

Inequalities in the incidence of infectious disease in the North East of England: a population-based study

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SUMMARY

The objective of this study was to measure the association between deprivation and incidence of 21 infectious diseases in the North East of England (2007–2011). We used count regression models with the Index of Multiple Deprivation and population/landscape data for small areas (~1500 persons). Deprivation significantly predicted incidence ($P < 0.05$) for 17 infectious diseases. The direction of association was broadly consistent within groups: increased incidence with increased deprivation for all three bloodborne viruses, 2/3 invasive bacterial diseases, 4/5 sexually transmitted infections (STI) and tuberculosis (TB); decreased incidence with increased deprivation for 5/6 infectious intestinal diseases (IID) and 2/3 vaccine-preventable diseases. Associations were removed for all but one IID (*E. coli* O157 infection) after accounting for recent foreign travel. Hepatitis C virus, TB and STI are priority infections for reduction of inequalities associated with deprivation in the North East of England.

Key words: Analysis of data, infectious disease epidemiology, modelling, prevention, public health.

INTRODUCTION

The consideration of health inequalities is at the forefront of public health in the UK [1], where their reduction is part of the mission for public health [2]. Discussion of health inequalities is generally restricted to non-communicable diseases [2] despite the established link between decreasing socioeconomic status and increased risk of a multitude of diseases, including infectious diseases [3].

The dedication of resources to narrowing health gaps must be guided by a wider appreciation of the complex and diverse social and societal determinants of health [4]. For infectious diseases these determinants

increase the risk of effective contact with the infectious agent either through an increased likelihood of exposure and/or an increased innate susceptibility to infection/progression to disease. Targets for intervention include those that act through behaviour, the proximate living environment, neighbourhood characteristics and individual-level predisposition (such as chronic diseases, mental health, nutrition) [3] as well as immunity through vaccination. Engaging in risky behaviour may be associated with a lack of individual empowerment for lower socioeconomic classes, the restriction of life choices and a tendency to have a more fatalistic view of health [3, 5].

For infectious diseases, a relatively deprived social environment can equate to an increased risk of infection in a variety of ways. Although this is not as well studied as it has been for non-communicable diseases, considerable evidence exists for an increased burden of certain infectious disease linked with (but not

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exclusively) reduced access to healthcare [6], overcrowding [7], social segregation [8] and poor or damp housing [9]. In addition, chronic diseases are often pre-disposing factors for infectious diseases and have a higher prevalence within disadvantaged populations [10] as do anxiety and depression [11, 12].

As social disadvantage and deprivation undoubtedly restrict life chances and life choices [3], behavioural risk factors are themselves, at least in part, linked to the social gradient by levels of risk associated with the social and structural environment [13]. A living environment with low social capital places an individual at increased risk of exposure to infections associated with behavioural risk [14]. Associations which have been found between deprivation and increased risk of hepatitis C virus (HCV) infection [15] and human immunodeficiency virus (HIV) infection [16] may represent functions of the social environment.

In order to understand the association between the living environment and levels of risk it is necessary to consider the causal pathway between living in a deprived neighbourhood and ill health [17]. For infectious disease the number of potential interventions may be considerable and highly specific to the epidemiology of individual infections or groups of infection. It is therefore logical to first assess the relationship between deprivation and infectious disease incidence within defined populations in order to determine which infections contribute to inequalities and subsequently identify clues to aetiology and potential targets for intervention.

The North East of England has a population of about 2.6 million persons and is largely ethnically homogeneous; 95% of the population reporting their ethnicity as white at the 2011 census [18]. The North East has a disproportionate level of deprivation: 33% of small area populations (average 1500 persons) are within the most deprived national quintile, the highest percentage of any region in England [19]. Here we have used count regression models to estimate the direction and size of inequalities associated with levels of deprivation and the 5-year (2007–2011) incidence of 21 different infectious diseases for small area populations in the North East of England.

METHODS

Infectious disease data

Case data was available for 21 different laboratory-confirmed infections with an annual incidence

>1 case/100 000 population and with geographical coding for individual cases available at postcode level. Cases with specimen dates between 1 January 2007 and 31 December 2011 were extracted from the Public Health England Centre North East surveillance system for infections of public health significance or the Genitourinary Medicine Clinic Activity Dataset (GUMCAD) (Table 1). Cases from the North East surveillance system were linked to population data by postcode of residence using the Office for National Statistics (ONS) Postcode Directory (2011 edition) (all ONS data available from www.ons.gov.uk). Data from GUMCAD contains geographical coding and no additional linkage was necessary. For data from the North East surveillance system, cases were removed where no postcode of residence was available (prisons and those cases where clinics, testing laboratories and health service centres were provided in lieu of a residential address), although for most infections these proportions were known to be small.

Given that substantial numbers of cases of infectious intestinal disease (IID) in England are associated with recent foreign travel, separate datasets were used with and without those cases where recent foreign travel was reported (all IID except campylobacteriosis, where data on recent foreign travel is not routinely recorded).

Small area data

Lower super output areas (LSOA) are small statistically bounded areas with a national average population of 1500 persons. Populations for LSOA were stratified by age group (0–15, 16–29, 30–44, 45–64, ≥ 65 years) using ONS mid-2010 population estimates. According to this data, the 1656 LSOA for the North East have an average total population size of 1774 persons (range 468–7031). The area of each LSOA (in km²) was calculated from area data freely available from ONS.

The ethnic diversity of each LSOA was coded as an ordinal variable based on the number of different ethnic groups (range 0–5) each making up $\geq 5\%$ of the LSOA population from the 2011 census. In addition, minority ethnic groups were defined as ethnic groups which alone made up $\geq 15\%$ of the population of a LSOA. This definition was chosen so that no LSOA in the North East had more than one minority ethnic group; 24 LSOA contained a minority ethnic group: Bangladeshi (8), Chinese (2), and Pakistani (14).

Table 1. *Infectious diseases and datasets used to measure the association between incidence and deprivation in the North East of England, 2007–2011*

Group	Dataset*	Cases (n)					Annual rate/ 10 000 persons (95% CI#)	Note
		All	No address/ out of area†	Prison/ health service	Foreign travel- associated‡	Included in models§ (%¶)		
BBV	HBV infection	914	11	127	11	776 (84.9)	0.59 (0.50–0.70)	New diagnoses (acute and chronic)
	HCV infection	1560	10	490	0	1060 (67.9)	0.81 (0.71–0.93)	New diagnoses (acute and chronic)
	HIV infection	254	48	—	—	206 (81.1)	0.20 (0.15–0.26)	New diagnoses
IBD	Invasive GAS infection	271	2	0	2	269 (99.3)	0.20 (0.15–0.27)	
	Invasive meningococcal infection	364	2	0	1	362 (99.5)	0.28 (0.22–0.35)	
	Invasive pneumococcal infection	1294	2	0	2	1292 (99.8)	0.99 (0.87–1.12)	Conjunctivitis excluded
IID	Campylobacteriosis	15112	32	13	265	15067(99.7)	11.56 (11.15–12.00)	
	Cryptosporidiosis	1096	0	1	247	1095 (99.9)	0.84 (0.73–0.96)	
	<i>E. coli</i> O157 infection	341	0	1	52	340 (99.7)	0.26 (0.20–0.33)	
	Giardiasis	191	0	0	69	191 (100.0)	0.15 (0.10–0.20)	
	Salmonellosis	2177	8	0	632	2169 (99.6)	1.66 (1.51–1.83)	
	Shigellosis	216	0	0	86	216 (100.0)	0.16 (0.12–0.22)	
STI	Chlamydia infection	31754	4763	—	—	26991(85.0)	25.89 (25.27–26.51)	Does not include NCSP data
	Genital herpes	4945	750	—	—	4195 (84.8)	4.02 (3.78–4.28)	First episodes only
	Genital warts	18465	2700	—	—	15765(85.4)	15.12 (14.65–15.60)	First episodes only
	Gonorrhoea	3506	586	—	—	2920 (83.3)	2.80 (2.60–3.01)	
	Syphilis	458	99	—	—	359 (78.4)	0.35 (0.28–0.42)	Diagnosis in IDU excluded
TB	Tuberculosis	500	3	4	1	493 (98.6)	0.38 (0.31–0.46)	
VPD	Measles	192	0	0	2	192 (100.0)	0.15 (0.10–0.20)	
	Mumps	1011	6	2	0	1003 (99.2)	0.77 (0.66–0.88)	
	Pertussis	248	0	0	0	248 (100.0)	0.19 (0.14–0.25)	

BBV, Bloodborne viruses; GAS, group A streptococcal; HBV, hepatitis B virus; HCV, hepatitis C virus; IBD, invasive bacterial diseases; IDU, infectious disease unit; IID, infectious intestinal diseases; NCSP, National Chlamydia Surveillance Programme; STI, sexually transmitted infections; TB, tuberculosis; VPD, vaccine-preventable diseases.

* Datasets are for the North East of England taken from either the Public Health England Centre North East surveillance system for laboratory-confirmed infections of public health significance or from the Genitourinary Medicine Clinic Activity Database (HIV and STI datasets) with specimen dates 1 January 2007–31 December 2011.

† Cases with either a missing residential address or a reported residential address outside the North East.

‡ For IID a separate dataset was modelled after removal of recent foreign travel-associated cases.

§ All cases minus those with no address/out of area and prison/health service.

¶ Percentage of the raw dataset.

|| Of the modelled dataset.

95% exact Poisson confidence interval.

The morphology of each LSOA was designated as urban, town and fringe, village or hamlet and isolated dwellings according to rural and urban area classification (RUAC) [20].

Index of Multiple Deprivation (IMD)

North East quintiles (Q1–Q5) of the 2010 Index of Multiple Deprivation [21] were used for all modelling: (Q1) 1·74–10·96; (Q2) 10·97–19·60; (Q3) 19·61–29·66; (Q4) 29·67–42·27; (Q5) 42·28–80·51.

Count regression modelling

Each infectious disease was modelled separately using the count of cases by LSOA as outcome and with the following explanatory variables: population sizes (1000 persons; continuous variable) for five age groups (0–15, 16–29, 30–44, 45–64, ≥ 65 years), area of LSOA in km² (quartiles; categorical variable, reference group smallest area), RUAC (categorical variable, reference group urban), minority ethnic group (if present; categorical variable, reference group no minority group), ethnic diversity (categorical variable, reference group no ethnic diversity) and IMD quintile (categorical, reference group least deprived quintile). The natural logarithm of the all-persons mid-2010 population size for each LSOA was entered into the model as an offset. A robust cluster variance estimator was used by clustering on the 12 local authority (LA) areas of the North East of England (median 122 LSOA per LA, range 58–320).

For each dataset the best-fitting model was selected according to a hierarchical approach: (1) fit of a Poisson model using the deviance goodness-of-fit test; (2) fit of a zero-inflated Poisson (ZIP) model assessed by the Vuong test [22] and Akaike's Information Criteria (AIC) relative to the Poisson model; (3) fit of a negative binomial model using a boundary likelihood ratio test (LRT) for improvement on the Poisson model and AIC for improvement upon ZIP; (4) fit of a zero-inflated negative binomial (ZINB) model assessed by the Vuong test relative to the negative binomial model and Akaike's Information Criterion (AIC) relative to the best fitting of the best-fitting model from (1)–(3). A reduction in AIC of $>2\cdot5$ was considered as a significant improvement in fit [23]. Rejection of the more parsimonious Poisson and negative binomial models by their zero-inflated equivalents required a significant Vuong test ($P < 0\cdot05$), irrespective of AIC scores.

Where the goodness of fit for a Poisson model was poor ($P < 0\cdot001$) the negative binomial model was selected by comparison of AIC score with the Poisson model without consideration of the boundary LRT.

The assumption of linearity for each age group population size was assessed for evidence of a monotonic relationship with outcome for adjusted quartiles of each variable for each final model [24]. The stability of coefficients of all predictors to the removal of outlying counts was assessed for each final model. Deviance (Poisson and negative binomial models) [23] or Pearson (ZIP and ZINB models) [25] residuals from each final model were visually assessed for fit to a normal distribution. Model coefficients were transformed to incidence rate ratios (IRR) and associations with deprivation measured using IRR for each IMD quintile using a significance of $P < 0\cdot05$ for coefficient z scores. All statistical analysis was performed using Stata v. 11·0 (StataCorp LP, USA).

RESULTS

Model selection

For 13 of the 21 datasets, the negative binomial was selected as the best-fitting model (Table 2). Of the remaining eight datasets, three were modelled using a Poisson and five using a ZIP model. For IID datasets (except campylobacteriosis), removal of recent foreign travel-associated cases resulted in selection of a different model for two datasets (Supplementary Table S1). Bimodality of residuals for the best-fitting model was evident for 12 datasets (Table 2).

Associations with deprivation

After adjusting for demographic and area factors, deprivation remained a significant predictor of incidence in at least one quintile for all but four of the infectious diseases (Table 3, Supplementary Fig. S1). With the exception of measles, shigellosis and giardiasis, associations reflect a monotonic trend with deprivation: incidence rates either decrease or increase consistently with increasing deprivation. The direction of this association was broadly determined by the nature of the infection: bloodborne viruses (BBV), invasive bacterial diseases (IBD) (with the exception of invasive group A streptococcal (GAS) infection), sexually transmitted infections (STI) (with the exception of genital herpes) and tuberculosis (TB) all have positive associations with deprivation whereas IID

Table 2. Count regression model selection for the association between deprivation and incidence of infectious diseases in the North East of England, 2007–2011

Group	Dataset	Mean count (variance)	Zero counts (%)	Poisson model		ZIP model		Negative binomial model				ZINB model				Final model	Residuals‡	
				GOF	AIC	Vuong	AIC	ΔAIC*	LRT	AIC	Ref.†	Δ AIC*	Vuong	AIC	Ref.†			ΔAIC*
BBV	HBV infection	0.5 (1.20)	73.13	0.5974	2688.15	0.0129	2646.69	41.46	<0.0001	2640.09	ZIP	6.5950	0.2645	2609.86	NB	30.2310	NB	Bimodal
	HCV infection	0.6 (1.78)	65.70	<0.0001	3297.41	0.0001	3208.84	88.57	<0.0001	3163.59	ZIP	45.2500	Did not converge				NB	Bimodal
	HIV infection	0.1 (0.17)	89.79	1.0000	1221.36	0.0359	1209.11	12.25	0.0090	1215.70	ZIP	-6.5900	<0.0001	1209.11	ZIP	0.0000	ZIP	Normal
IBD	Invasive GAS infection	0.2 (0.16)	85.08	1.0000	1547.07	0.2220	1546.04	1.03	0.5000	1547.07	Poisson	0.0000	n.a.	1546.04	Poisson	1.0290	Poisson	Bimodal
	Invasive meningococcal infection	0.2 (0.2)	80.92	1.0000	1833.24	0.4435	1833.14	0.10	0.2410	1897.69	Poisson	-64.4500	Did not converge				Poisson	Bimodal
	Invasive pneumococcal infection	0.8 (0.88)	47.77	0.0004	3824.18	0.2869	3820.83	3.35	0.1130	3820.71	Poisson	3.4660	0.5002	3822.71	NB	-2.0000	NB	Bimodal
IID	Campylobacteriosis	9.1 (16.90)	0.06	<0.0001	8968.73	0.5015	8970.73	-2.00	<0.0001	8851.94	Poisson	116.7970	0.6873	8853.94	NB	-2.0000	NB	Normal
	Cryptosporidiosis	0.6 (0.93)	57.67	<0.0001	3701.46	0.0004	3643.18	58.27	<0.0001	3635.16	ZIP	8.0190	Did not converge				NB	Bimodal
	<i>E. coli</i> O157 infection	0.2 (0.31)	84.72	1.0000	1849.14	0.0002	1769.68	79.45	<0.0001	1772.10	ZIP	-2.4170	0.1860	1767.69	ZIP	1.9950	ZIP	Normal
	Giardiasis	0.1 (0.13)	89.79	1.0000	1181.32	0.2797	1179.32	2.01	0.0750	1179.25	Poisson	2.0710	Did not converge				Poisson	Bimodal
	Salmonellosis	1.3 (1.68)	30.56	<0.0001	4954.11	0.0639	4944.17	9.94	<0.0001	4932.55	Poisson	21.5590	0.3544	4931.58	NB	0.9740	NB	Bimodal
	Shigellosis	0.1 (0.17)	89.19	1.0000	1322.53	0.0375	1303.02	19.51	<0.0001	1304.63	ZIP	-1.6160	<0.0001	1303.02	ZIP	0.0000	ZIP	Normal
STI	Chlamydia infection	16.3 (114.75)	0.12	<0.0001	12286.15	0.2136	12402.45	-116.30	<0.0001	10794.84	Poisson	1491.3100	0.5013	10796.84	NB	-2.0000	NB	Normal
	Genital herpes	2.5 (5.53)	14.67	<0.0001	6519.80	0.0004	6463.26	56.54	<0.0001	6380.17	ZIP	83.0880	0.1768	6378.25	NB	1.9220	NB	Bimodal
	Genital warts	9.5 (37.40)	0.12	<0.0001	9719.94	0.1753	9712.69	7.25	<0.0001	9208.55	Poisson	511.3900	0.5019	9210.55	NB	-2.0000	NB	Normal
	Gonorrhoea	1.8 (3.88)	28.44	<0.0001	5515.32	0.0006	5463.17	52.15	<0.0001	5436.05	ZIP	27.1220	0.1525	5432.93	NB	3.1230	NB	Bimodal
	Syphilis	0.2 (0.31)	83.64	1.0000	1820.41	0.0033	1782.72	37.69	<0.0001	1790.35	ZIP	-7.6330	Did not converge				ZIP	Normal
TB	Tuberculosis	0.3 (0.68)	80.13	1.0000	1925.97	0.0974	1918.59	7.38	0.0030	1918.35	Poisson	7.6240	0.2148	1975.60	NB	-57.2530	NB	Bimodal
VPD	Measles	0.2 (0.35)	93.78	1.0000	1272.75	Did not converge			<0.0001	997.65	Poisson	275.0984	0.2136	994.67	NB	2.9823	NB	Normal
	Mumps	0.6 (1.36)	59.78	0.0006	3351.60	0.0146	3327.67	23.93	<0.0001	3323.82	ZIP	3.8510	0.1771	3319.82	NB	4.0010	NB	Bimodal
	Pertussis	0.1 (0.20)	87.98	1.0000	1508.98	0.0042	1464.64	44.34	<0.0001	1462.52	ZIP	2.1230	0.4800	1462.50	ZIP	2.1360	ZIP	Normal

AIC, Akaike's Information Criterion; BBV, bloodborne viruses; GAS, group A streptococcal; GOF, goodness of fit; HBV, hepatitis B virus; HCV, hepatitis C virus; IBD, invasive bacterial diseases; IID, infectious intestinal infections; n.a., not available; LRT, likelihood ratio test; NB, negative binomial; STI, sexually-transmitted infections; TB, tuberculosis; VPD, vaccine-preventable diseases; ZINB, zero-inflated negative binomial; ZIP, zero-inflated Poisson.

* Difference in AIC between the model of interest and the reference model.

† Reference model for testing.

‡ Distribution of residuals for the final model assessed by eye.

Table 3. Associations between deprivation and the incidence of infectious diseases for lower super output areas in the North East of England, 2007–2011

Group	Dataset	Model	IMD regional quintile*															No. of significantly associated quintiles†
			Q1				Q2				Q3			Q4			Q5	
			IRR	IRR	95% CI	<i>P</i> value	IRR	95% CI	<i>P</i> value	IRR	95% CI	<i>P</i> value	IRR	95% CI	<i>P</i> value	IRR	95% CI	<i>P</i> value
BBV	HBV infection	NB	1.00	1.16	0.70–1.90	0.569	1.10	0.78–1.54	0.598	1.21	0.79–1.85	0.373	2.56	1.62–4.06	<0.001	+1		
	HCV infection	NB	1.00	1.76	1.22–2.54	0.002	2.94	2.05–4.20	<0.001	4.36	2.63–7.21	<0.001	9.43	6.62–13.43	<0.001	+4		
	HIV infection	ZIP	1.00	1.06	0.58–1.93	0.857	1.35	0.87–2.09	0.182	1.89	0.98–3.66	0.059	2.17	1.15–4.11	0.017	+1		
IBD	Invasive GAS infection	Poisson	1.00	0.74	0.47–1.16	0.183	1.07	0.79–1.46	0.665	1.07	0.74–1.53	0.725	1.14	0.66–1.97	0.648	0		
	Invasive meningococcal infection	Poisson	1.00	0.92	0.51–1.66	0.777	1.52	1.06–2.16	0.021	2.28	1.36–3.81	0.002	2.46	1.44–4.17	0.001	+3		
	Invasive pneumococcal infection	NB	1.00	1.22	0.99–1.48	0.052	1.36	1.13–1.63	0.001	1.60	1.40–1.82	<0.001	2.03	1.61–2.55	<0.001	+3		
IID‡	Campylobacteriosis	NB	1.00	0.95	0.90–1.01	0.091	0.91	0.84–0.98	0.015	0.86	0.78–0.94	0.001	0.77	0.68–0.87	<0.001	–3		
	Cryptosporidiosis	NB	1.00	0.99	0.81–1.21	0.915	0.94	0.79–1.12	0.514	0.96	0.72–1.27	0.772	0.76	0.61–0.93	0.010	–1		
	<i>E. coli</i> O157 infection	ZIP	1.00	0.87	0.64–1.20	0.396	1.03	0.75–1.42	0.845	0.51	0.30–0.87	0.014	0.69	0.48–0.98	0.041	–2		
	Giardiasis	Poisson	1.00	1.04	0.74–1.46	0.807	0.67	0.40–1.10	0.112	0.46	0.29–0.74	<0.001	0.73	0.46–1.14	0.167	–1		
	Salmonellosis	NB	1.00	1.12	0.97–1.30	0.124	1.06	0.92–1.22	0.409	1.03	0.91–1.16	0.649	0.98	0.91–1.16	0.730	0		
	Shigellosis	ZIP	1.00	0.62	0.40–0.96	0.033	0.63	0.43–0.94	0.023	0.99	0.69–1.43	0.964	0.33	0.22–0.51	<0.001	–3		
STI	Chlamydia infection	NB	1.00	1.20	1.13–1.28	<0.001	1.44	1.34–1.55	<0.001	1.64	1.50–1.79	<0.001	1.79	1.58–2.02	<0.001	+4		
	Genital herpes	NB	1.00	1.10	1.02–1.18	0.632	1.19	1.12–1.28	0.425	1.39	1.28–1.52	0.484	1.40	1.26–1.55	0.485	0		
	Genital warts	NB	1.00	0.97	0.86–1.09	0.014	1.08	0.90–1.29	<0.001	1.06	0.89–1.27	<0.001	1.07	0.89–1.27	<0.001	+4		
	Gonorrhoea	NB	1.00	1.20	1.04–1.38	0.009	1.57	1.30–1.90	<0.001	1.83	1.58–2.13	<0.001	2.61	2.28–2.99	<0.001	+4		
	Syphilis	ZIP	1.00	2.01	1.47–2.76	<0.001	2.01	1.49–2.72	<0.001	2.40	1.44–3.99	0.001	3.83	2.46–5.96	<0.001	+4		
TB	Tuberculosis	NB	1.00	1.13	0.78–1.65	0.516	1.63	1.16–2.29	0.005	1.96	1.23–3.12	0.005	3.87	2.78–5.38	<0.001	+3		
VPD	Measles	NB	1.00	0.35	0.15–0.85	0.021	0.99	0.64–1.52	0.953	1.08	0.53–2.19	0.825	0.81	0.30–2.14	0.665	–1		
	Mumps	NB	1.00	1.00	0.87–1.14	0.975	0.89	0.68–1.15	0.367	0.82	0.62–1.08	0.164	0.58	0.43–0.79	<0.001	–1		
	Pertussis	ZIP	1.00	0.87	0.59–1.29	0.482	0.71	0.44–1.13	0.147	0.96	0.70–1.32	0.818	0.81	0.50–1.33	0.403	0		

BBV, Bloodborne viruses; CI, confidence interval; GAS, group A streptococcal; HBV, hepatitis B virus; HCV, hepatitis C virus; IBD, invasive bacterial diseases; IID, infectious intestinal infections; IMD, Index of Multiple Deprivation; IRR, incidence rate ratio; NB, negative binomial; STI, sexually-transmitted infections; VPD, vaccine-preventable diseases; ZIP, zero-inflated Poisson.

* IRR for North East quintiles of the 2010 IMD have been adjusted for age distribution, size of lower super output area, urban/rural classification, presence of minority ethnic groups and population heterogeneity. IMD quintile 1 (Q1) is the least deprived quintile and quintile 5 (Q5) the most deprived quintile; values in bold represent significant associations ($P < 0.05$).

† The direction of the association relative to the least deprived quintile (Q1): +, quintiles associated with increased rates of infection, –, quintiles associated with decreased rates of infection.

‡ Includes travel-associated cases.

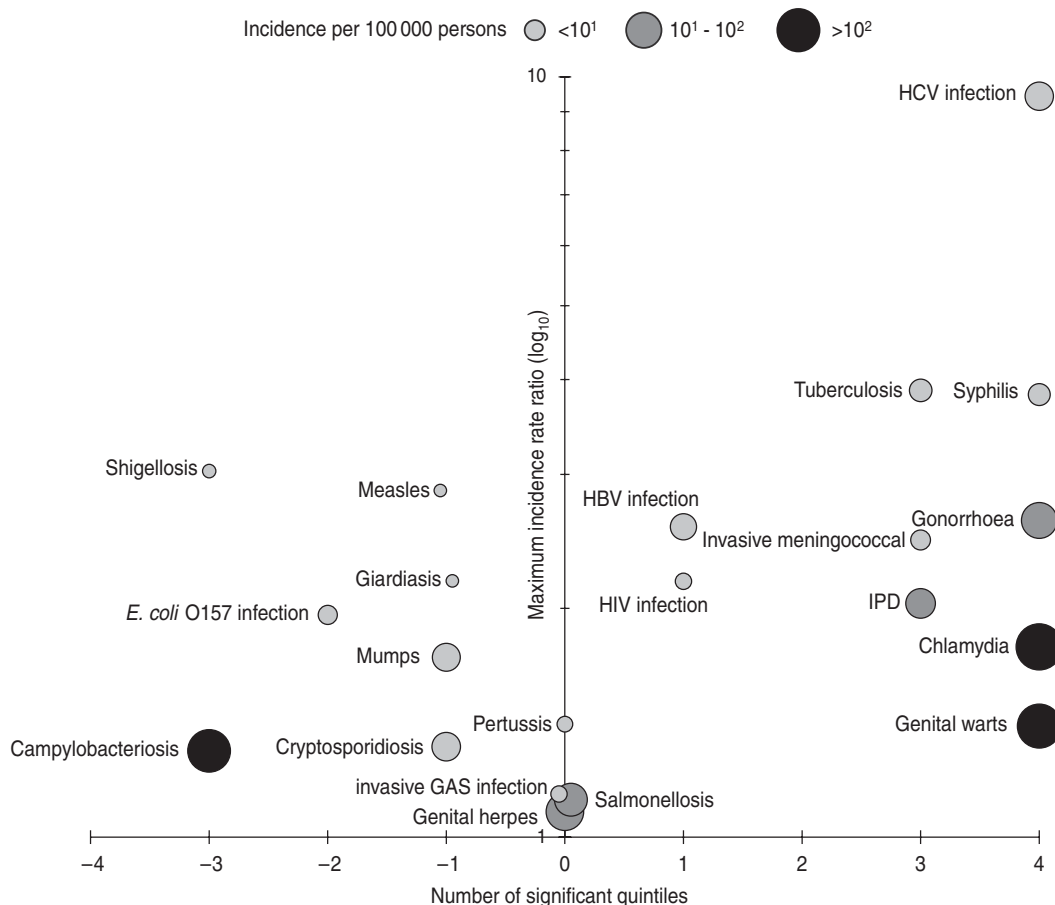


Fig. 1. Associations between deprivation and the incidence of infectious diseases in the North East of England, 2007–2011. The number of significant quintiles indicates the number of Index of Multiple Deprivation 2010 quintiles significantly associated ($P < 0.05$) with an increased incidence rate (1–4) or a decreased incidence rate (–1 to –4) after adjusting for age distribution, size of lower super output area, urban/rural classification, presence of minority ethnic groups and ethnic diversity in a multivariable count regression model. The size and shading of each data point reflects the incidence of each infection.

(except salmonellosis) have a negative association with deprivation. The association of increased rates of IID with less deprived areas was no longer evident after removal of cases associated with recent foreign travel for all datasets other than *E. coli* O157 infection (Supplementary Fig. S1, Supplementary Table S2).

The association of incidence rate with deprivation was assessed in terms of direction (either a positive or negative association), scope (the number of quintiles for which a significant association was found) and magnitude (the highest IRR for positive associations and the reciprocal of the lowest IRR for negative associations). Together, these components were used to produce a graphical representation of inequalities associated with each infection (Fig. 1). STI (except genital herpes) exhibit clear increases in incidence associated with deprivation; this is particularly marked for chlamydia and genital warts as

these infections have the highest incidence of any infection in this study. HCV infection, TB and syphilis have the greatest magnitude of any association (Table 3, Fig. 1). This is particularly evident for HCV infection where the IRR for Q5 is considerably higher than any other infection and the gradient across all five quintiles steeper than those other infections positively associated with deprivation (perhaps with the exception of TB which rises sharply across Q3–Q5). Syphilis, although associated with significantly increased rates for Q2–Q5, has a moderate gradient compared to HCV infection.

Of those infections with a negative association with deprivation (Fig. 1), campylobacteriosis stands out in having both a high incidence and scope, although we have been unable to perform a subgroup analysis after removal of recent foreign travel-associated cases for this infection. After removal of recent foreign

travel-associated cases from the cryptosporidiosis, giardiasis and shigellosis datasets the significant negative association between deprivation and incidence is no longer present (Supplementary Table S2). Measles and mumps have significantly higher rates of infection in less deprived areas but with relatively low incidence rates and the magnitudes of these inequalities are slight when compared to those on the right hand side of the central axis (Fig. 1).

DISCUSSION

This study was undertaken to further understand how the living environment influences the incidence of infectious diseases for disadvantaged populations in the North East of England. The focus of this study is a contextual one; based upon the areas where people live and the associations between characteristics of that environment and the health of the population who make their homes there [26]. Inferences drawn from this approach are for populations, rather than individuals. Clearly, considerable inequalities exist in the North East of England across a range of infectious diseases.

BBV

The association between HCV infection and deprivation stands out in this study as representing a substantial inequality which, as it likely reflects the distribution of people who inject drugs, i.e. the largest risk group for HCV infection in England [27], may be modifiable. In turn, the lack of substantial inequalities for HIV and HBV infection may reflect the low prevalence of these infections in the North East of England [28, 29]. Whether or not case ascertainment rates for BBV are associated with deprivation due to targeted testing of high-risk populations requires further study.

IBD

The association between increased deprivation and increased incidence for IBD found here supports previous studies of invasive pneumococcal disease (IPD) and meningococcal disease in England [30–33]. The social environment has been linked to the risk of IPD [30] and other potentially invasive bacteria through risk associated with overcrowding [7], malnutrition [34] and first-hand [35] or second-hand [36] exposure to cigarette smoke.

For invasive GAS infection, it may be that following improvements in housing and hygiene, factors which have in the past been thought to contribute to a higher burden of GAS infection [37], these are no longer contributing risk factors for invasive GAS infection in the North East of England. It may also be that the dynamics of carriage and invasive infection differ for invasive GAS infection compared to IMD and IPD (where a clear association between incidence and deprivation exists).

IID

We found no significant association between deprivation and autochthonous IID for all datasets except *E. coli* O157 infection. The association between decreased rates of *E. coli* O157 infection with increasing deprivation after the removal of recent foreign travel-associated cases may reflect a different pattern of exposures compared to the other IID and/or a case ascertainment bias. For salmonellosis, analysis at the genus-level may have masked associations with deprivation beyond this level [38, 39].

The negative associations between total incidence of IID and increased deprivation supports evidence from other studies for campylobacteriosis [39, 40], cryptosporidiosis [41], giardiasis [41] and shigellosis [39]. However, after removal of recent foreign travel-associated cases (for IID other than campylobacteriosis) there were no associations with deprivation other than for *E. coli* O157 infection. The inference here is that associations between IID and deprivation reported in previous studies may have been confounded by foreign travel. It seems plausible that foreign travel, and the associated exposure to the causative agents of IID, is more common for those living in areas of low deprivation. Details of recent foreign travel were not available for most campylobacteriosis cases; however, given the high numbers of expected travel-associated cases [42] it would be surprising should the negative associations for this infection not be also be reduced after removal of recent foreign travel-associated cases.

Rates of presentation to primary care for IID have been shown to be associated with increased deprivation in England [43] and the USA [44]. The negative relationship between deprivation and rates of total IID found here suggests that other variation, in either or both of the incidence of laboratory confirmable disease or of laboratory testing rates, is also associated with deprivation, and outweighs the higher rates of

presentation expected with increased deprivation. Elucidation of such factors would clarify the relationships between IID and deprivation.

STI

STI represent a clear target for reducing infectious disease inequalities in the North East of England and form a substantial burden (particularly chlamydia and genital warts). Our findings are largely consistent with evidence from other settings for chlamydia [45, 46], genital herpes [45], genital warts [45], gonorrhoea [45, 47, 48] and syphilis [49]. Although the complexity of risk for STI is great, the breakdown in social networks within communities (and the associated loss of social capital) can result in a reduction in trust, support and adherence to social norms. Such losses in social cohesion can then lead to increased risk of exposure for the population to the infectious agents causing STI [50]. Strengthening social networks within deprived areas of the North East of England could be considered as a potential structural target for prevention of STI [14].

TB

TB diagnoses are clearly associated with deprivation in the North East of England, fitting with previous national [51] and global studies [52]. The North East of England has the lowest rate of any region in England for diagnosed TB cases assessed to be as a result of a recent transmission event (~10%) [53] and a higher proportion of older cases (22% aged ≥ 65 years for this study) compared to England as a whole (14% aged ≥ 65 years for 2011) [53]. Hence many of the cases in this study are as a result of exposure within the UK at some (unknown) time in the past. Ideally, the date of effective exposure would have been associated with a contemporaneous deprivation index to examine the association between deprivation and rates of infection, but this was not possible. However, current levels of deprivation for the living environment may also have an association with the risk of an active infection (i.e. one which is diagnosed for the first time). Furthermore, any intervention strategies need also to consider extant transmission networks and exposure locations for future diagnosed cases. These associations could be studied by stratification of cases by ethnic group, but this would best be undertaken in a high-incidence area.

Vaccine-preventable diseases

We found limited evidence of inequalities associated with measles and mumps. The incidence of cases of measles, mumps and pertussis since the introduction of childhood vaccination is obviously closely linked to vaccine coverage and infection rates may be difficult to study over relatively short time periods due to the cyclical nature of their epidemics [54]. Vaccine coverage may [55, 56] or may not [57] also reflect the social gradient and disentangling all of these processes to understand the contribution of deprivation to contemporary rates of infection may be particular to different settings and populations. Although we included only laboratory-confirmed cases of vaccine-preventable disease the proportion of notified cases which are laboratory confirmed does not appear to change substantially with IMD quintile for measles, mumps or pertussis (results not shown) and suggests that case ascertainment rates (through laboratory confirmation) are not confounding the association between incidence and deprivation.

Small areas where large mumps outbreaks associated with higher education institutions had occurred appeared as outliers within the mumps dataset and removal of these outlying data points had no substantial impact on associations with deprivation (results not shown). Our data does not include the recent increase in pertussis cases across England and it is unknown whether this national increase may be associated with deprivation.

Limitations

In measuring the association between infectious disease incidence and deprivation we have attempted to adjust for confounding variables as much as was realistically possible given data availability at a small area level. Although we were able to adjust for potential confounding by age distribution, population size, population density, ethnicity and rurality, residual confounding suggests that for some infections unknown predictors of incidence remain after adjustment for these factors. When taking a broad, population-level approach to such a complex issue, adjustment for very specific explanatory variables which may be strong predictors of incidence for specific infections or groups of infections is not always possible. However, the consistency of analytical methodology here can be seen as a strength of the study: no

inherent bias exists in our attempt to understand the effects of deprivation on any one particular infection or group of infections (other than perhaps the removal of recent foreign travel-associated cases from IID). We plan to use multi-level models in further studies in order to explore the nature of residual confounding at the small area level by building further contextual factors into models [58].

We used a single indicator of deprivation (albeit one which is composed of many closely related domains, chosen to reflect varying forms of disadvantage) which provides no insight into which specific factors are associated with the pathway between exposure and infection. This measure also limits direct discussion of causality to residential areas, within which we have implicitly assumed that health outcomes are determined. Although such assumptions are required for population studies of this nature, individual-level risk is also derived from exposures and risk factors which exist in other settings, such as the workplace, which can only realistically be captured using an individual-level approach.

According to the 2011 census, the population of the North East has increased by around 20000 persons since 2001. As a consequence of this change in population size, 69 LSOA in the North East were re-drawn according to the 2011 census as the LSOA populations had become either too large or too small: 70 LSOA were created as a result and do not have an IMD score (as this was last modified in 2010). Although LSOA prior to this re-drawing can be mapped to 2011 LSOA, due to merging and complex changes to some areas, 19 pairs of LSOA have been mapped here to the same 2011 LSOA. As such, 19 sets of LSOA used the same ethnicity data.

Case ascertainment rates require consideration in epidemiological studies of this kind and certainly analysis of some of the less severe infections selected here may have included a bias where ascertainment rates may have been associated with levels of deprivation. Implicitly, we have assumed that case ascertainment rates are not associated with deprivation. Although this might not be true for all infections (e.g. HCV) [15], by adjusting for the rural/urban nature of small area populations we have adjusted for at least some potential confounding due to distance from primary healthcare services. Although we made no adjustment for the presence of recognized outbreaks, the proportion of cases associated with outbreaks for each infection was very small and we do not feel that this will have impacted on the findings and the

interpretation of how deprivation is associated with the burden of each infection.

Our outcome measure does not represent a measure of the infectious disease burden; a measure of this kind would include both morbidity and mortality, such as disability adjusted life years (DALYs) [59]. Our measured impact of infections (the number of laboratory-confirmed cases) is therefore a relative underestimate of burden for infections where mortality is high (such as for invasive GAS infection) [60] or where long-term consequences can be considerable (such as for HIV infection) [61]. Just as very severe or long-term debilitating infections are underweighted by using incidence alone, very common yet often mild infections such as those with influenza virus and norovirus are rarely laboratory confirmed in England, yet their burden to the population and cost to the health system are high [62, 63]. No small area surveillance data is available to assess associations with deprivation for pathogens of this nature and this is accepted as a missing component of this study.

Implications

Strategies to reduce inequalities associated with infectious diseases (through altering behaviour, the living environment, neighbourhood characteristics, vaccination coverage or individual-level risk factors) have the ultimate aim of producing long-term effects through tackling health inequalities at their core [64, 65]. This may require focused research to determine how very specific factors associated with deprivation may have influence on the causal pathway between exposure and infection for individuals who are part of a disadvantaged population associated with a (relatively) high incidence of infection.

This study recommends that HCV infection, TB and STI should be considered as priority infections for reduction of inequalities associated with deprivation in the North East of England – their incidences represent broad and substantial inequalities for disadvantaged populations. IPD and invasive meningococcal infection both have a lower incidence but are also strongly associated with deprivation and opportunities to address these infections should also be taken. Research into interventions to prevent these infections should specifically examine the mechanisms of transmission and progression to disease (where appropriate) that result in these inequalities. Public health programmes should target the most affected and

disadvantaged populations with the aim of ultimately reducing the burden for these populations.

SUPPLEMENTARY MATERIAL

For supplementary material accompanying this paper visit <http://dx.doi.org/10.1017/S0950268814000533>.

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DECLARATION OF INTEREST

None.

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