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Giardiasis in North West England: faecal specimen requesting rates by GP practice

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SUMMARY

Many cases of giardiasis in the UK are undiagnosed and among other things, diagnosis is dependent upon the readiness of GPs to request a specimen. The aim of this study is to assess the rate of specimens requested per GP practice in Central Lancashire, to examine the differences between GP practices and to estimate the pattern of unexplained spatial variation in the practice rate of specimens after adjustment for deprivation. To achieve this, we fitted a set of binomial and Poisson regression models, with random effects for GP practice. Our analysis suggests that there were differences in the rate of specimens by GP practices ($P < 0{\cdot}001$) for a single year, but no difference in the proportion of positive tests per specimen submitted or in the rate of positive specimens per practice population. There was a difference in the cumulative rate of positive specimens per practice population over a 9-year period ($P < 0{\cdot}001$). Neither the specimen rate per practice for a single year nor the cumulative rate of positive specimens over multiple years demonstrated significant spatial correlation. Hence, spatial variation in the incidence of giardiasis is unlikely to be confounded by variation in GP rate of specimens.

Key words: Diarrhoea, gastrointestinal infections, giardiasis, public health, water-borne infections.

INTRODUCTION

Giardiasis is a parasitic disease caused by the protozoan *Giardia duodenalis* (also called *Giardia lamblia* or *Giardia intestinalis*) and is a common cause of human gastroenteritis. *Giardia* is found in all parts of the world, with the highest incidence in developing countries with poor sanitary conditions [1]. It is also common in developed countries, with around 3000 cases annually in the UK [2], although the true number is likely to be higher as many cases are undiagnosed. Identified risk factors for giardiasis include foreign travel, contact with fresh water, countryside activities or person-to-person transmission [3]. Giardiasis has also been associated with farm animal contact [4] and with consumption of mains tap water as opposed to bottled water, with a dose–response relationship observed [5]. Risk of giardiasis is thought to be higher for males, children and adults aged 30–40 years [6, 7]

The reported incidence of giardiasis in the UK is likely to underestimate the true incidence for several reasons. Patients do not always present to their

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General Practitioner (GP) when they have symptoms and because diarrhoeal specimens are not routinely tested for *Giardia* infection in the UK. Ascertainment also depends on the readiness of GPs to request a faecal specimen from patients presenting with gastroenteritis. The Health Protection Agency (HPA, now Public Health England) issued guidelines to GPs in 2007, updated in 2010 [8] on when to request a specimen, but how widely they are used is unknown. Additionally, among specimens that are sent for laboratory testing, there are differences in ascertainment due to variation in laboratory testing protocols, and in the sensitivity and specificity of the diagnostic tests. There is no standard *Giardia* diagnostic protocol for NHS laboratories. Laboratories may use criteria to avoid testing specimens that are considered likely to be negative for *Giardia*, such as only testing specimens related to travel, specimens from children or specimens from patients with prolonged diarrhoea. These criteria may be different for different laboratories and may rely on the GP adding a note, e.g. about recent travel, on the request form. For diagnosis, laboratories may prefer the traditional method of microscopy and are reluctant to introduce newer, more sensitive methods like enzyme immunoassay (EIA), due in part to the additional costs.

This paper is concerned with specimens tested for giardiasis in Central Lancashire. Since 2002 all faecal specimens submitted by GPs in Central Lancashire have been tested for infection with *Giardia* by the Preston laboratory. Previously, the laboratory method used to detect *Giardia* was light microscopy of faecal specimens but this was relatively insensitive. In 2002, the Preston laboratory introduced a monoclonal EIA antigen detection method (Giardia/Cryptosporidium CHEK®, Techlab, USA). Positive results indicating the presence of *Giardia* were confirmed by light microscopy until April 2006, after which an immunochromatographic assay (RIDA®QUICK Giardia, R-Biopharm Rhone Ltd, Germany) was used. This has been associated with a trebling of diagnosed infections, with the increase most marked in males aged 25–44 years [9]. Since then, all specimens in Central Lancashire have been processed using this assay. There is now a period of over 10 years in which every faecal specimen requested from patients presenting to a GP with diarrhoeal disease has been routinely assessed at the Preston laboratory for *Giardia* infection using a sensitive test. The aim of this study is to use these data to assess the 'practice-level specimen requesting rates' (rate of specimens), i.e. the number of faecal specimens requested as a proportion of the practice population per year, in Central Lancashire, to examine the differences between GP practices and to estimate the pattern of unexplained spatial variation in the rate of specimens after adjustment for deprivation. If there is a pattern in GP requesting rates, it is possible that the pattern of giardiasis incidence will be confounded by some characteristic of the GP practice or the GP practice's location.

To achieve these objectives, we investigated the rate of specimens, the rate of positive specimens per specimens tested, and the rate of positive specimens per 1000 population for 2011 by GP practices in Central Lancashire. We also analyse the cumulative rate of specimens which tested positive for giardiasis during 2003–2011, since the counts of positive specimens are low, this longer period provides more information and allows us to make inference about the rate of positive specimens. We fit statistical models to characterize the magnitude and significance of any differences in rates. Then we identify any spatial pattern in rate of specimens and assess its potential contribution to the spatial distribution of giardiasis in Central Lancashire. If no spatial correlation is found, we can eliminate spatial variation in rate of specimens as a contribution to the spatial variation in the rate of giardiasis.

METHODS

Data

The study area was Central Lancashire, an administrative district consisting of the Local Authorities (LAs) Chorley, South Ribble and Preston. There were 60 GP practices in the study region. Figure 1 shows LA boundaries and locations of GP practices. Data on numbers of faecal specimens sent for analysis and on the laboratory results were obtained from several sources and linked via a unique identifier, the GP practice code. Data on the total number of faecal specimens sent for testing by GP practice in 2011, the most recent year available, was obtained from the laboratory at Royal Preston Hospital. Data for other years could not be obtained due to the time required to code the data appropriately for this study. Data on the GP practice populations for 2012 was obtained from the Lancashire and South Cumbria Agency (LaSCA). The GP practice populations include all of the people registered with each GP practice in 2012. The database holding population information is

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Fig. 1. Index of multiple deprivation (IMD) scores by GP practice. Larger circles correspond to higher IMD scores, shading of dark grey to white circles indicates low to high IMD scores.

constantly updated and due to the way the data is stored, it is not possible to obtain archive information, therefore only data from 2012 was available. Information on faecal specimens which tested positive for giardiasis in 2003–2011 was obtained from surveillance data held by the Cumbria and Lancashire Health Protection Unit. For each specimen that tested positive, the GP practice and date of test was recorded.

Deprivation for each GP practice was classified at the Lower Super Output Area (LSOA) level using the English Indices of Deprivation 2007 [10] as an index of multiple deprivation (IMD). The IMD is a single summary measure based on seven domains of deprivation: Income Deprivation; Employment Deprivation; Health Deprivation and Disability; Education, Skills and Training Deprivation; Barriers to Housing and Services; Crime; and Living Environment Deprivation. We scaled the IMD by 1000 for ease of interpretation of the resulting estimates after fitting the model.

Statistical analysis

To investigate potential differences in specimen requesting rates between GPs, we fitted a set of binomial regression models and a Poisson regression model, both with random effects [11], we designated these models 1 and 2, respectively. We fitted model 1 to each of the following outcomes: (i) the rate of specimens sent to the laboratory by practice during 2011 per 1000 practice population, (ii) the rate of specimens sent for analysis by practice that were found positive for *Giardia*, per 1000 specimens in 2011, and (iii) the rate of positive specimens by practice from 2011 per 1000 practice population. In each model independent variables were GP practice and IMD. (See online Supplementary Material for further details.)

Model 2 uses the Poisson approximation to the binomial for ease of fitting, and expands model 1 to include time (see Supplementary Material). The general trend is included as a factor for year and seasonality (week) is modelled by harmonic regression. The dependent variable was the cumulative rate of positive specimens by practice from 2003 to 2011 (i.e. total number of positive specimens from 2003 to 2011) per 1000 practice population. Independent variables were week within year (0–52), year (2003–2011), IMD and GP practice.

Inference

The random effects in models 1 and 2 describe the differences in rates between GP practices adjusted for IMD. In order to assess whether there are significant

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Table 1. *Descriptive statistics for main input and output variables*

Variable	Mean	S.D.	Min	Max
Practice population	5 857	4 183	1 486	18 705
Index of multiple deprivation	24·23	18·12	3·20	67·54
Rate of specimens in 2011 per 1000 population	17·47	8·11	0·00	43·00
Rate of positives in 2011 per 1000 specimens	8·13	12·30	0·00	58·82
Rate of positives in 2011 per 1000 population	0·13	0·17	0·00	0·67
Cumulative rate of positives in 2003–2011 per 1000 population	0·77	0·69	0·00	3·61

differences between GP practices (i.e. the variance σ^2 of the random effects is significantly different from zero), models 1 and 2 were compared to corresponding models which do not have a random effect. The significance of the random effect was assessed using a non-standard likelihood ratio (LR) test according to Self & Liang [12], in which the P value for the test is half the P value obtained using the χ^2_1 distribution.

Diagnostic test for residual spatial correlation

Models 1 and 2 assume there is no spatial correlation between the responses. We conducted a test for spatial correlation between the random effects to investigate this using the variogram of the fitted random effects (see Cressie [13] and Supplementary Material for further details).

RESULTS

The mean practice population was 5857 [standard deviation (S.D.) = 4183]. The IMD score at the site of GP practices had a mean of 24·23 (S.D. = 18·12). This is slightly higher than the UK average for LSOAs of 21·67 [14]. IMD scores varied across the study region, ranging from 3·20 to 67·54, with GP practices in city centres having higher IMD scores than rural GP practices (Fig. 1).

The GP practice was recorded for 40% (307/770) of positive specimens on the surveillance database. The mean specimen requesting rate across all GP practices in 2011 was 17·47 (S.D. = 8·11) per 1000 practice population (Table 1, Fig. 2). The specimen rate varied from 0–43 per 1000 practice population, although there was no apparent spatial clustering by testing rate (Fig. 3). The mean rate of positives per 1000 specimens in 2011, 8·13 (S.D. = 12·30), gives an indication of the magnitude of the proportion of these specimens which are giardiasis cases. The mean rate of positives in 2011 per 1000 practice population was 0·13 (S.D. = 0·17). The mean cumulative rate of positives for 2003–2011 per 1000 practice population was 0·77 (S.D. = 0·69). There was no clear link between location and rate of positives in 2003–2011, or between location and rate of positives in 2011 only, with high rates observed close to lower rates (Figs 4 and 5).

Fitted models

The effect of IMD was not significant for any of the outcomes (Table 2). The random effect for GP practice was significant for the rate of specimens from 2011 per 1000 practice population (LR P value $< 0{\cdot}001$) indicating a difference between GP practices.

The variances of the random effects for the rate of specimens from 2011 which tested positive per 1000 specimens (model 1ii) and for the rate of positive specimens from 2011 per 1000 practice population (model 1iii) was estimated as zero (LR P value = 0·500), indicating there is no observable difference in these measures in GP practices.

The rate of positive specimens per 1000 population varied during 2004–2011 compared to 2003 and the trend for year was significant in the model (LR P value $< 0{\cdot}001$). There was a decrease in the rate of giardiasis in 2007–2009 with those years having around half the number of positive specimens compared to 2003 (Fig. 6). This was followed by a marked increase in the rate of giardiasis in 2010 and 2011 with around twice the number of cases in those years compared to 2003. The effect of seasonality in the model was significant (LR P value = 0·032) and the trend had an amplitude of 0·2 (Fig. 7). This indicates a lower rate of giardiasis for weeks 10–17, i.e. a one fifth decrease in positive specimens in spring compared to winter, and a higher rate of giardiasis in weeks 35–45, i.e. a one fifth increase in positive specimens in autumn. The random effect for GP practice was also significant (LR P value $< 0{\cdot}001$) indicating a difference between GP practices.

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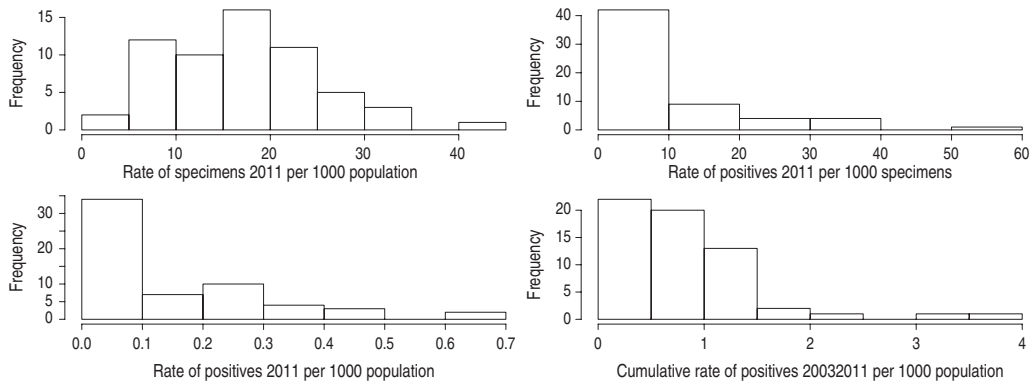

Fig. 2. Histograms of main output variables showing the spread of values for different GP practices.

Fig. 3. Rate of specimens in 2011 per 1000 population by GP practice. Larger circles correspond to higher rates of specimens, shading of dark grey to white circles indicates low to high rates of specimens.

Diagnostic test for residual spatial correlation

The variogram for the rate of specimens (Fig. 8*a*) mostly lies within the reference band, apart from between distances of about 3000–6000 m. There was no overall trend in the variogram and no *a priori* reason for interest in the GP specimen requesting behaviour at 3000–6000 m, therefore the variogram provides little evidence of a spatial pattern in the values of the random effects. The *P* value from a formal test was 0.079. This supports the observation in Figure 3 of no clear link between location and specimen requesting rate.

The variogram for the cumulative rate of positive specimens per population from 2003 to 2011 (Fig. 8*b*) lies completely within the reference band. Again, there is no overall trend in the variogram, and with a *P* value of 0·604, the variogram provides no evidence of a spatial pattern in the values of the random effects. This supports the observation made previously of Figure 4 of no clear link between location and specimen requesting rate.

DISCUSSION

We have presented the results of the analysis of specimen requesting rates to assess variability in these rates between GP practices. Our analysis suggests that there are differences in the rate of specimens for 2011 for

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Fig. 4. Rate of positives in 2003–2011 per 1000 population by GP practice. Larger circles correspond to higher rates of positives, shading of dark grey to white circles indicates low to high rates of positives.

Fig. 5. Rate of positives in 2011 per 1000 population by GP practice. Larger circles correspond to higher rates of positives, shading of dark grey to white circles indicates low to high rates of positives.

different GP practices but no significant differences among GP practices in the rate of positive specimens per 1000 specimens tested or in the rate of positive specimens per 1000 population. There was a difference by GP practice in the cumulative rate of positive specimens during 2003–2011 per 1000 population; however, there was no spatial pattern to specimen rate or the cumulative rate of positive specimens.

This is the first study to look at GP requesting rates of faecal specimens in the context of *Giardia*. Other

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Table 2. *Results of fitting binomial regression models (model 1) and a Poisson regression model (model 2) to the outcome variables*

		IMD		Random effect for GP practice	
Model	Outcome variables	Regression estimate, β (95% CI)	*P* value	Variance	Likelihood ratio, *P* value
Model 1i	Specimens to laboratory per 1000 practice population, 2011	0·849 (−7·410 to 9·108)	0·840	0·319	<0·001
Model 1ii	Positive specimens per 1000 specimens, 2011	11·367 (−4·221 to 26·955)	0·153	0·000	0·500
Model 1iii	Positive specimens per 1000 practice population, 2011	11·296 (−4·089 to 26·680)	0·150	0·000	0·500
Model 2	Positive specimens per 1000 practice population, 2003–2011	−3·480 (−14·885 to 7·926)	0·550	0·294	<0·001

IMD, Index of multiple deprivation; CI, confidence interval.

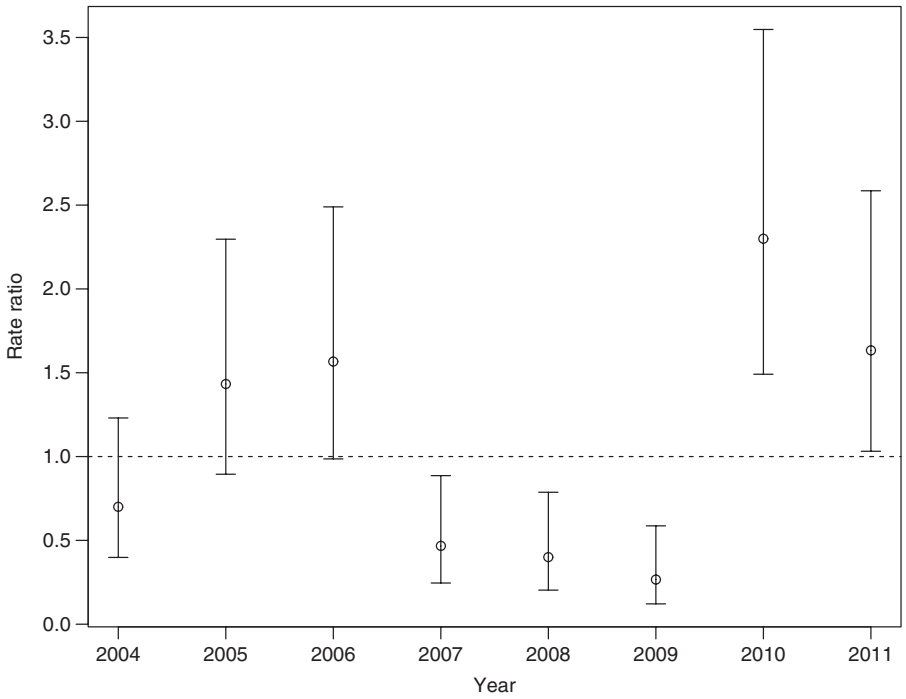

Fig. 6. The rate ratio of positive specimens per 1000 practice population in each year and positive specimens per 1000 practice population in 2003, with 95% confidence intervals. A rate ratio of 1 indicates no difference between the rate of positive specimens in that year and the rate of positive specimens in 2003.

papers have not conducted a detailed analysis of specimen requesting rates, despite the information this type analysis can add to the issue of under-diagnosis of giardiasis. In this paper, we add to the body of information on GP requesting rates and how they may contribute to the number of reported cases of giardiasis. Our method of analysis could be repeated in other geographical regions if appropriate data from routine *Giardia* testing become available.

The dataset provides complete enumeration of faecal specimens over a contiguous geographical region. Since all faecal specimens are tested for *Giardia*, the rate of positive specimens is not subject to laboratory testing bias due to selective testing. This provides a complete picture of the study region.

There are several limitations with the data we had available, which may impact on the results. The GP practice code was only recorded for 40% (307/770)

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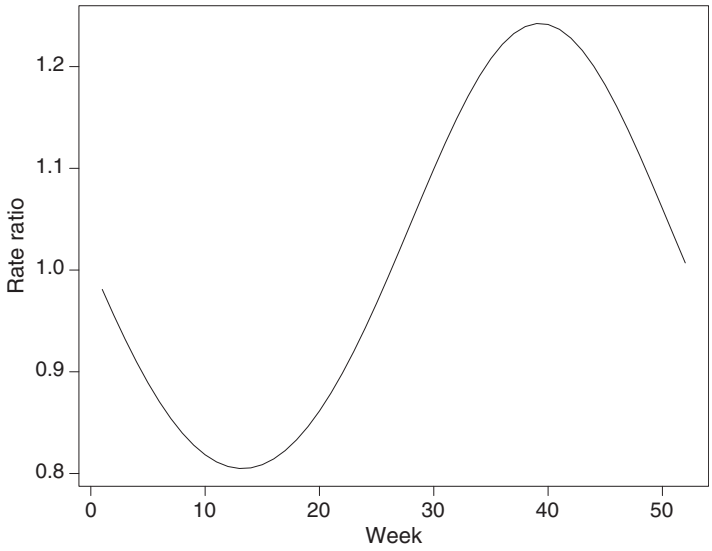

Fig. 7. The rate ratio of positive specimens in 2003–2011 per 1000 practice population in each week (1–52) and positive specimens in 2003–2011 per 1000 practice population in week 0, showing seasonality. A rate ratio of 1 indicates no difference between the rate of positive specimens in 2003–2011 per 1000 practice population in that week and the rate of positive specimens in 2003–2011 per 1000 practice population in week 0.

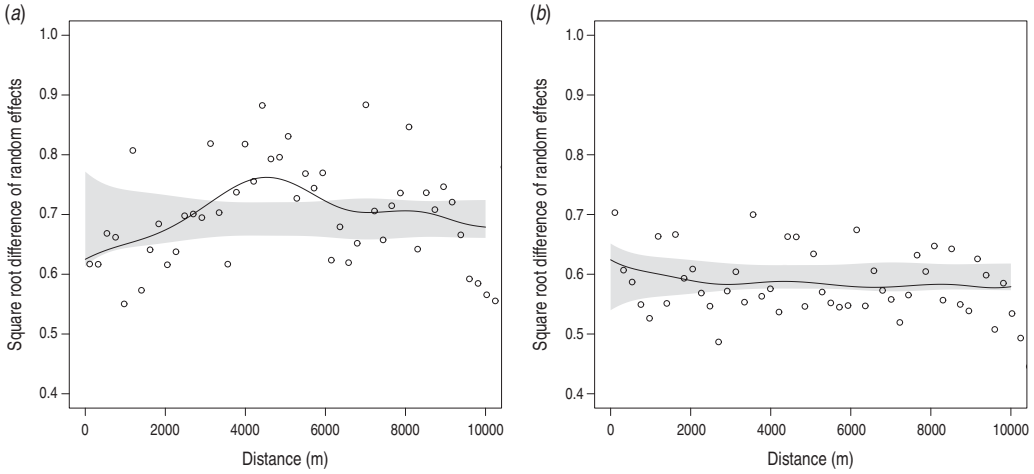

Fig. 8. Variograms of fitted random effects for (*a*) rate of specimens and (*b*) rate of positive specimens in 2003–2011, with reference bands. Each point is the average over the pairs of observations in the bin (a small range of distances).

of positive specimens on the surveillance database. This was due to an administrative issue and there is no systematic pattern in whether GP practice was recorded, so this should not affect conclusions of differences between GP practices. Data were most complete from 2010 onwards. In addition, some (estimate <5%) of the recorded GP names and addresses for the laboratory requests in 2011 did not correspond with recognized practice names from LaSCA. This means the number of specimens in our data is only a proportion of the total specimens requested and this proportion may not be the same for all GP practices. Moreover, while we have case data available for 2003–2011, we only have GP specimen requesting data for 2011. GP specimen requesting rates may have changed between 2003 and 2011.

It is possible that the results are affected by differences in healthcare-seeking behaviour for diarrhoea across the study region. Data on this are not available at the level of the participating practices, and therefore we were unable to assess the effect.

There may be concern about the differing requesting rates between GP practices. However, other

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studies have suggested that while there may be differences in specimen requesting rates between different GP practices, there are no common themes between those with low, medium or high requesting rates, in terms of criteria used to decide whether to request a specimen and of questions asked by GPs to patients concerning factors such as recent travel or visits to farms [15].

The differences between GP practice for two of our outcome measures was not significant (the rate of specimens from 2011 which tested positive per 1000 specimens and the rate of positive specimens from 2011 per 1000 practice population). This could indicate there is no actual variation between GP practices, but it could also be explained by the low number of positive specimens, making any difference undetectable. This demonstrates the benefit of investigating the cumulative rate of positive specimens from 2003 to 2011 in addition to those from 2011 only. In our interpretation of these results, we have made the assumption that the GP practice populations remained constant over the period 2003–2011 as we only have data for the 2012 population. We think this is reasonable because the population in the area has not changed greatly over the period: for 80% of LSOAs in the study area, population change has been less than 20% (19·69% for 80% of urban LSOAs, 17·40% for 80% of rural LSOAs) and for 80% of LSOAs the change in mean age has been less than 3·75 years (3·70 for 80% of urban LSOAs, 3·84 for 80% of rural LSOAs) between the 2001 and 2011 censuses [16, 17]. However, using data from this extended period provides larger counts of positive specimens than from just one year and so allows us to make inferences about positive specimens rather than only total specimens requested. While there are differences between GP practices in the rate of specimens from 2011 and the cumulative rate of positive specimens from 2003 to 2011, the spatial analysis indicates that there is no spatial pattern. This means that any analysis of spatial variation in *Giardia* incidence is unlikely to be confounded by variation in GP reporting rates.

Although IMD is commonly associated with disease incidence, it is not significant here. The IMD score used here is a measure of the IMD at the location of the GP practice and while patients are expected to live reasonably close to their GP practice, IMD can change over small distances and this measure may not accurately reflect the IMD of the patients.

The mean rate of positives in 2011 per 1000 practice population was 0·13, greater than one ninth of the mean cumulative rate of positives in 2003–2011 per 1000 practice population, which is what we would expect if the rate was constant over time. However, this may also reflect the poorer quality of data earlier in the study period.

In a follow-up study, we will investigate the presence of spatio-temporal clusters in case-control data in the same region. The results of this study are reassuring as any clusters found in the case-control data could be genuine clusters or could be the result of differences in GP behaviour in terms of specimen requesting rates. This analysis suggests that the chance of this type of confounding occurring will be reduced.

SUPPLEMENTARY MATERIAL

For supplementary material accompanying this paper visit http://dx.doi.org/10.1017/S0950268814002350.

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DECLARATION OF INTEREST

None.

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