* related condition.

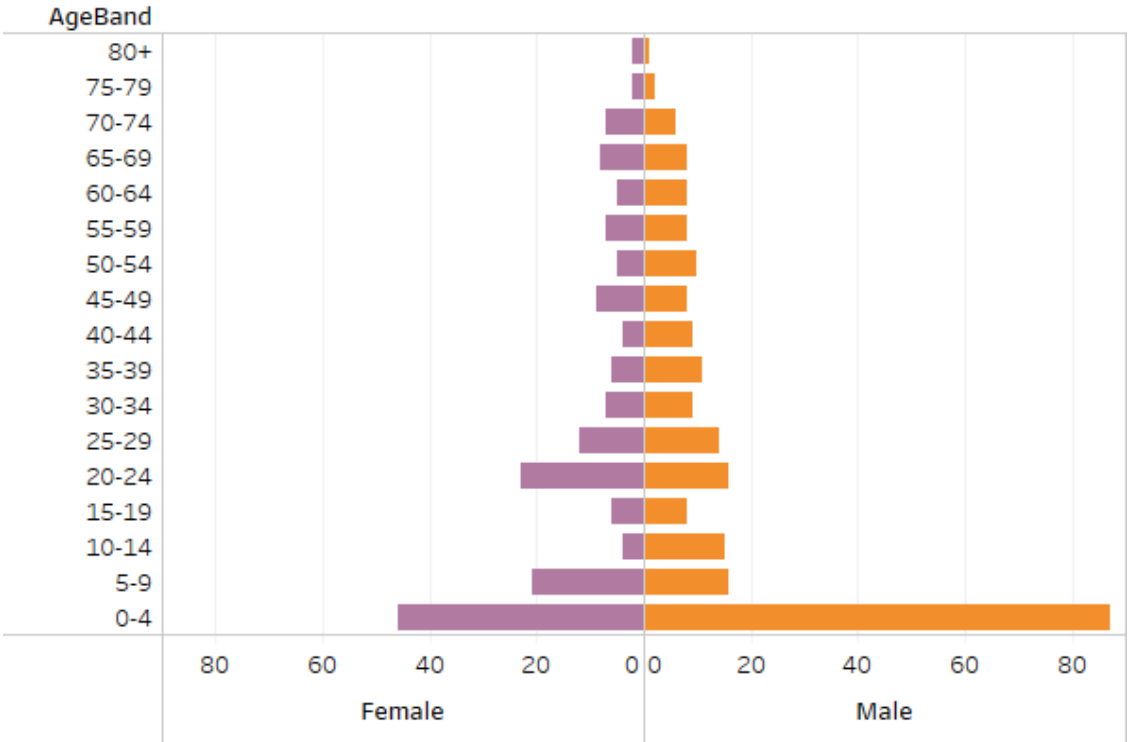
There was some variation in the proportion of cases admitted and discharged on the same day, with a low of 7.6% in 2013 and a high of 11.9% in 2014 but no overall trend (Table 16).

Table 16: Percentage of Hospital Admissions Discharged Same Day, by Year

Year	SameDayDis..	Same Day Dis %
2013	61	7.6
2014	106	11.9
2015	86	10.2
2016	82	10.6
2017	72	8.5
Grand Total	407	9.8

There was no statistical significance in the proportion of males and females discharged on same day.

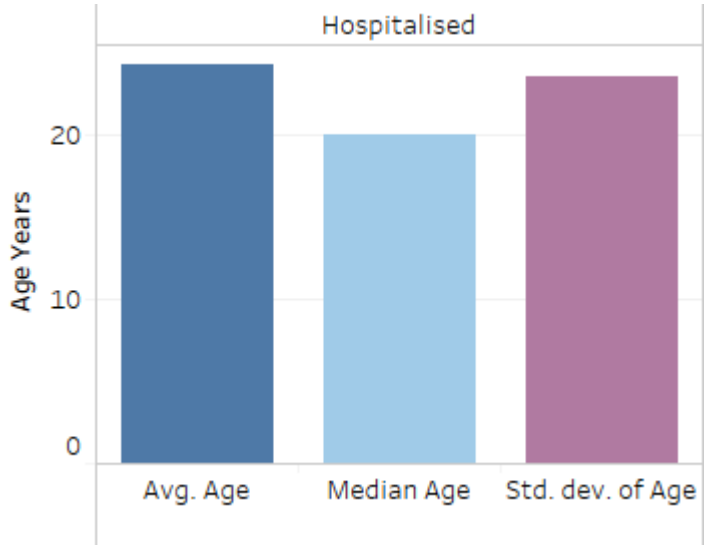
Figure 26: Same Day Hospital Discharge by Age Band and Sex



As shown in Figure 26 same day admission and discharge was most frequent in the youngest age group, in this group the 133 cases with same day admission and discharge accounted for 52.8% of all cases hospitalised in this age group.

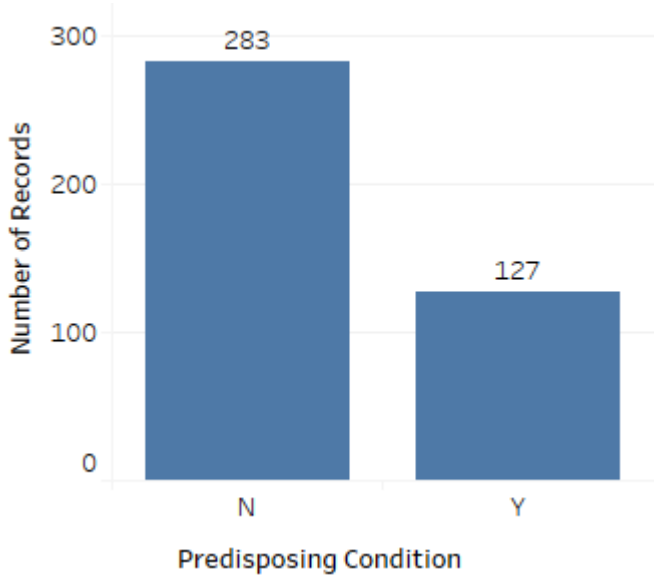
The median age of those not kept in overnight was 20 (Figure 27), while for those who were kept in it was 55. The median age for those not hospitalised for a *Campylobacter* related condition was 49.

Figure 27: Same Day Discharge Age, Mean and Median



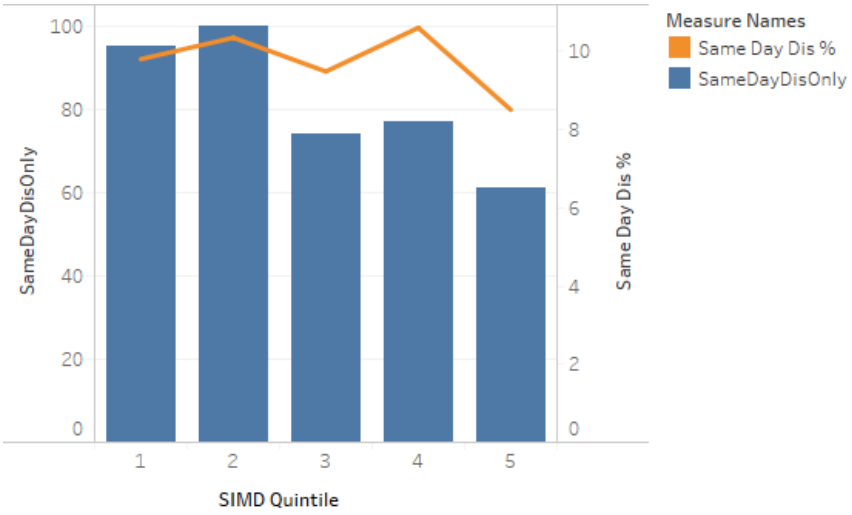
Among the cases hospitalised but not kept overnight 69.1% (Figure 28) did not have a predisposing condition (indicated in either hospitalisation or prescribing data) while 30.9% did have a predisposing condition. This compares with 47.8% of cases kept overnight who had a predisposing condition. This difference was significant with a p value <0.001.

Figure 28: Same Day Discharge Cases with Predisposing Conditions



There was some difference according to deprivation with more cases in more deprived areas being admitted to hospital and discharged on same day than those in less deprived areas (Figure 29), but this difference was not significant.

Figure 29: Percentage of Same Day Discharge Cases by Deprivation Category



Long Stay Characteristics

A total of 438 cases (1.5% of confirmed cases and 10.4% of hospitalised cases) were kept in hospital for 10 nights or more. It is possible that for those cases their extended stay was due to factors other than their *Campylobacter* infection.

A higher proportion of females than males had a long stay in hospital (Table 17) but this difference was not statistically significant.

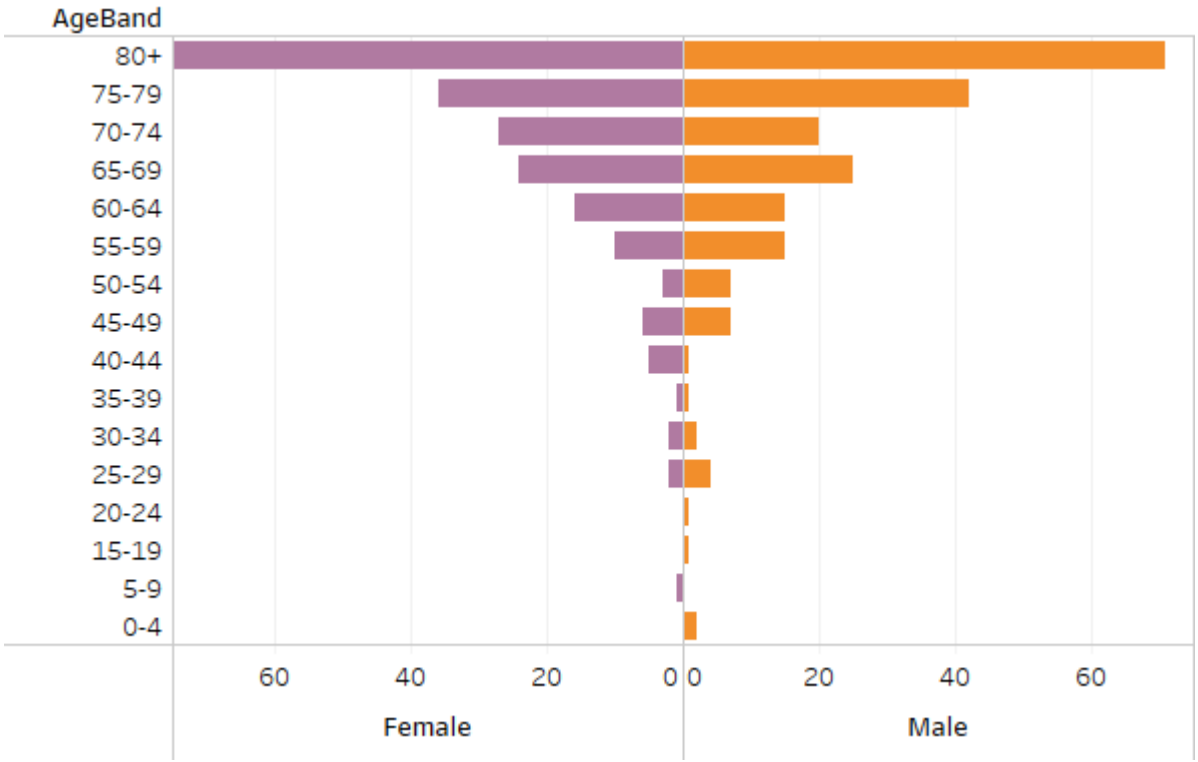
Table 17: Long Stay, Percentage by Sex

Sex	Cases	Hospitalis..	Hosp%	LongStay	LongStay%
F	14,180	2,008	14.2	224	11.2
M	15,784	2,185	13.8	214	9.8
Grand Total	29,964	4,193	14.0	438	10.4

Long stay cases increased with each 5-year age band over 55-59 (Figure 30*).

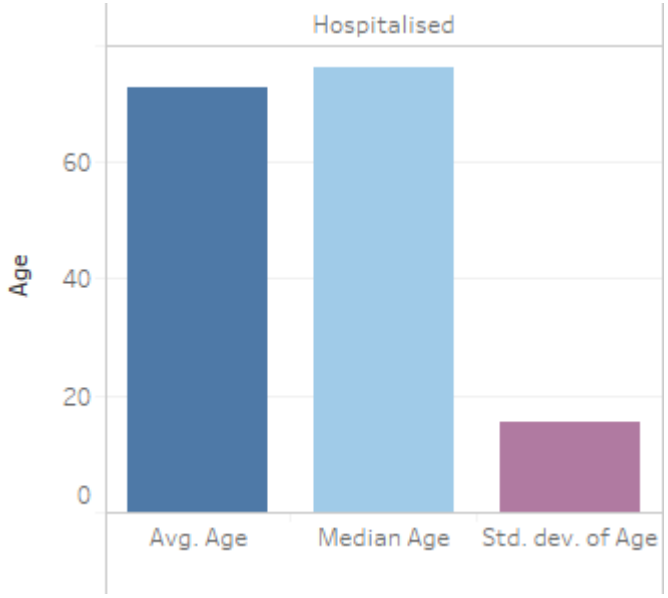
*No cases in 10-14 age-band had a long stay

Figure 30: Long Stay Cases Age Band and Sex



The mean age of long stay (10 days or more) cases was 72.5 (SD 15.5), with the median being 76.

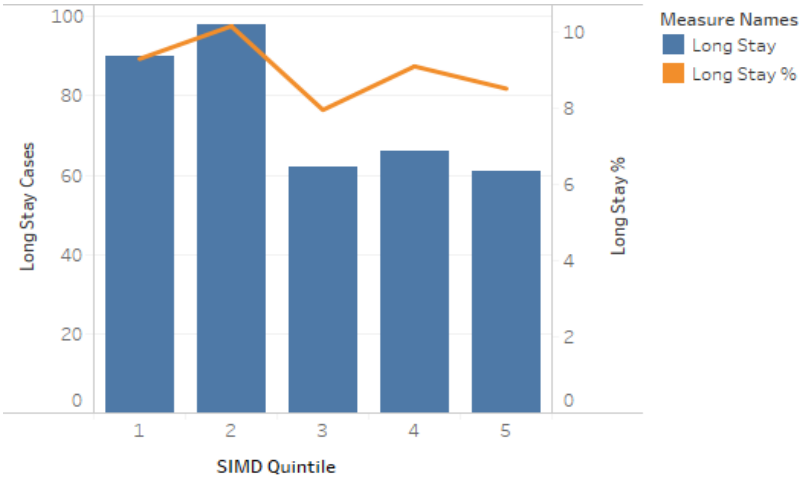
Figure 31: Long Stay Cases Mean and Median Age



A total of 171 (39%) long stay cases had a predisposing condition indicated in hospital and/or prescribing data and 117 (26.7%) had a stay in a Geriatric Ward.

There was no particular pattern in the proportion of long stay cases and deprivation with 9.3% in the most deprived category and 8.5% in the least deprived (Figure 32).

Figure 32: Percentage of Long Stay Cases by Deprivation



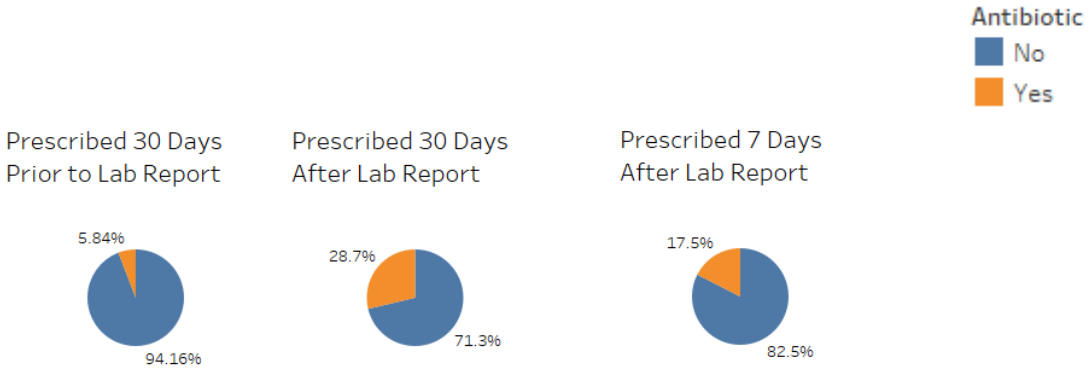
Antibiotic Prescribing

A total of 5.8% of *Campylobacter* cases were prescribed an antibiotic in the 30 days prior to their laboratory report (Figure 33) and increased to just under 29% in the 30 days subsequent to lab report. Of those, 17.5% were prescribed within 7 days of laboratory report. A total of 665 cases were prescribed an antibiotic in the 30 days prior to lab result and also in the 30 days after lab result.

From the available data it was not possible to ascertain whether antibiotics were prescribed in response to *Campylobacter* infection, therefore all results relating to clinical outcomes following antibiotic use should be considered as associations rather than cause and effect.

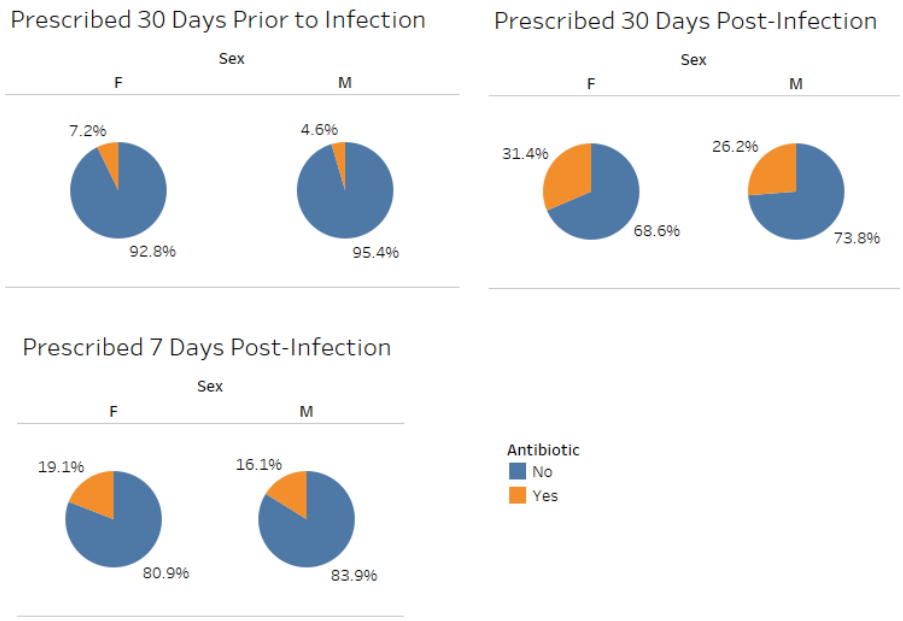
Figures detailing the percentage of the Scottish population as a whole who were prescribed antibiotics each month were not available but the proportion of the Scottish population that received at least one course of antibiotics was 28.3% in 2017 compared to 31.5% in 2013 (https://hpspubsrepo.blob.core.windows.net/hps-website/nss/2647/documents/1_SONAAR-report-2017-revised-november-2019.pdf).

Figure 33: Antibiotic Prescribing Proportions Pre and Post Lab Report



The proportion of antibiotic prescribing pre and post-infection was consistently higher in females than males (Figure 34). A chi square test showed this difference was statistically significant with a p value <0.001.

Figure 34: Antibiotic Prescribing Proportions Pre and Post Lab Report by Sex



A greater proportion of cases living in the most deprived areas were prescribed antibiotics (Table 18, Table 19) in the 30 days pre (7.1% vs 4.8%) and post infection (31.5% vs 28.2%) than those in the least deprived areas. The difference between areas within 7 days of infection (Table 20) wasn't as great (18.7% vs 17.3%). The difference in proportions categorised by deprivation in cases prescribed antibiotics either 30 days before laboratory report specimen date or 30 days after report is significant, with a p value <0.001.

A study by Covvey JR[42] et al found patients in Scotland in the most deprived SIMD quintile had an overall antibiotic prescription rate that was 36.5% higher than those in the least deprived quintile; in our data this difference was greater with 47.9% more cases in SIMD 1 prescribed an antibiotic 30 days prior to their specimen date compared to cases in SIMD 5, the least deprived area.

Table 18: Prescribed Antibiotic in 30 Days Pre-Specimen Date SIMD %

	SIMDQuintile				
Antibiotic..	1	2	3	4	5
No	4,715	5,452	5,670	6,159	6,125
	92.9%	93.8%	94.3%	94.3%	95.2%
Yes	363	361	345	370	307
	7.1%	6.2%	5.7%	5.7%	4.8%

Table 19: Prescribed Antibiotic in 30 Days Post-Specimen Date, SIMD %

	SIMDQuintile				
Antibiotic..	1	2	3	4	5
No	3,479	4,059	4,346	4,782	4,615
	68.5%	69.8%	72.3%	73.2%	71.8%
Yes	1,599	1,754	1,669	1,747	1,817
	31.5%	30.2%	27.7%	26.8%	28.2%

Table 20: Prescribed Antibiotic in 7 Days Post-Specimen Date, SIMD %

	SIMDQuintile				
AntiB7Day..	1	2	3	4	5
No	4,129	4,778	4,987	5,415	5,321
	81.3%	82.2%	82.9%	82.9%	82.7%
Yes	949	1,035	1,028	1,114	1,111
	18.7%	17.8%	17.1%	17.1%	17.3%

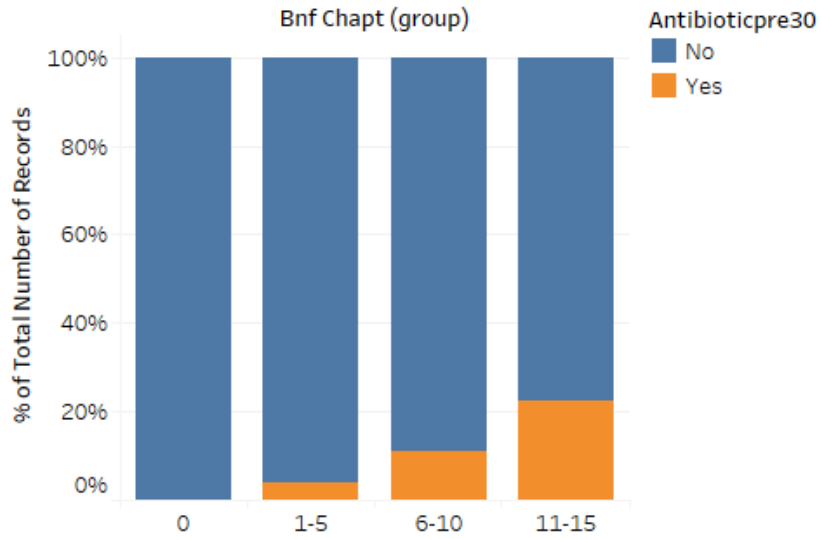
The most frequently prescribed antibiotics in the seven days subsequent to the specimen date were macrolides (Table 21). This class of antibiotics is often used to treat common bacterial infections. This suggests that many of these antibiotics may have been used to treat the *Campylobacter* infection given they were prescribed so close to the specimen date.

Table 21: Top 5 Antibiotics Prescribed 7 Days Post-Specimen Date

Antib7DaysList	
Clarithromycin	39.4%
Erythromycin	34.7%
Ciprofloxacin	21.5%
Trimethoprim	2.5%
Amoxicillin	1.9%

The higher the number of comorbidities the more likelihood there was of being prescribed an antibiotic. Among those with prescriptions of between 11-15 BNF chapters in the 12 months preceding specimen date, 22.6% had been prescribed an antibiotic in the 30 days prior to their specimen date compared with 4.1% for those with prescriptions from 1-5 BNF chapters (Figure 35).

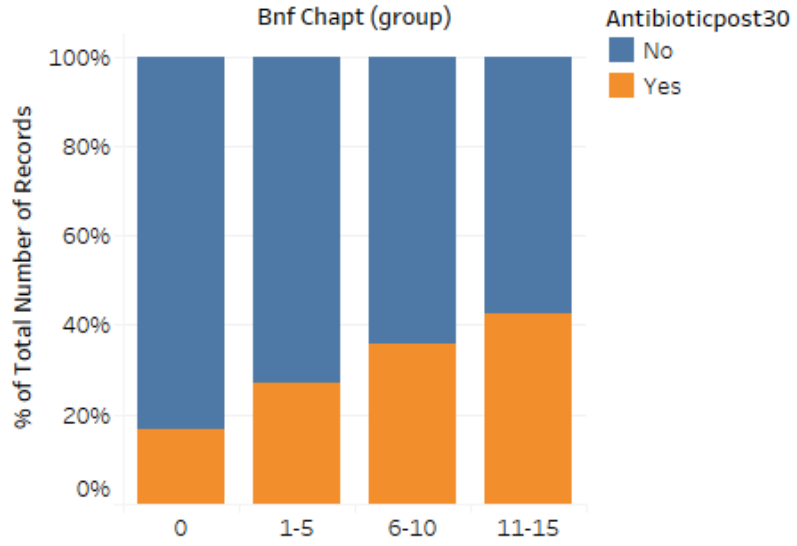
Figure 35: Percentage of Cases Taking Antibiotics in 30 days Prior to Specimen Date, by number of BNF Chapters Prescribed



A similar trend was observed with respect to antibiotics in the 30 days post *Campylobacter* report, with 16.7% of those with no previous BNF chapter prescriptions being prescribed an antibiotic in the 30 days subsequent to specimen date, compared with 42.4% of those who had been prescribed from

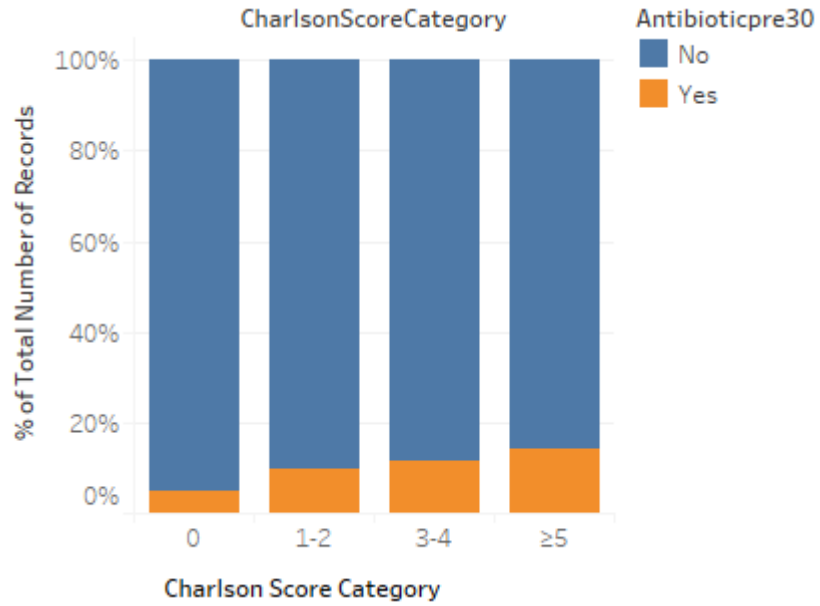
the most chapters (11-15) in the 12 months preceding their positive laboratory specimen date (Figure 36).

Figure 36: Percentage of Cases Taking Antibiotics in 30 days Post-Specimen Date, by Number of BNF Chapters Prescribed



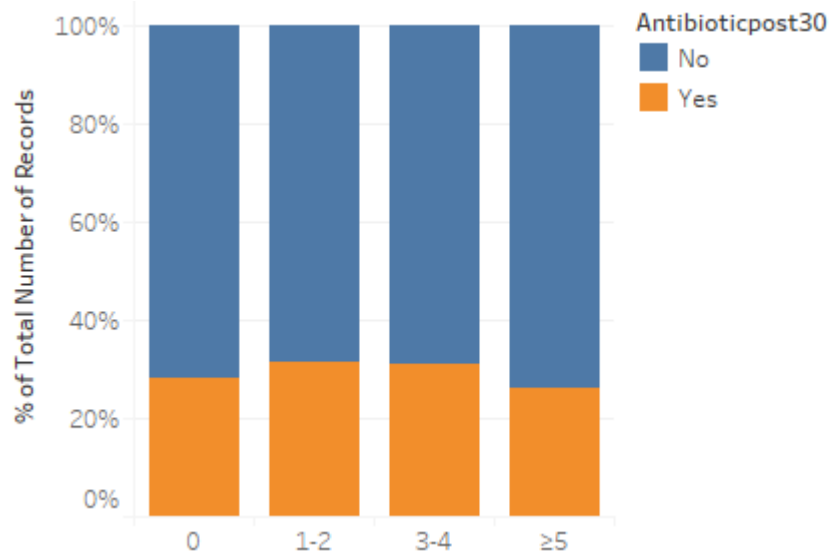
A similar pattern was observed using the Charlson Comorbidity Index (CCI) as an indicator of comorbidity for those prescribed an antibiotic in the 30 days prior to infection, with 5% of *Campylobacter* cases with no CCI score prescribed an antibiotic compared with 14.1% of those with a score of 5 or more (Figure 37).

Figure 37: Percentage of Cases Taking Antibiotics in 30 days Prior to Specimen Date, by Charlson Score



This pattern was not the same for those prescribed an antibiotic in the 30 days after their specimen date with a more even distribution of prescribing proportions ranging from 28.3% in those with no Charlson score to 26% in those with a Charlson score of five or higher (Figure 38).

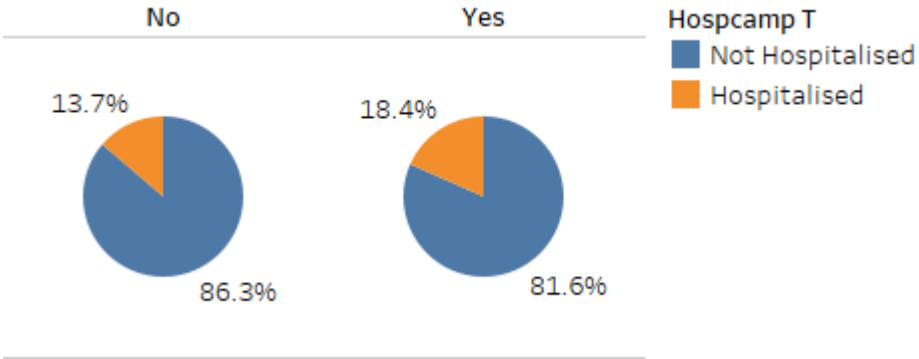
Figure 38: Percentage of Cases Taking Antibiotics in 30 days Post-Specimen Date, by Charlson Score



A higher proportion of cases who were prescribed antibiotics in the community in the 30 days prior to their laboratory report were hospitalised than those who did not have an antibiotic prescribed (Figure 39).

A higher proportion of cases prescribed antibiotics pre or post-infection (combined field) were hospitalised than those not prescribed antibiotics. A chi-square test showed this difference was signifcant (p<.001). As described above, those with the greatest number of comorbidities as defined both by the number of BNF chapters and Charlson score had a higher rate of antibiotic use 30 days pre and post *Campylobacter* report, and therefore this association of higher hospitalisation among those prescribed antibiotics is likely to be confounded by their underlying health status and therefore should be viewed with caution.

Figure 39: Hospitalisation % For Cases Prescribed Antibiotics 30 Days Pre-Specimen Date



Proton Pump Inhibitor Prescribing

A total of 34% of cases were prescribed protein pump inhibitors (PPI) in the 90 days preceding their positive specimen date (Table 22). This compares with a figure of 18.4% for use of prescription PPIs in the Scottish population as a whole in 2015, based on data obtained from ISD.

PPIs were the most commonly prescribed item in Scotland in 2015 with a total of 3.47 million dispensed. A study in England in 2018[43] estimated 40% of elderly (over 60 years old) adults were prescribed PPIs.

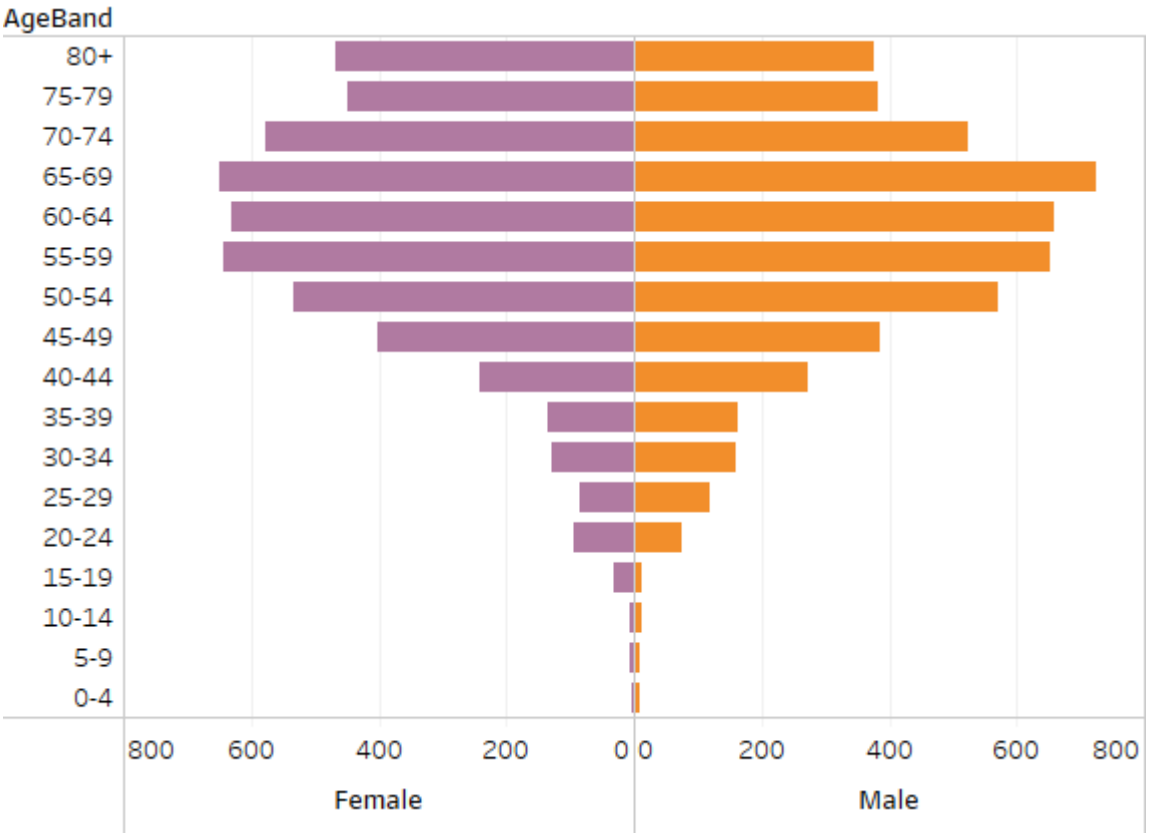
These figures do not include the use of PPIs available for purchase without a prescription, therefore their use cannot be captured as part of the analysis.

Table 22: PPI % Use 90 Days Pre Specimen Date

PPIpre90	Cases	% of Total ..
No	19,759	65.9%
Yes	10,205	34.1%

Use of prescription PPIs was higher among females (39.6%) compared to males (34.7%) (Figure 40); this difference in proportions was significant ($p<0.001$). PPI use was rare in young cases (1.3% for the 0-4 year olds), increasing steadily with age up until the 75-79 age group where use was 65.3%, while in the oldest cases usage was 63.4%.

Figure 40: PPI Use 90 Days Prior to Specimen Date, 2013-2017 by Age Band and Sex



A higher proportion of cases were prescribed a PPI in the 90 days prior to infection in more deprived areas, with 38.9% prescribed PPI in the most deprived areas compared to 29.5% in the least deprived areas (Table 23).

This difference was statistically significant.

Table 23: PPI Use 90 Days Pre Specimen Date and Deprivation

PPIpre90	SIMDQuintile	Cases	% of Total ..
No	1	3,103	61.1%
	2	3,589	61.7%
	3	4,033	67.0%
	4	4,416	67.6%
	5	4,532	70.5%
Yes	1	1,975	38.9%
	2	2,224	38.3%
	3	1,982	33.0%
	4	2,113	32.4%
	5	1,900	29.5%

Hospitalisation rates were higher (Table 24) among PPI users (18.2%) compared with non-PPI users (11.8%). This difference was statistically significant.

Table 24: PPI Use 90 Days Pre-Specimen Date, Hospitalisation Percentage

PPIpre90	Cases	Hospit..	Hosp%
No	19,759	2,336	11.8
Yes	10,205	1,857	18.2

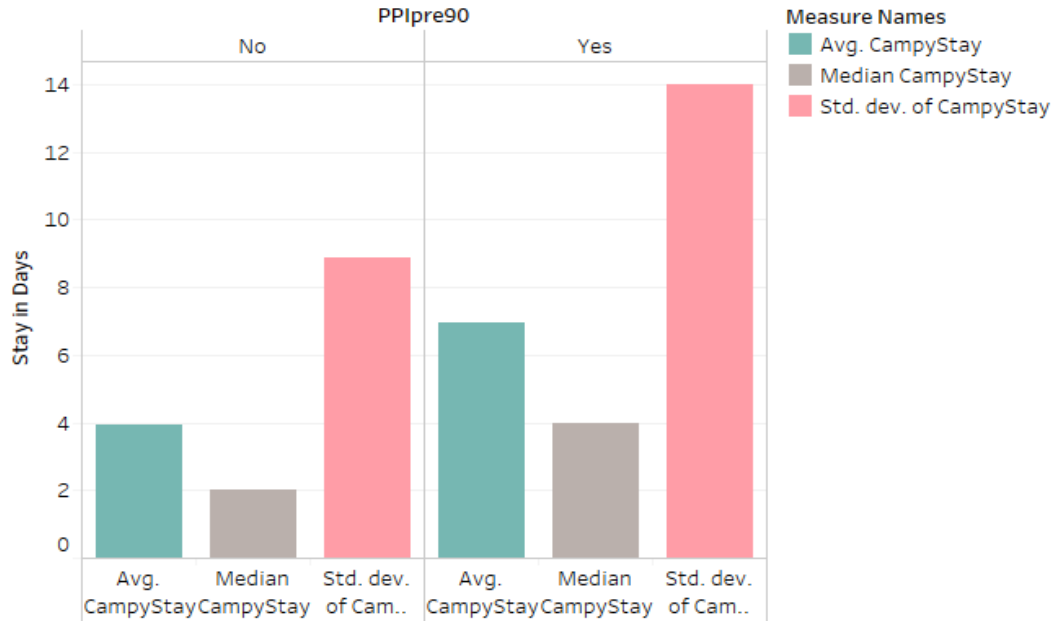
Recognising that age is an important factor in PPI use, when this analysis was run on the 65 and older age group the difference in the hospitalisation rate was still significant, with 16.4% of cases in this age group without a PPI prescription admitted to hospital compared with 22.9% with a PPI prescription (Table 25).

Table 25: PPI Use 90 Days Pre-Specimen Date, Hospitalisation Percentage by Broad Age

PPIpre90	Agebroad	Cases	Hospit..	Hosp%
No	<18	3,024	454	15.0
	18-64	13,940	1,423	10.2
	65+	2,795	459	16.4
Yes	<18	68	20	29.4
	18-64	5,982	887	14.8
	65+	4,155	950	22.9

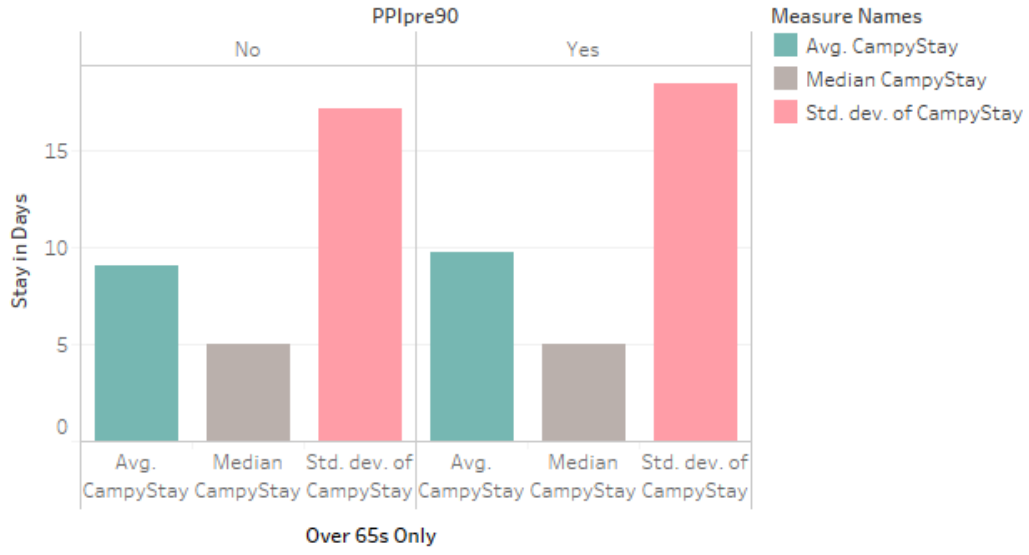
Overall, among those cases who were hospitalised, mean length of stay was longer for PPI users (7.2 days) than those who did not use a PPI (4.0 days) (Figure 41). This difference in mean stay length was significant ($p<0.001$). Median stay length was 4 days for those using PPI, compared to 3 days for those who did not (Figure 41). As previously noted, age is a strong predicator of PPI use and strongly related to duration of stay, which explains this association.

Figure 41: Mean & Median Length of Stay for Cases Prescribed a PPI in 90 Days Prior to Specimen Date



When this analysis was restricted to those aged 65 years and over the mean duration of admission was 9.0 days for those without a PPI prescription and 9.7 days for those with a PPI prescription (Figure 42) and this difference was not significant.

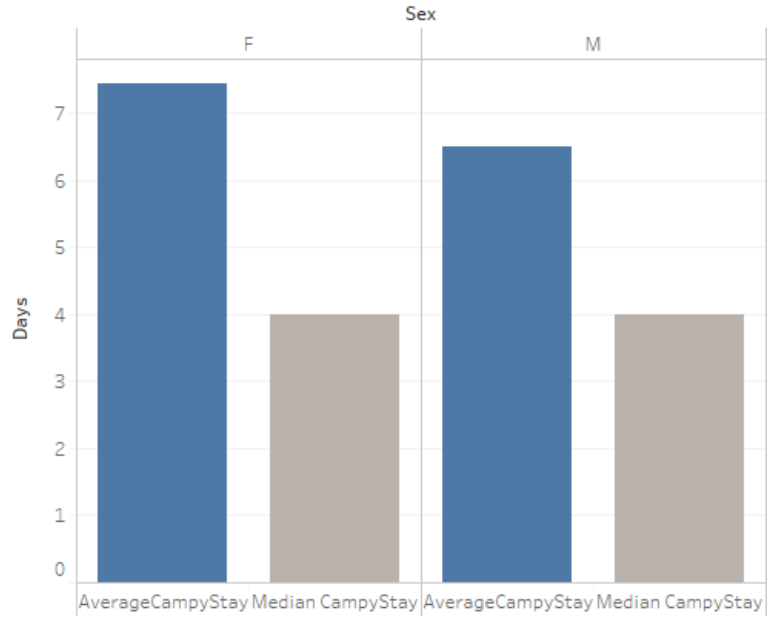
Figure 42: Mean & Median Length of Stay for Cases Prescribed a PPI in 90 Days Prior to Specimen Date in Over 65s Only



Among all ages, the mean stay for females (7.7 days) who had been prescribed a PPI in the 90 days prior to infection was longer than the mean stay for males prescribed a PPI (6.7 days).

This difference was statistically significant.

Figure 43: Mean & Median Length of Stay for Cases Prescribed a PPI in 90 Days Prior to Specimen Date by Sex



Anti-diarrhoeal Prescribing

Many anti-diarrhoeal drugs are available without a prescription and use of non-prescription drugs by *Campylobacter* cases could not be captured, and therefore the data on anti-diarrhoeal prescribing should be viewed with caution. The proportion of cases prescribed an anti-diarrhoeal drug in the 30 days prior to infection was 7.8% (Table 26) and rose to 15.1% (Table 27) for those prescribed in the 30 days after infection.

There was no significant difference in prescribing between males and females either pre or post-infection.

Table 26: Anti-Diarrhoeal Prescribing % in 30 Days Prior to Specimen Date

Antidiarrpre..	Cases	% of Total Number ..
N	27,641	92.2%
Y	2,323	7.8%

Table 27: Anti-Diarrhoeal Prescribing % in 30 Days Post-Specimen Date

Antidiarrpost..	Cases	% of Total Number ..
N	25,442	84.9%
Y	4,522	15.1%

Use of anti-diarrhoeal drugs was more common in older cases (Figure 44, Figure 45).

Figure 44: Anti-Diarrhoeal Prescribing Proportions in 30 Days Prior to Specimen Date by Age Band

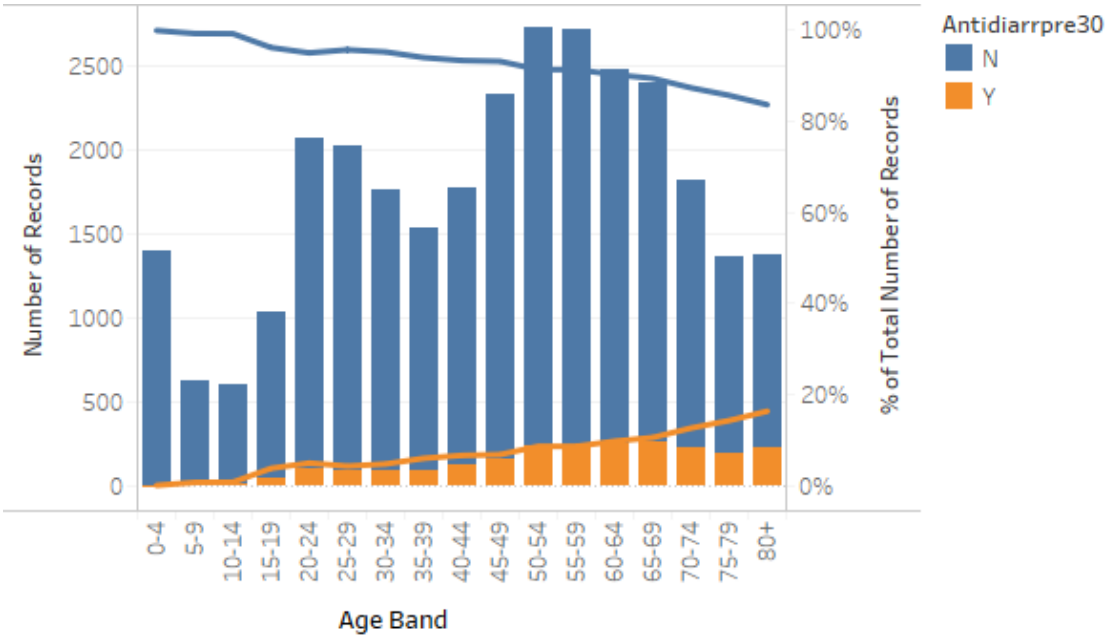
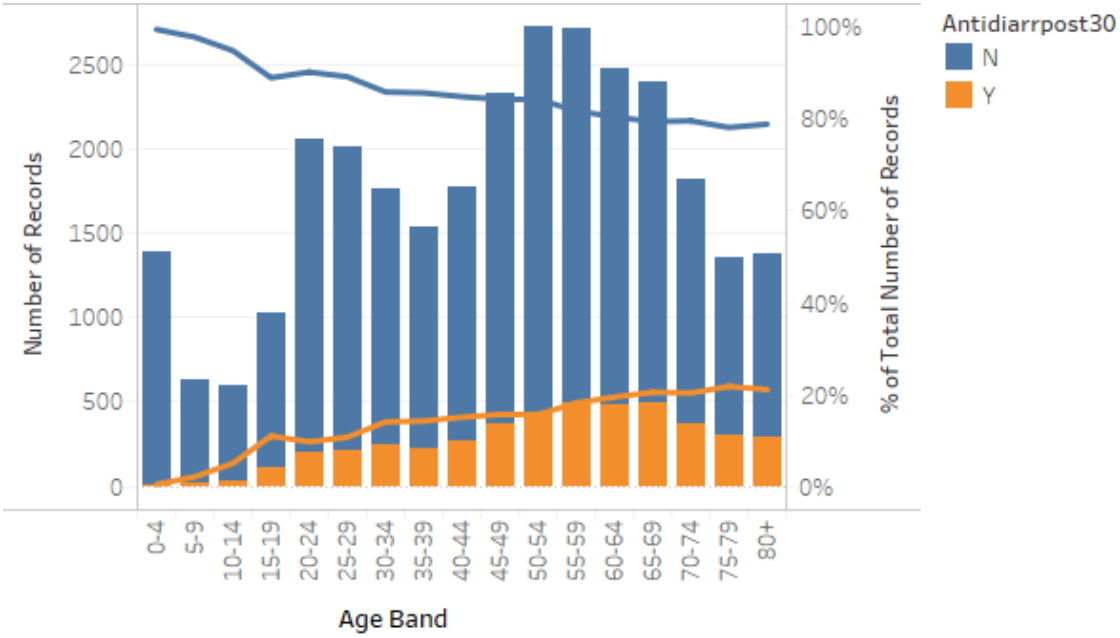


Figure 45: Anti-Diarrhoeal Prescribing Proportions in 30 Days Post- Specimen Date



By deprivation, use was highest in the most deprived quintile both pre and post-infection. In the 30 days prior to specimen date the proportion of cases in the most deprived category prescribed anti-diarrhoeals was double that of cases in the least deprived category (Table 28). This difference was also evident in the 30 days following specimen date (Table 29).

Table 28: Anti-Diarrhoeals Prescribed 30 Days Pre-Specimen Date by Deprivation

Antidiarrpre30	Simd2012 Sc Quintile	Cases	% of Total Number ..
N	1	4,532	89.2%
	2	5,312	91.4%
	3	5,544	92.2%
	4	6,095	93.4%
	5	6,066	94.3%
Y	1	546	10.8%
	2	501	8.6%
	3	471	7.8%
	4	434	6.6%
	5	366	5.7%

Table 29: Anti-Diarrhoeals Prescribed 30 Post-Specimen Date by Deprivation

Antidiarrpost30	Simd2012 Sc Quintile	Cases	% of Total Number ..
N	1	4,143	81.6%
	2	4,860	83.6%
	3	5,110	85.0%
	4	5,594	85.7%
	5	5,639	87.7%
Y	1	935	18.4%
	2	953	16.4%
	3	905	15.0%
	4	935	14.3%
	5	793	12.3%

Hospitalisation rates were higher (15.8%) among those prescribed anti-diarrhoeals in the 30 days prior to infection (Table 30) than those who were not (13.8%) prescribed an anti-diarrhoeal. This was significant with a p value of 0.006.

Table 30: Anti-Diarrhoeal Prescribing and Hospitalisation % in 30 Days Pre Specimen Date

Antidiarrpre30	Hospcamp T	Cases	% of Total N..
N	Not Hospitalised	23,815	86.2%
	Hospitalised	3,826	13.8%
Y	Not Hospitalised	1,956	84.2%
	Hospitalised	367	15.8%

When considering anti-diarrhoeals prescribed 30 days post specimen date (Table 31)the proportion hospitalised was lower (10.1%) than the proportion not hospitalised (14.7%). This was significant, with a p value < 0.001.

Table 31: Anti-Diarrhoeal Prescribing and Hospitalisation % in 30 Days Post- Specimen Date

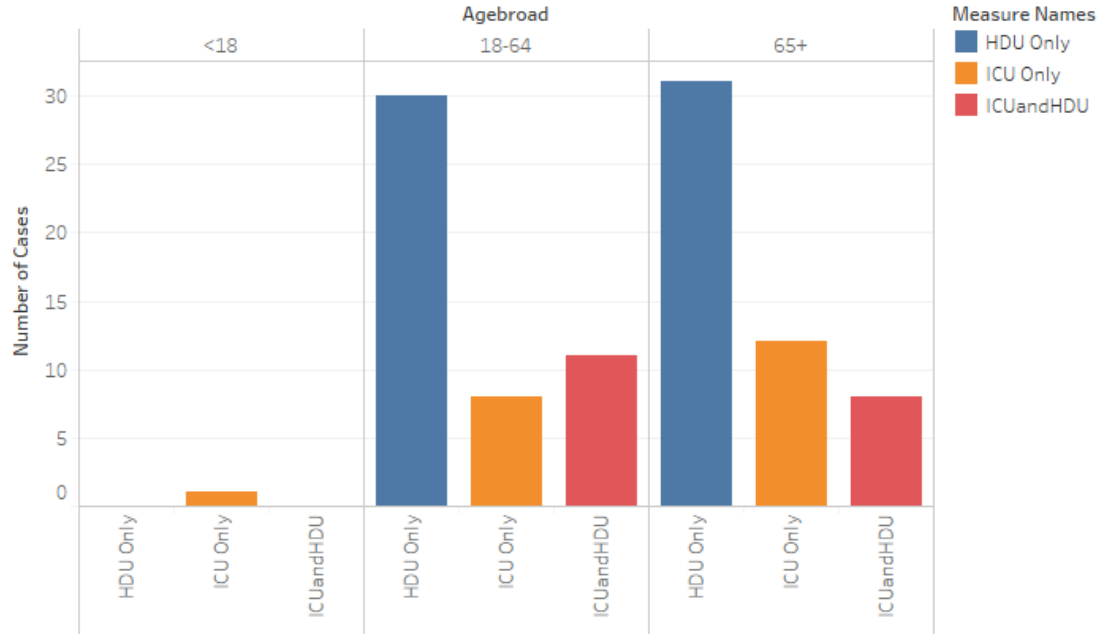
Antidiarrpost30	Hospcamp T	Cases	% of Total N..
N	Not Hospitalised	21,704	85.3%
	Hospitalised	3,738	14.7%
Y	Not Hospitalised	4,067	89.9%
	Hospitalised	455	10.1%

For those cases who were hospitalised, mean stay length was not significantly different among those who were prescribed anti-diarrhoeal drugs either pre or post- specimen date, compared to those who were not prescribed anti-diarrhoeal drugs. However it is important to note the prescribing data is only capturing the prescriptions for anti-diarrhoeal treatments within the community and not those prescribed within hospital.

Hospital Wards

Among the total of 4193 cases who were admitted to hospital for a *Campylobacter* related condition 101 (2.4%) were coded with a stay in either ICU or HDU, with 19 cases recording a stay in both units. Among these 101 cases, 51 (50.1%) were aged 65 years and over and 49 (48.5%) were aged between 18 and 64.

Figure 46: HDU or ICU Admissions by Broad Age Group



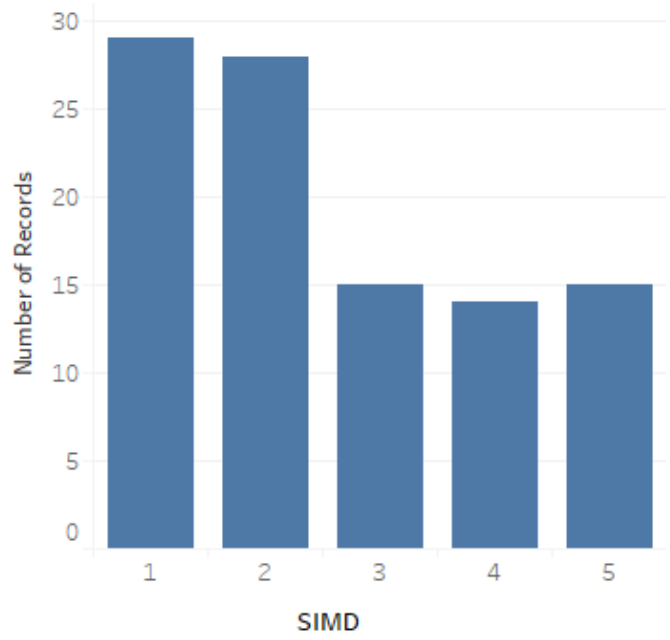
Of the 101 cases 70 (69.3%) were males compared with 31 (30.7%) females admitted to HDU or ICU.

Table 32: HDU or ICU Admissions by Sex

	Sex	
	F	M
HDU Only	16	45
ICU Only	9	12
ICUandHDU	6	13

When the data on HDU and ICU admission is broken down by SIMD (Figure 47)the numbers in each deprivation category are small, but among those cases requiring admission to HDU or ICU, nearly twice as many were from the most deprived quintile compared with the least deprived.

Figure 47: HDU/ ICU Admissions by Deprivation Category



The average stay in either HDU or ICU was 4.3 days.

The significant facility for hospitalised cases records the admission ward type but cases may then have been transferred to another ward(s) following admission. The coding for Table 33 includes the most common admission ward code in the dataset, which is defined as Other (inc. the Clinical Facilities of Standard Specialty Ward 1K, Day Bed Unit 1J).

Table 33: Number of Cases Admitted to Each Ward Type

Significant Facility (group)	Cases
DayBedUnit&Oth	2,855
AcuteAssess	984
ChildUnit	258
AllOther	57
HDU	28
ITU	11
Grand Total	4,193

Severe Outcomes

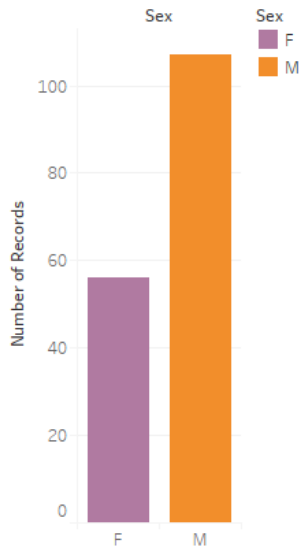
A variable indicating the presence of one the following outcomes was created: death (of any cause) within 30 days of *Campylobacter* specimen date, or among those cases hospitalised for *Campylobacter*, admission to ICU or HDU. This allowed the calculation of the proportion of cases for whom a severe outcome was recorded and to determine their characteristics and compare those characteristics to cases for whom outcomes were not severe.

A total of 163 cases recorded a severe outcome, which is less than 0.6% of *Campylobacter* cases. Just over 40% of those with a severe outcome had underlying health conditions.

More male cases (107) had a severe outcome recorded in the dataset (Figure 48) than female cases (56).

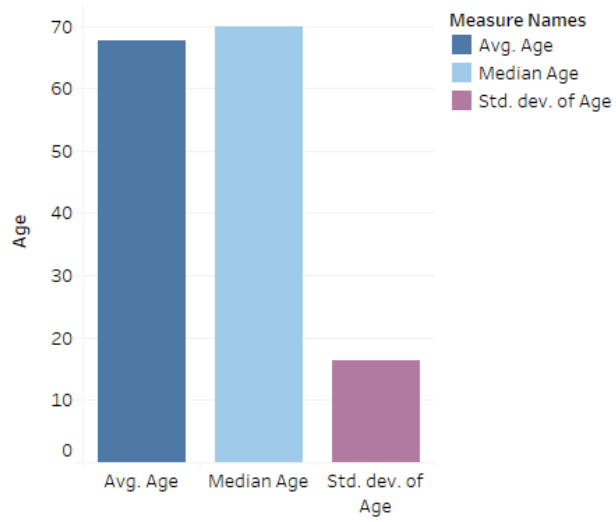
Of the73 deaths recorded within 30 days of *Campylobacter* laboratory result, 11 were directly attributable to *Campylobacter* enteritis, while the others included causes such as myocardial infarction and leukaemia.

Figure 48: Severe Outcomes by Sex



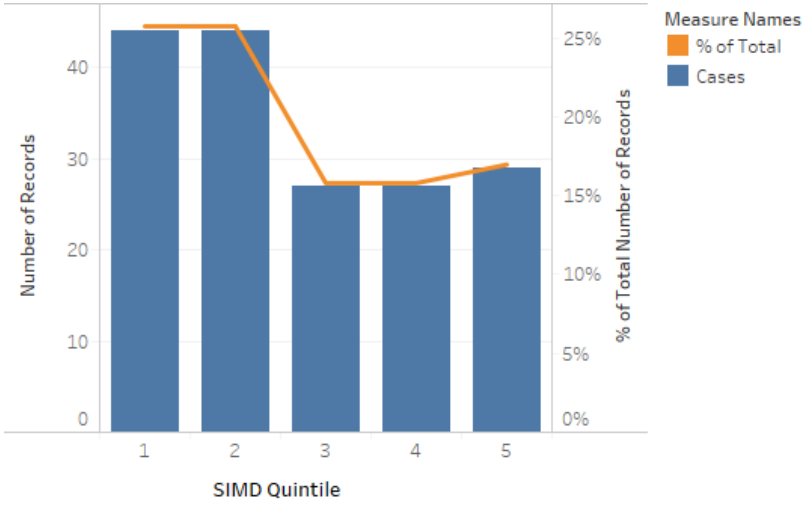
The mean age of 67.7 years for cases with a severe outcome (Figure 49) was more than 20 years above the mean age for all *Campylobacter* cases (46.2 years), this difference was not surprising given the higher rates of underlying medical conditions among the older population which is likely to be a factor in severe outcome.

Figure 49: Severe Outcomes, Age Mean, Median & SD



The proportion of cases with severe outcomes was higher in more deprived categories (Figure 50). This difference was statistically significant ($p<0.003$). As underlying health conditions were higher in the more deprived groups, this is likely to have impacted on the higher rate of severe outcome in this group.

Figure 50: Severe Outcomes by Deprivation Category



Guillain-Barré Syndrome

There were ten recorded cases of GBS in the dataset, this is an incidence of 33 per 100 000 cases of *Campylobacter* and accounts for 0.03% of cases. In Keithlen et al[21] they reported that 0.07% of *Campylobacter* cases developed GBS.

Table 34 shows distribution of these GBS cases by broad age band and sex. Three of the ten cases were among females and 7 among males. Half the cases (5/10) were aged 65 years and over.

Table 34: Guillain-Barré Syndrome Cases by Broad Age Band and Sex

	Sex	
Agebroad	F	M
<18	0	0
18-64	1	4
65+	2	3

Sequelae

When both hospitalisation and prescribing data were used to identify the presence of sequelae, a total of 2991 (9.9%) cases were recorded as having some form of sequelae in the 12 months following their infection (Table 35). These included episodes of hospital care for conditions or prescriptions for drug classes associated with conditions that were not present in the data for the 12 months prior to infection. From the available data however, it is not possible to determine that the sequelae were directly related to the episode of *Campylobacter* infection, it is also possible that some of the classes of drugs used in assigning the presence of the sequelae conditions were in fact prescribed for a different condition.

The presence of the following conditions in the SMR01 data in the 12 months following infection (but not present in the previous 12 months) were flagged: reactive arthritis (ReA), irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), ulcerative colitis (UC), Crohn's disease (CD), coeliac disease, and chronic gastritis. The creation of flags to identify the presence of sequelae used the same methods as those used to identify the presence of predisposing conditions. Where a condition was recorded in the SMR01 data both before and after the episode of infection, or the prescribing data indicated that prescriptions for a class of drugs (e.g. drugs used in bowel conditions or immunosuppressants) were used, then the condition appearing in the SMR01 data following the infection was not flagged as a sequela.

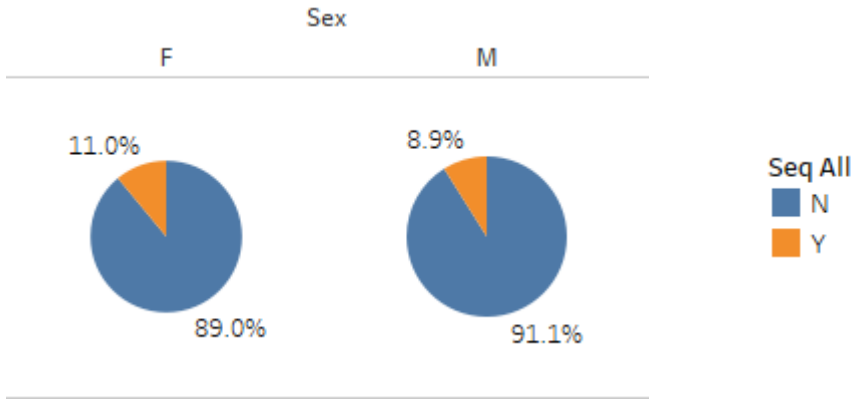
For each condition, two variables indicating its presence as a sequelae were created: one using only hospitalisation data (presence of hospitalisation for a condition in the 12 months following infection when it was absent in the hospitalisation data in the 12 months before), and the other using hospitalisation and prescribing data (presence of a condition in the hospitalisation data in the 12 months following infection where it was absent in the hospitalisation data for the 12 months before, and its absence was also indicated by the classes of drugs prescribed in the 12 months prior to infection).

Table 35: Sequelae Identified Using SMR and Prescribing Data

Seq All	Cases	%
N	27,205	90.1%
Y	2,991	9.9%

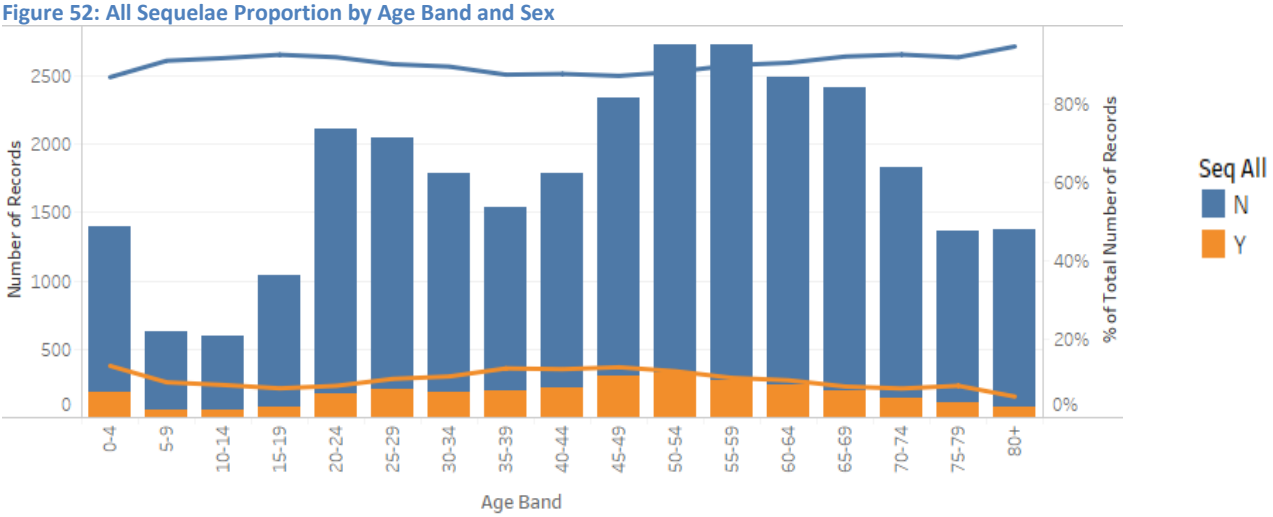
A higher proportion of females (11.0%) developed sequelae than males (8.9%) and this difference was significant (p<0.001).

Figure 51: Sequelae Identified Using SMR01 and Prescribing Data, % by Sex



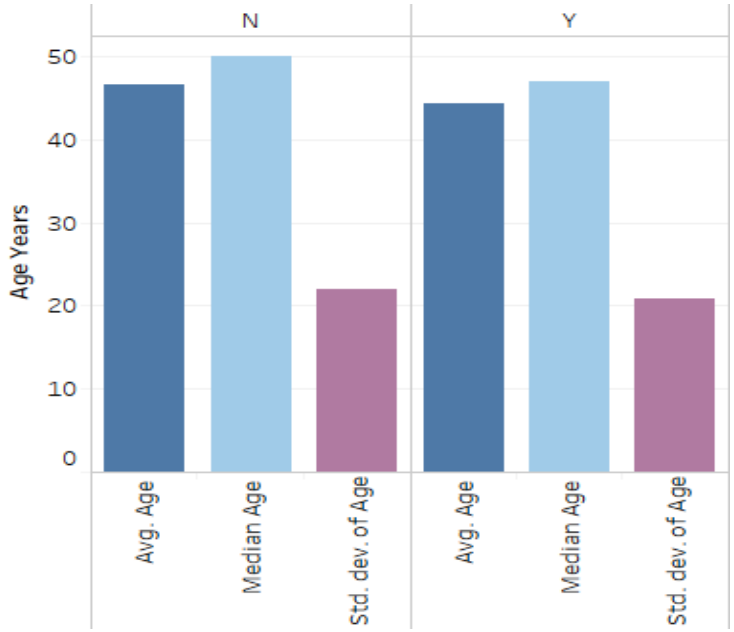
The proportion of those developing sequelae (Figure 52) was highest in the 0-4 age band (13.1%), followed by the 45-49 age band (12.9%), however this may also be a reflection of the diagnoses of conditions in this age group (0-4 yrs) that hadn't previously been diagnosed due to age, and therefore may not be a direct consequence of the *Campylobacter* infection

Figure 52: All Sequelae Proportion by Age Band and Sex



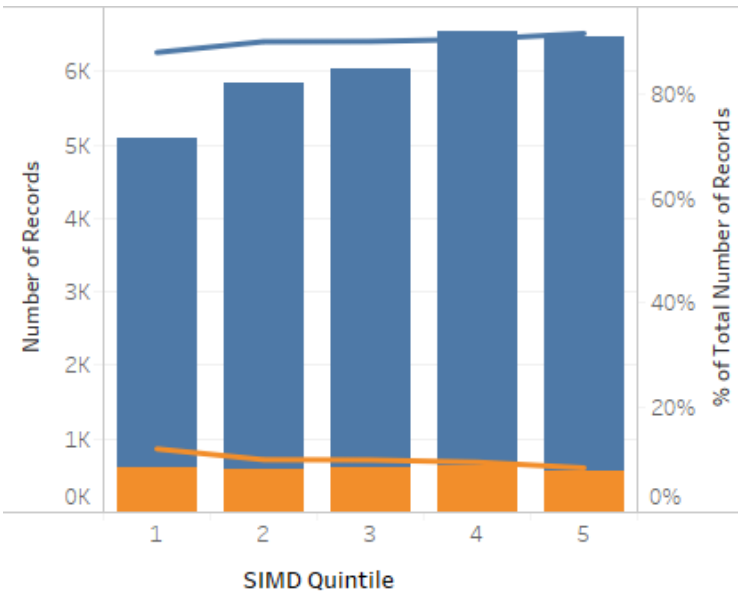
The difference in mean age for those developing sequelae (44.4) and those who did not (46.6) was statistically significant (p<0.001). Very low rates of sequelae were identified in those in the oldest age group. This may also reflect that for some of these cases there may not have been a full year of follow-up SMR01 data, due to unrelated death in the 12 months following *Campylobacter* infection.

Figure 53: Mean and Median Age in Cases Who Did and Didn't Develop Sequelae



There was no significant difference in the proportion of cases developing sequelae in most deprived area compare to the least deprived (Figure 54).

Figure 54: All Sequelae, Proportion by Deprivation Category



The proportion of those developing sequelae denoted by orange line.

Sequelae by Specific Condition

Figures for the number of cases developing the following conditions were first obtained using only hospitalisation records, and then where applicable were re-calculated using both hospitalisation and prescribing data. Where hospitalisation data only was used, the numbers indicate individuals who received hospital treatment for the condition in question during the 12 months following their *Campylobacter* diagnosis, but who did not receive treatment for that condition during the 12

months before their *Campylobacter* infection. It is, however, possible they had the condition in the 12 months prior to their *Campylobacter* infection, but did not require hospitalisation for it. When prescribing information was used, the total includes cases who received hospital treatment for the condition in question during the 12 months following their *Campylobacter* infection, and received neither hospital treatment in the 12 months before nor prescriptions for drug classes relevant to their condition during those 12 months. It was not possible to obtain information on drug prescriptions for specific conditions, therefore prescription data could not be used to flag the presence of specific sequelae developing post-infection. The methodology described for this analysis identified cases for whom the given conditions appeared to be new, however it is possible that the admissions identified following infection were the result of flare-ups of previously existing conditions.

Table 36: Specific Sequelae Identified Using SMR and Prescribing Data

Sequelae	**New cases identified in the dataset using only SMR01 data**	**New cases identified in the dataset using hospitalisation and prescribing data**
Ulcerative colitis	31*	16*
Crohn's disease	43	40
Inflammatory Bowel Disease	102	8
Irritable Bowel Syndrome	37	6
Chronic gastritis	13	2
Coeliac disease	8	-
Reactive arthritis	10**	-

*The difference in these two results is explained by the fact the second number excludes cases with a hospitalisation for UC following infection for whom a prescription for a bowel-related condition or an immunosuppressant was present in the 12 months before infection, in order to define 'true' new cases of UC.

**When only hospitalisation data were used, 9 cases were recorded as developing reactive arthritis within 30 days of the lab sample date. A further 1 case developed arthritis during the rest of the year following diagnosis, giving an incidence of 0.033%. When prescribing data was also used, a total of 2696 (8.9%) cases were recorded as developing any form of arthritis during the year following diagnosis. However it is important to note that as 44% of these 2696 cases were aged over 50 years this may merely reflect the natural course of this illness.

Table 37: Incidence of Specific Conditions per 100,000 Using SMR01 Data Only

Condition	Incidence as sequelae in *Campylobacter* population per 100,000	Incidence in Scottish population per 100,000 in 2017
Ulcerative colitis	102.66	26.06
Crohn's disease	142.40	23.90
Inflammatory Bowel Disease	337.79	52.32
Irritable Bowel Syndrome	122.96	36.52
Chronic gastritis	43.05	21.70
Coeliac disease	26.49	15.39

It was not possible to compare the incidence of arthritis, as figures for the incidence of reactive arthritis were not available for the Scottish population as a whole.

As Table 37 shows, the incidence of each condition was higher among the *Campylobacter* cases in the 12 months following *Campylobacter* infection than among the Scottish population as a whole, however it is important to note this data is not stratified by age

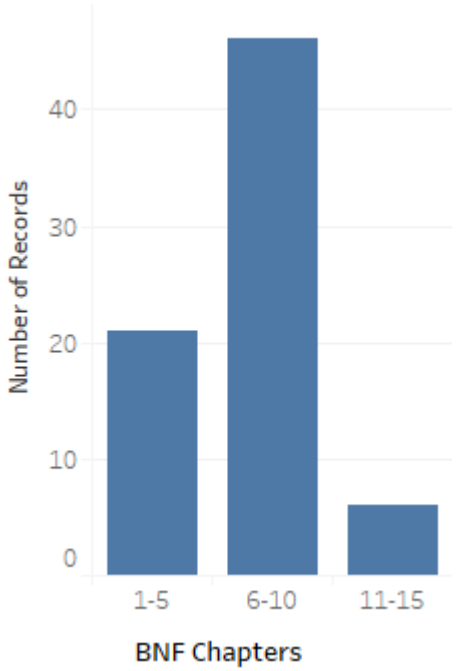
Deaths

Over the 5-year period, 12 cases died with *Campylobacter* enteritis recorded as the main cause of death, giving a 5-year mortality rate of 0.04%. Their mean age was 75.5 (SD 13.1), median age 75. All of these cases were hospitalised within 8 days of their infection and five of them had a predisposing condition which required hospitalisation within the 12 months preceding their *Campylobacter* specimen date.

An additional 62 cases died within 30 days of their *Campylobacter* report but *Campylobacter* enteritis was not recorded as the cause of death, of these, 52 (84%) were aged over 65 years. Of those over 65 years of age, 45 had a range of underlying condition recorded in the dataset including myocardial infarction and cancer. Others may have had other underlying conditions which were not the specific comorbidities included in this data linkage.

Using the number of BNF chapters prescribed within one year of laboratory report as an indication of the extent of comorbidity it shows that 52 (70%) of the cases that died had been prescribed from a minimum of six unique BNF chapters in the 12 months preceding their positive laboratory specimen for *Campylobacter* (Figure 55).

Figure 55: Deaths Within 30 Days of Specimen Date by Number of BNF Chapters Prescribed



Discussion

Demographics

The age profile of laboratory confirmed cases of *Campylobacter* has remained relatively stable over time (Figure 2) with a bimodal distribution with peak in young children and a second higher peak in the incidence among older adults, which is similar to that reported by Riddle et al. [29].

The trend in our results for higher incidence rates in the adult population than in children is in contrast with some literature which shows a decrease in cases with increasing age Scallan et al [8]. It is, however, in keeping with studies in the rest of the UK [5] showing that older age groups are the emerging risk population for *Campylobacter* infection. This was also supported by the descriptive study conducted in England and Wales [37] which found higher incidence rates in older age groups in the last 20 years.

The work on inverse trends in *Campylobacter* in Switzerland [41] found that the median age of cases increased from 25 in 1988 to 39 in 2013, the median age in this Swiss study was younger than in our study where the median age was 49 years.

The finding of a higher incidence of *Campylobacter* in males (120 per 100,000) compared to females (102 per 100,000) was in consensus with findings by Nichols at a[37] this higher incidence was consistent across the age bands (Figure 4). Despite the higher incidence in males in all age groups, the absolute number of cases was higher among female than males in the older age groups, reflecting the higher average life expectancy among females and a larger female population in the older age groups.

Hospitalisation and mortality

The overall hospitalisation rate of 14% (12.6% with an overnight stay) is at the higher end of hospitalisation rates recorded in the literature, albeit there is great variation with CDC (Centers for Disease Control and Prevention) reporting a hospitalisation rate of 15% for *Campylobacter* in the USA[4;44] and Ruzante et al[10] reporting a rate of 5.1% in Canada. In the UK, Gillespie et al[5] recorded a hospitalisation rate of 10% in England and Wales for the year between 1990 and 2007. The direct comparison of hospitalisation rates between studies is problematic due to differences in study design and healthcare structure and access. It is also of note that in our analysis we were able to capture those cases who were admitted and discharged on the same day, while others may have only included those with an overnight stay. Despite these difficulties in cross study comparisons, the rate reported here is at the higher end of that reported elsewhere. This could be partial attributable to higher rates of underlying conditions in the Scottish populations than in other study populations. As noted by Walsh et al[45], Scotland has the lowest life expectancy in Western Europe along with the widest mortality inequities.

Our results were consistent with findings in the literature that hospitalisation rates were higher in infants than in older children [3] and with those reported in the literature, showing that both hospitalisation and mortality were more common in cases over 65 year [4;44]. The mean (5.3 days) and median (3 days) length of hospital stay was similar to those reported in the literature for comparable settings: Schmultz et al. reported a mean of 3 days for Swiss cases [46] and a median of 7 days, while Samuel et al[7]., reported a mean of 4.6 days for a US-based study.

Among the cases with the longest stays, a high proportion of individuals were aged over 65 (78%). Comparatively few (42%) had predisposing conditions requiring hospitalisation. These results suggest that age is a more important determinant of stay length than underlying conditions. The higher frequency of females among the cases who were hospitalised for 10 nights or more may be an artefact of the fact these cases were primarily from older age groups, where females tend to outnumber males.

Two distinct trends with SIMD were observed. Among the population there was a higher incidence of *Campylobacter* in the least deprived compared to the most deprived areas, but once an individual develops *Campylobacter* those in the most deprived areas were significantly more likely to be admitted to hospital than those in the least deprived areas, however among those admitted there was no significant difference in duration of stay.

The phenomenon of hospitalisation being associated with increased deprivation may be attributable to a tendency among cases in more deprived areas to delay seeking healthcare in concurrence with a general trend in healthcare-seeking behaviour reported by the literature [47-49], or to a higher prevalence of underlying conditions among this group.

The proportion of cases hospitalised in urban areas was higher than in rural ones (Table 11) this is likely to be a reflection of the concentration of the most deprived areas within large urban conurbations. While hospitalisation rates increased over the 5 years from 13.3% in 2013 to 14.9% in 2017, the median length of stay remained the same, at 3 days, while mean stay ranged from a low in 2016 of 5.1 days to a high of 5.7 days in 2017, but with no overall trend in duration over the study period.

The proportion of hospitalised cases who were admitted and discharged on the same day varied from year to year with no discernible trend. The same was true of long stay cases.

It is possible to suggest a number of factors that may have contributed to this increasing trend for hospitalisation; it may reflect a change in clinical practice, where cases are more likely to be admitted at an earlier stage on infection, or alternatively cases are presenting at A&E rather than to primary care, which may impact on patient management. Whilst the trend has been for an increase in the proportion of cases hospitalised, the laboratory reports for the first three years (2013-2015) are over 6,000 while in the last two years are below 6,000, so it may be that a lower proportion of non-hospitalised cases are being sampled and laboratory confirmed, resulting in an apparent rise in hospitalisation rates. Differences may also be attributable to differences in circulating strains over the 5 year period, with some associated with greater severity of disease therefore more likely to result in hospitalisation, unfortunately typing of *Campylobacter* is not routinely conducted in Scotland so there is no information available on circulating strains. The trends presented here are limited to five years, it will be important to monitor how the rate of hospitalisation changes over the next few years and explore the driving factors. Over the longer term the increase in the older population in whom hospitalisation rates are higher may impact on overall trends.

While there was a higher incidence of *Campylobacter* among males, hospitalisation was more common among female cases, potentially due to the fact hospitalisation was more common among older cases, a higher percentage of whom were female. Severe outcomes however, were more common among male cases. This may be attributable to differences in healthcare seeking behaviour

between males and females, or to a higher prevalence of specific underlying conditions associated with more severe clinical outcomes in males.

Prescribing

One of the unique features of this study compared to many of the published papers was the ability to look at community prescribing for antibiotics, anti-diarrhoeal drugs and PPIs.

Figure 33 shows the increase in antibiotic prescribing in the 7 and 30 days post laboratory report, increasing from a baseline of 5.8% in the 30 days prior to laboratory report to 17.5% and 28.7% in the 7 and 30 days post laboratory report respectively. It would be reasonable to assume that much of this increase is attributable to prescriptions as a consequence of the *Campylobacter* infection, especially as the predominant antibiotics prescribed (Table 21) are macrolides, which are often used to treat common bacterial infections.

This is the first study in the UK to be able to describe prescribing trends for *Campylobacter* infection. In the 30 days pre laboratory report antibiotic prescribing was higher (7.1%) among cases in the most deprived SIMD compared to the least (4.1%), which is consistent with a recognised trend of higher antibiotic prescribing in more deprived areas[42] but at 7 days post laboratory report there was little difference across the quintiles.

The data showed that PPI use was higher among the laboratory confirmed cases (34%) than the general population of Scotland (18%), which is consistent with the findings of a number of studies of PPI being a risk factor for *Campylobacter* infection [14-16].

Among cases, PPI use showed a strong correlation with age with higher use among older cases (Figure 40) and among those in more deprived areas (Table 23). Brophy et al. [2] suggest that the increased risk of illness from *Campylobacter* in the presence of PPI use may in fact result from the presence of specific underlying conditions associated with PPI use such as concurrent immunosuppressant medication. It is of note that hospitalisation rates were higher both overall and also in the over 65 years only among those with PPI use compared to those without.

Sequelae and complications

The percentage of cases recorded as developing GBS (0.033%) was consistent with the 0.07% (95% CI 0.03% - 0.15%) reported in the review by Keithlin et al. [21].

The number of cases recorded in the linked data as developing reactive arthritis requiring hospital admission (0.033%) was lower than figures reported in the literature for reactive arthritis development overall (1.7%-2.86%[17;21;39]) The number reported as taking medication for arthritis (all types not just reactive) in the year following infection (8.9%) is considerably higher than figures reported in the literature for reactive arthritis development and contrasts with findings reported by Garg et al., [50] of no increased risk of prescriptions for arthritis following infection with *Campylobacter*. However it is important to note that the prescribing data analysed here reflects drugs used for arthritis generally and not specifically reactive arthritis, which limits direct comparison across studies. Also as 44% of new prescriptions for drugs for arthritis were among cases aged over 50 years it may also in part reflect natural history of the condition and age of diagnosis.

The number developing IBS (0.13-0.15% of cases, depending on whether prescribing data was taken into account) is considerably lower than rates reported in the literature ranging from 4%[21] to 8%[39].

This will almost certainly be because in many cases those developing IBS may consult their GP but would be treated neither by hospitalisation nor by prescription medication, and also reflects issues with the accurate diagnoses of IBS, which unlike many other conditions has no definitive diagnostic test.

Implications of findings

This work has provided a detailed insight into the burden of *Campylobacter* infection, including the fact that overall 14% of cases require admission to hospital and the factors associated with hospitalisation in particular age, deprivation and underlying medical conditions. Knowing the groups most likely to require hospitalisation may be valuable material for clinicians in the early recognition of more severe infection.

Whilst the overall aim of the FSS *Campylobacter* strategy is to reduce the total number of cases, it is possible that targeted work aimed at both those groups most likely to acquire *Campylobacter* infection and those at greatest risk of hospitalisation upon infection may help to reduce the overall burden of *Campylobacter* on both individuals and the health service in Scotland. The study has identified a number of factors associated with hospitalisation including age, deprivation, underlying medical conditions and PPI use. This may become increasingly important with the aging population – the group not only with the highest rates of hospitalisation but also the longest stays.

The work has shown that a substantial number of cases are prescribed antibiotics, possibly for their *Campylobacter* infection. Understanding some of the factors associated with prescribing including clinical presentation, duration of symptoms etc will be important in the overall antimicrobial resistance strategy and the stewardship of prescribing. It also raises the question of whether routine AMR testing of isolates will be required.

Limitations

The results of this study only provide information on confirmed cases of *Campylobacter* therefore it is not possible to gather information on the characteristics of cases who may have experienced acute symptoms of infection and not received a laboratory diagnosis, and in particular the proportion who may have progressed to develop sequelae post-infection. The IID2 study estimated that for every laboratory confirmed case reported to national surveillance approximately 9 occur in the community [51]. It is likely that most cases with illness severe enough to require hospitalisation will have had a stool sample tested, so it is unlikely that the numbers of hospitalised cases is significantly under reported in our study.

The one year follow-up period for identifying the development of sequelae maybe an insufficient length of time for the development of some sequelae associated with *Campylobacter*, and is a relatively short time for some of the sequelae considered in the analysis (i.e. coeliac disease). Keithlin et al's[21] review found follow up times as long as three years for GBS and IBS. They also found that smaller studies reported higher numbers of sequelae, whilst bigger studies maybe only capture more severe cases.

The work conducted in Lancashire [52] reported a high number of cases (100 out of 155) noted some new symptoms such as joint pain within four weeks of their *Campylobacter* infection. None of them required hospitalisation or hospital referral as a result of these symptoms and those who reported musculoskeletal sequelae had symptoms lasting for a mean of 8.4 days. Other than using a

questionnaire based data gathering methodology, most of these low-level potential sequelae would not be detected.

The study was also unable to capture data from primary care for sequelae that did not result in a prescription which may have underestimated some conditions or those treated with over the counter medication. Further studies might consider a longer follow-up period. However, increasing the length of follow-up needs to be balanced against the increasing occurrence of other events the individual may experience that also contribute to the development of conditions that may be a sequelae of *Campylobacter* infection, resulting in an over estimation of the contribution of *Campylobacter* infection.

The prescribing data was limited to community prescribing and therefore would not have captured those drugs prescribed in hospital, which may have underestimated the proportion of cases who received antibiotic or anti-diarrhoeal treatment for their *Campylobacter* infection.

Strengths

This study was able to bring together and link a number of datasets to provide a comprehensive picture of the burden of *Campylobacter* infection in Scotland. The use of 5 years' worth of cases not only provided a large dataset for analysis but also allowed some trends to be looked at over time, in particular overall hospitalisation rates.

By using national datasets, the study was not dependant on case participation on questionnaires, which is not only resource intensive, but is also prone to bias by those willing to participate in the study.

The use of both Charlson score and BNF chapter prescriptions to estimate the overall underlying health of the cases provided an indicator that was not restricted to the identification of individual ICD10 codes, although this approach was also used.

Further work

Similar work is planned for some of the other key enteric pathogens, once complete the results from the *Campylobacter* analysis will be compared to those for other pathogens.

Health economic work is ongoing using the data generated in this analysis to assign healthcare costs associated with *Campylobacter* infection.

With a focus on antimicrobial resistance it will be important to understand some of the factors related to antibiotic prescribing for *Campylobacter* infection, the impact this has on reducing the duration of illness and the potential for the development of resistance.

The findings from this work can be used by those in FSS and other agencies to help identify groups where targeted interventions may have the greatest impact in reducing the burden of *Campylobacter* infection.

When more data becomes available for *Campylobacter*, trends across longer time periods will be analysed. Syntax written for the above analysis can be re-run once more data becomes available.

Conclusion

Incidence of confirmed cases of *Campylobacter* remained relatively stable over the 5-year period of interest, and there was no significant difference in the demographic characteristics of cases over the period.

The rate of hospitalisation of confirmed cases of *Campylobacter* was 14%. Hospitalisation was more common among more deprived cases, older age groups and females. Over the 5 year time period there were 14 deaths attributable to *Campylobacter*.

These results are for the most part consistent with findings reported in the literature, and provide new insights into the associations between deprivation and *Campylobacter* infection, hospitalisation and clinical outcomes following infection.

Appendices

Literature search strategy

The below table shows the search strategy used to interrogate PubMed and MEDLINE.

Database	Search terms
Pubmed	(*Campylobacter*[Title) AND sequelae[Title]
	(campylobact*[Title]) AND sequel*[Title/Abstract]
	(campylobact*[Title]) AND burden*[Title/Abstract]
	((campylobact*[Title/Abstract]) AND long-term[Title/Abstract]) AND outcome[Title/Abstract]
	((campylobact*[Title/Abstract]) AND hospitali*[Title/Abstract])
	(campylobact*[Title/Abstract]) AND risk factor*
	Campylobacter AND meningitis
	campylobact* and chronic sequela/ae
	campylobact* AND risk factor*
	Campylobact*[Title/Abstract] AND hospital admission* campylobact* and co-morbidi*
	campylobact* and comorbidi*
	campylobact* and linkage
	campylobact* and predispos*
	campylobact* and prescription*
	campylobact* and prescrib*
	campylobact* and immunosuppress*
	campylobact* and diabet*
	campylobact* and omeprazole
	campylobact* and lansoprazole
	campylobact* and PPI
	campylobact* and protein pump inhibitor*
	campylobact* and protein-pump inhibitor*
	campylobact* and antibiot*
	campylobact* and antibacterial*
	campylobact* and cancer
	campylobact* and gastro-oesophageal reflux disease
	campylobact* AND incidence
	campylobact* AND antibiotic
	campylobact* AND repeated admission
	campylobact* AND repeated infection
	campylobact* AND recurrent infection
	campylobact* AND recurring infection
	campylobact* AND relapsing infection
	campylobact* and steroid
	(campylobact*[Title/Abstract]) AND death (human)
	(campylobact*[Title/Abstract]) AND mortality (human)
	(campylobact*[Title/Abstract]) AND morbidity
	campylobact* and bowel cancer
	campylobact* and colorectal cancer

	campylobact* and gastric cancer
	campylobact* and stomach cancer
	campylobact* and co-infection
	campylobact* and coinfection
Medline	(campylobact* and sequel*)
	(camplobact*[Title/Abstract]) AND risk factor*
	(campylobact*[Title/Abstract]) AND risk factor* AND hospitali*)
	campylobact* and hospitali*

ICD-10 codes

The table below shows the ICD-10 codes used to identify the presence of specific conditions in the linked *Campylobacter* data.

	Condition	**ICD-10 code(s)**
Predisposing and chronic conditions	Chronic liver disease	K70-K77
	Alcoholic liver disease	K70
	Hypogammaglobulinemia	D800, D801, D807
	Immunodeficiency	D80-D84
	Neoplasms	C00-D48
	Diabetes mellitus	E10-E14
	Ulcerative colitis	K50
	Crohn's disease	K51
	Irritable bowel syndrome	K58
	Inflammatory bowel disease	K528, K529
	HIV/AIDs	B20, B21, B22, B24
	Coeliac disease	K900
	Chronic gastritis	K293, K294, K295
Presenting symptoms	*Campylobacter* enteritis	A045
	Bacterial intestinal infection	A048
	Diarrhoea and gastroenteritis of presumed infectious origin	A09
	Abdominal and pelvic pain	R10
	Nausea and vomiting	R11
	Dehydration	E86
	Diarrhoea	A090; K591
	Gastroenteritis	A09
	Myalgia	M791
	Bacteraemia	A499
	Toxic mega colon	K593
	Sepsis	A41
	Hemolytic-uremic syndrome	D593
	Peritonitis	K65
	Hypovolemic shock	R571
	Malaise	R53
	Intestinal obstruction	K56
	Enterocolitis	A099
	Viral intestinal infection, unspecified	A084

Complications	Bacteraemia	A499
	Toxic mega colon	K593
	Sepsis	A41
	Hemolytic-uremic syndrome	D593
	Aortic aneurysm	I71
	Peritonitis	K65
	Gastrointestinal haemorrhage, unspecified	K922
	Hypovolemic shock	R571
	Endocarditis	I330, I339, I38X, I39
	Pleuritis	R091
	Myocarditis	I410, I514, I012, I40
	Acute pancreatitis	K85
	Pericarditis	I30
	Guillan Barré syndrome	G610
	Inflammatory polyneuropathy	G61
	Polyneuropathy, unspecified	G629
	Reactive arthropathies	M02
	Immunoproliferative small intestinal disease	C883
	Malaise	R53
	Intestinal obstruction	K56
Sequelae	Ulcerative colitis	K51
	Crohn's disease	K52
	Irritable bowel syndrome	K58
	Inflammatory bowel disease	K528, K529
	Intussusception	K561
	Reactive arthropathies	M02
	Immunoproliferative small intestinal disease	C883
	Coeliac disease	K900
	Chronic gastritis	K293, K294, K295

BNF codes

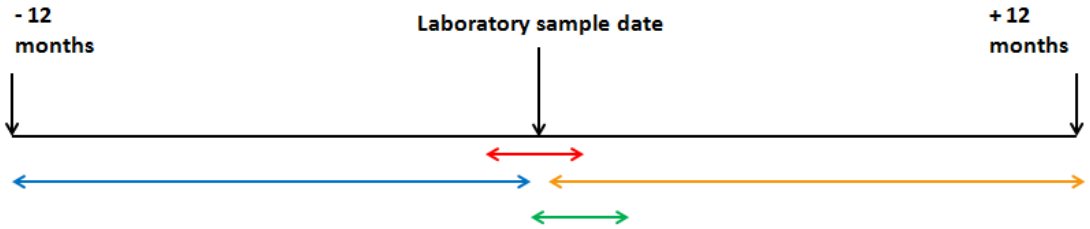
The following codes were used to identify the drug classes corresponding to the predisposing conditions and sequelae of interest in the prescribing data.

Drug class	BNF code
protein pump inhibitors	1.3.5
Immunosuppressants	8
Antibiotics	5.1
chronic bowel disorders	1.5
Cancer	8
Arthritis	10.1
Diabetes	6.1

Timeline for data linkage

Figure 1 shows the timeline used for linkage of the *Campylobacter* data

Timeline showing periods of interest for identifying hospitalisation, presenting symptoms, complications, sequelae and predisposing conditions in the linked data



- Hospitalisations & deaths in the ± 14 days around the laboratory sample date: specialisations and diagnoses recorded
- Hospitalisations & deaths in the 30 days from the sample date: complications
- Records of sequelae in hospitalisation, prescription and mortality data in the 12 months following the sample date
- Records of predisposing conditions in hospitalisation and prescribing data during the 12 months before the sample date.

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