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Social determinants of infectious diseases: a public health priority

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Vulnerable groups are disproportionately affected by infectious diseases in every European Union (EU) Member State [1]. The level and distribution of wealth within a society plays a significant role in determining vulnerabilities to communicable diseases. A clear association between social welfare spending and mortality across EU countries has been reported [2]. The current measles outbreak in Bulgaria is a stark reminder of the urgency to act on social determinants of infectious diseases in Europe [3]. Since the onset of the outbreak in April 2009, over 23,429 measles cases and 24 deaths have been reported, 90% of which have been in the Roma ethnic community [4]. The majority of cases (>60%) were younger than 15 years and one third (30%) had not received the full course of measles-mumps-rubella (MMR) vaccination (Mira Kojouharova, personal communication June 2010). A number of factors converged to precipitate this epidemic: virus importation from Germany, socio-economic and health system reform, social marginalisation, crowded living conditions and a high degree of mobility among Roma communities (Mira Kojouharova, personal communication June 2010. Such socio-economic conditions could be fertile ground for outbreaks of other vaccine-preventable diseases (e.g. diphtheria, polio), if the agents were to be introduced into these or similar communities. Indeed, social determinants of infectious diseases are a significant public health issue throughout Europe. For instance, tuberculosis (TB) prevalence in EU Member States is inversely correlated with wealth and its distribution at an ecological level (Figure): with increasing socio-economic equality, TB rates drop [5].

Thus, addressing social determinants of infectious diseases in Europe becomes a public health priority. It is not purely an issue of solidarity and social justice. Elevated infectious disease incidence/prevalence rates in vulnerable populations pose a health threat not only to them, but also to society at large: for example, high TB rates in prisons in the former Soviet Union served as a reservoir that inoculated the overall resurgence of TB in the general population [6].

The vast majority (89%) of Europeans demand from their governments urgent actions against poverty, according to a Eurobarometer survey from 2009 [7]. The EU and its Member States have in fact committed to tackling poverty and social exclusion, yet 79 million people – 16% of Europe's population – continue to live below the poverty line (set at 60% of their country's median income) [8]. Since socio-economic inequalities lead to differential health outcomes, the strategic objectives laid down in the European Commission White Paper 'Together for health: A strategic approach for the EU 2008-2013' promote solutions to inequities in health that are linked to social, economic and environmental factors [9]; these issues are closely linked to the European Commission's overall strategic objective of Solidarity. The World Health Organization has also laid out a plan of action to tackle social determinants of health in 2008 [10]. The Portuguese EU Presidency focused on migrant health issues and, more recently, the Spanish EU Presidency embedded health inequalities in the political agenda and discussed monitoring social determinants of health, assessed progress and suggested areas of research [11]. The Belgian EU Presidency will now follow up on these initiatives with a conference on 8 and 9 November 2010, entitled 'Reducing Health Inequalities from a Regional Perspective'. The focus of the conference will be: 'What works and what does not'.

Eurosurveillance has dedicated this special issue to social determinants of infectious diseases to address some of these challenges. One paper in this issue presents different intervention strategies to reduce inequalities in infectious diseases and discusses 'what works and what does not' [12]. Two papers provide new insights about the social determinants of listeriosis [13,14]. While the incidence is relatively low, Europe has experienced a steady increase in incidence over the years [15]. Listeriosis is a potentially serious infection caused by consumption of food contaminated with the bacterium *Listeria monocytogenes*. Food products can be contaminated with *Listeria* during processing or preparation, and most cases are domestically acquired. *L. monocytogenes* is capable of multiplying in a refrigerator at +4°C and as little as 100 cfu/g is considered a health risk for healthy adults, however main risk groups for listeriosis are young children,

pregnant women, immunocompromised and elderly people [16,17]. While appropriate food storage is nonetheless important, especially in the home, preventing the initial food contamination is even more important.

Gillespie *et al.* demonstrate that human listeriosis in England is associated with neighbourhood deprivation [13]. They rank geographic areas in England according to an index of multiple deprivation (IMD) by taking into account a number of socio-economic factors: income, employment, health deprivation and disability, barriers to housing and services, living environment, crime and disorder, and education, skills and training. *Listeria* incidence increased with rising IMD (least to most deprived). The authors suggest that health education tailored to vulnerable groups should be intensified. Unfortunately, vulnerable groups tend not to respond well to health promotion interventions [12]. The resilience of *L. monocytogenes* to propagate even

under refrigeration suggests that governments should enforce regulations for food hygiene during processing, packaging and sales to prevent contamination at the source.

The paper by Mook *et al.* specifically addresses pregnancy-related listeriosis among ethnic minorities in England and Wales between 2001 and 2008 [14]. The authors take advantage of a number of data sets to assess the listeriosis risk and document a significant incidence increase among ethnic minorities in recent years [14]. While ethnicity is not inevitably linked to vulnerability, ethnic minorities tended to reside more in deprived areas [18]. In light of shifting migration patterns in Europe this apparent incidence increase has an epidemic potential that should be closely monitored.

Tick-borne encephalitis (TBE) is nowadays preventable through vaccination but nevertheless has experienced

FIGURE

Wealth inequality and tuberculosis prevalence rates in the European Union[a], 2006
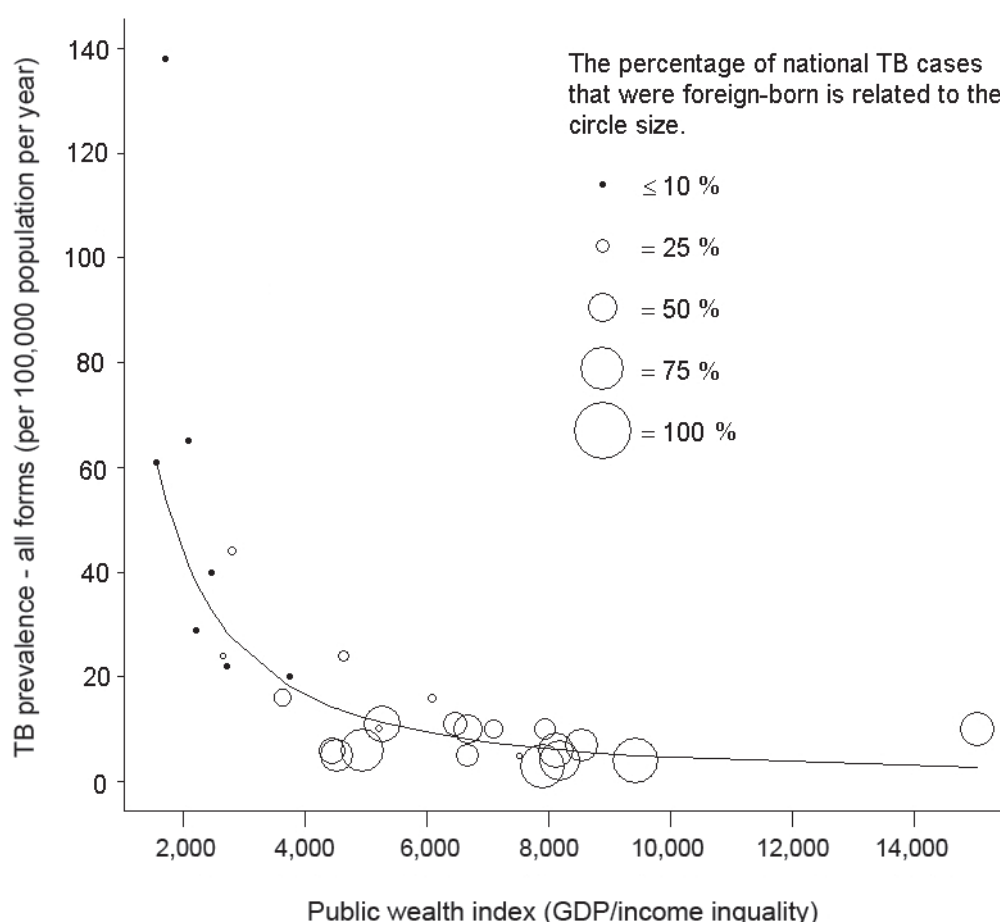
GDP: gross domestic product; TB: tuberculosis.

[a] Includes 27 EU Member States plus Norway and Iceland.

The Public Wealth Index divides a nation's economic wealth (as measured with Eurostat data on GDP in Purchasing Power Standards per capita) by its level of social cohaesion (using Eurostat's inequality of income distribution ratio). Effectively, this metric takes the relative high level of wealth in Europe into account while also controlling for its distribution. It favours very wealthy countries with low income inequality ratios: the top five scores on the public wealth index were generated by Luxembourg, Norway, Denmark, Sweden and the Netherlands.

Reproduced from Suk J, Manissero D, Büscher G and Semenza JC. Wealth inequality and TB elimination in Europe. Emerging Infectious Diseases. 2009;15(11):1812-4 [5].

an upsurge in Europe in recent years, with cases reported from new areas, including Norway and some parts of Germany that had not previously reported TBE [19,20]. Previous studies have shown that factors such as climate variations that directly or indirectly influence the transmission of the virus, the vector, the vertebrate wildlife, or people's behaviour, are correlated with variations of TBE incidence over time [21]. An article by Randolph et al. in this issue of Eurosurveillance proposes that during periods of rapid political change, socio-economic factors will play a prominent role in changing disease risk [22]. In the early 1990s, following political independence from the former Soviet Union, TBE rates surged in most central and eastern European (CEE) countries.

The studies summarised in Randolph et al. suggest strong correlations across eight CEE countries between TBE rates and the percentage of household expenditure on food. Randolph suggests mushroom picking as an alternative source of income in times of high unemployment as a driver of these rates. In Latvia, higher TBE rates were observed after forest cutting activities (probably through exposure of forest workers), at times of low economic activity (in a national level analysis), or in populations with low education levels (in a regional level analysis). Weather patterns are also described to play a role in determining human exposure to ticks, whether related to mushroom foraging or to recreational activities. These intriguing suggestions call for epidemiologic case control studies to account for potential confounders. Such studies would truly advance the field. For example, Randolph points out, in line with previous studies, that under more stable socio-economic conditions, TBE emergence may rather be the consequence of enhanced zoonotic cycles.

Today, in the wake of the financial crisis, rising unemployment and public debt in many EU countries lend further weight to the notion emphasised in all papers in this issue: socio-economic determinants of infectious diseases are a public health priority, perhaps even more urgently now than in recent times.

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Reducing health inequalities and monitoring social determinants of health in the European Union: a priority of the Spanish Presidency of the European Union 2010

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Many health problems and most causes of premature death are conditioned by social factors such as education, employment and working conditions, income, living environment and social exclusion which affect the population unequally and are largely outside of the remit of the health sector. Addressing the social determinants of health and working to achieve health equity are among the most important current public health challenges in Europe and worldwide [1].

The term 'health equity' can be described as relating to differences in population health which can be traced to unequal social and economic conditions. Those differences can be considered as systemic and avoidable and therefore be seen as unjust. Europe could and should demonstrate the potential of public health policies in terms of their benefits for health and health equity. In this sense, special attention needs to be given to vulnerable groups. As an example, protecting the health of vulnerable and marginalised groups is both an end in itself and an essential element of tackling the HIV/AIDS epidemic [2-3].

An important priority of the Spanish Presidency of the European Union (EU), January – June 2010, was to address health inequalities and the monitoring of social determinants of health in the EU. Other EU Presidencies, the European Parliament, the European Commission (EC), the World Health Organization (WHO) and further international organisations have previously addressed socially determined health inequalities through different approaches [4-9]. However, there are indications that such inequalities may be growing, aggravated by increased unemployment and uncertainty arising from the current economic crisis [10-12].

In order to achieve its objective to monitor social determinants of health and reduce health inequities the Spanish Presidency organised a series of events where policy makers and technical experts discussed and exchanged experiences from an intersectoral perspective.

At the March 2010 meeting of the employment, social policy, health and consumer affairs (EPSCO) Council, health ministers came to a common agreement on the importance of finding mechanisms to reduce the socially determined health inequalities in the EU and agreed on possible strategies for working further on the monitoring of social determinants of health [13]. The adoption of the conclusions on "Equity and Health in All Policies: Solidarity in Health" by the June EPSCO Council meeting where the Council of the EU urged all Member States to recognise the impact of the social determinants of health in shaping health status and the implications of this impact for their health and social systems, also progressed discussions [13]. A situation analysis report, commissioned by the European Commission, the WHO, the International Labour Office, universities and other relevant organisations was published and has become a relevant reference in the field [1].

The Spanish Presidency highlighted the relevance and importance of tackling socially determined health inequalities in the EU. The steps taken during the Presidency will provide a basis for reaching consensus on suggestions and best ways for implementing policies at national and international levels.

Members of the Technical Committee for the priority of the Spanish Presidency on "Monitoring Social Determinants of Health and the Reduction of Health Inequalities" are: D Catalán Matamoros (DGSPySE_inter@msps.es), K Fernández de la Hoz, P Campos Esteban, B Merino Merino, RM Ramírez Fernández, I Hernández Aguado.

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Human listeriosis in England, 2001–2007: association with neighbourhood deprivation

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Listeriosis is a rare but severe food-borne disease that predominantly affects pregnant women, the unborn, newborns, the elderly and immunocompromised people. Despite the high mortality rate of the disease, its socio-economic determinants have not been studied in detail, meaning that health inequalities that might exist in relation to this disease are not apparent. Laboratory surveillance data on listeriosis cases reported in England between 2001 and 2007 were linked to indices of deprivation and denominator data using patients' postcodes. Incidence relative to increasing quintiles of deprivation was calculated by fitting generalised linear models while controlling for population size. Patient food purchasing and consumption data were scrutinised and compared with commercial food purchasing denominator data to further quantify the observed differences in disease incidence. For all patient groups, listeriosis incidence was highest in the most deprived areas of England when compared with the most affluent, and cases were more likely to purchase foods from convenience stores or from local services (bakers, butchers, fishmongers and greengrocers) than the general population were. Patients' risk profile also changed with increasing neighbourhood deprivation. With increased life expectancy and rising food prices, food poverty could become an increasingly important driver for food-borne disease in the future. While United Kingdom Government policy should continue to focus on small food businesses to ensure sufficient levels of food hygiene expertise, tailored and targeted food safety advice on the avoidance of listeriosis is required for all vulnerable groups. Failure to do so may enhance health inequality across socio-economic groups.

Introduction

Listeriosis is a rare but severe food-borne disease caused by the opportunistic bacterium *Listeria monocytogenes*. Pregnant women, the unborn, newborns, the elderly and immunocompromised people are most commonly affected, with high associated mortality reported. Symptoms range from mild influenza-like or gastrointestinal illness to miscarriage, stillbirth, septicaemia, meningitis or encephalitis. Throughout the 1990s approximately 110 cases were reported annually in England and Wales, but from 2001 to 2008 an average of 188 annual cases were reported. The reasons for this increase – which has occurred almost exclusively in patients aged 60 years or older presenting with bacteraemia – are largely unknown [1]. Similar increases have been reported elsewhere in Europe [2,3].

The socio-economic determinants of human listeriosis have not been studied in detail before, despite numerous population-based studies of the disease [4-12]. Some studies have described the socio-economic aspects of suspected (i.e. undiagnosed) [13-16] and confirmed [17-24] gastrointestinal infections, but health inequalities that might exist in relation to listeriosis have not been investigated. A longitudinal study of human listeriosis in Bristol in England between 1983 and 1992 found that social classes I and II (higher social classes) were over-represented among cases when compared with the general population (45% versus 28%) [25]. Only 29 cases were included in this study, however, and social class data were only available for 20 of these, hence the estimates were subject to sampling variability (note the 95% confidence intervals (CI) around the above proportions: 45% (95% CI: 23.2 to 66.8) and 28% (95% CI: 27.8 to 28.2)). In order to systematically study the role of neighbourhood deprivation in human listeriosis for a larger population and over a longer time period, English national laboratory surveillance data for the period 2001 to 2007 were interrogated.

National surveillance for listeriosis in England and Wales is coordinated by the Health Protection Agency Centre for Infections. Following the voluntary referral of *L. monocytogenes* isolates for confirmation and subtyping [26-28] and/or local electronic reporting of confirmed cases, standardised clinical and epidemiological data are sought from hospital microbiologists and public health practitioners respectively [29]. The data are supplied through completion of questionnaires, which have been in use since 1990 (for hospital microbiologists) and 2005 (for public health practitioners) [29]. Epidemiological data are not routinely sought when the patient is deceased but are sometimes received. All data are stored in a bespoke database.

Methods
Case definitions

For the purposes of surveillance, a case of listeriosis is defined as a person with a clinically compatible illness from whom *L. monocytogenes* was isolated from a normally sterile site. Cases are classified further as pregnancy-associated (all maternal–fetal patients and neonatal patients, with a mother–baby pair considered a single case) or non pregnancy-associated (when the illness occurs in patients more than one month of age). Patients' ethnicity – classed as 'ethnic' if deemed to be from an ethnic minority, or 'non-ethnic' if not – was assigned to all cases using patients' names (surname and first name as available). It is important to note that this classification, undertaken by two of the authors (IAG and PM), is distinct from patients' own classification of their ethnicity, based on the 2001 United Kingdom (UK) census [30] and captured on the standardised epidemiological questionnaire. Due to restrictions in the availability of denominator data, our study was limited to cases reported from laboratories in England.

Analysis 1. Listeriosis incidence calculations

On the basis of their home postcode, cases were assigned to the Office for National Statistics' lower super output areas (LSOAs) – the smallest geographical area for which aggregated census data are routinely released, comprising 32,482 areas in England and containing on average 1,500 residents per area. We then calculated the number of all non pregnancy-associated cases, non pregnancy-associated cases aged 60 years or older and pregnancy-associated cases resident in each LSOA in each year from 2001 to 2007. Respective population data (the number of all people, all people aged 60 years or older and all live births) for each LSOA in each year were obtained from the Office for National Statistics (the number of conceptions by LSOA were unavailable). These data were combined with 2007 multiple and individual indices of deprivation [31], giving 227,374 observations.

Subsequent data manipulation and analyses were undertaken using Stata version 10 [32].

The 2007 indices of deprivation consist of seven dimensions of deprivation (income; employment; health deprivation and disability; education, skills and training; barriers to housing and services; crime and disorder; living environment) which are weighted and combined [33] to create the overall index of multiple deprivation. A rank is also provided for each dimension and the overall index, where one is the most deprived LSOA and 32,482 the least. Variables were created to represent quintiles of each dimension rank and the index of multiple deprivation, but coded to compare the least deprived LSOAs with the most. As there were instances where there were no live births in certain LSOAs in some years, data for pregnancy-associated cases were grouped further (sums of cases and population counts;

TABLE 1

Characteristics of listeriosis cases included or excluded in the study on the basis of postcode availability, England, 2001–2007 (N=1,242)

Factor	Postcode available	
	Yes (n=1,179) Number (%)[a]	No (n=63) Number (%)[a]
Study year		
2001	112 (86)[b]	18 (14)[b]
2002	106 (81)[b]	25 (19)[b]
2003	202 (91)[b]	20 (9)[b]
2004	193 (100)[b]	0 (0)
2005	179 (100)[b]	0 (0)
2006	176 (100)[b]	0 (0)
2007	211 (100)[b]	0 (0)
Case type		
Non pregnancy-associated	1033 (88)	51 (81)
Pregnancy-associated	146 (12)	12 (19)
Age group		
<60 years	385 (33)	31 (49)
≥60 years	783 (66)	27 (43)
Unknown	11 (1)	5 (8)
Ethnicity (based on name)		
Ethnic	140 (12)	12 (19)
Non-ethnic	1033 (88)	44 (70)
Undetermined	6 (1)	7 (11)

[a] Column percentage, unless stated otherwise.
[b] Row percentage.

TABLE 2

Incidence of listeriosis in relation to various markers for increasing deprivation, England, 2001–2007 (N=1,242)

Increasing deprivation quintile	Incidence relative to the least-deprived quintile (95% confidence interval)			
	All cases	Non-pregnancy-associated cases		Pregnancy-associated cases[a]
		All	≥60 years	
Indices of multiple deprivation				
1 (least)	1	1	1	1
2	1.02 (0.84–1.23)	0.98 (0.80–1.20)	0.94 (0.74–1.18)	1.16 (0.54–2.51)
3	0.93 (0.77–1.13)	0.98 (0.81–1.20)	0.96 (0.76–1.21)	0.94 (0.42–2.10)
4	1.16 (0.97–1.40)	1.09 (0.90–1.33)	1.21 (0.96–1.52)	2.34 (1.24–4.40)
5 (most)	1.38 (1.16–1.65)	1.27 (1.05–1.53)	1.36 (1.09–1.71)	2.20 (1.18–4.08)
Income				
1 (least)	1	1	1	1
2	0.98 (0.82–1.19)	0.99 (0.82–1.21)	0.97 (0.77–1.22)	1.26 (0.58–2.74)
3	0.77 (0.63–0.94)	0.83 (0.67–1.02)	0.83 (0.66–1.06)	1.21 (0.56–2.62)
4	1.18 (0.98–1.41)	1.16 (0.96–1.40)	1.24 (1.00–1.55)	2.38 (1.24–4.60)
5 (most)	1.25 (1.05–1.49)	1.17 (0.97–1.42)	1.31 (1.04–1.64)	2.10 (1.10–4.00)
Employment				
1 (least)	1	1	1	1
2	1.18 (0.97–1.43)	1.15 (0.94–1.41)	1.10 (0.87–1.39)	1.35 (0.62–2.95)
3	1.15 (0.95–1.40)	1.17 (0.95–1.43)	1.07 (0.84–1.36)	1.32 (0.63–2.76)
4	1.22 (1.01–1.48)	1.16 (0.95–1.43)	1.22 (0.96–1.55)	2.31 (1.18–4.52)
5 (most)	1.61 (1.34–1.93)	1.50 (1.24–1.82)	1.43 (1.14–1.80)	2.68 (1.41–5.08)
Health deprivation and disability				
1 (least)	1	1	1	1
2	0.97 (0.80–1.18)	0.92 (0.75–1.13)	0.98 (0.77–1.24)	1.04 (0.47–2.33)
3	1.13 (0.93–1.36)	1.08 (0.89–1.32)	1.12 (0.89–1.42)	1.19 (0.55–2.59)
4	1.17 (0.97–1.41)	1.09 (0.90–1.33)	1.24 (0.98–1.56)	2.12 (1.09–4.12)
5 (most)	1.54 (1.29–1.84)	1.37 (1.14–1.66)	1.48 (1.18–1.85)	2.58 (1.36–4.89)
Education, skills and training				
1 (least)	1	1	1	1
2	0.88 (0.73–1.06)	0.87 (0.72–1.06)	1.02 (0.82–1.28)	2.10 (1.10–4.03)
3	0.84 (0.69–1.01)	0.78 (0.64–0.95)	0.89 (0.70–1.12)	1.78 (0.91–3.46)
4	1.01 (0.84–1.20)	0.95 (0.78–1.14)	1.11 (0.89–1.39)	2.29 (1.23–4.27)
5 (most)	1.08 (0.90–1.28)	1.02 (0.85–1.23)	1.20 (0.96–1.50)	1.73 (0.92–3.26)
Barriers to housing and services				
1 (least)	1	1	1	1
2	0.88 (0.74–1.06)	0.96 (0.79–1.16)	0.95 (0.76–1.19)	0.60 (0.35–1.02)
3	0.87 (0.72–1.04)	0.95 (0.78–1.15)	1.03 (0.83–1.29)	0.86 (0.52–1.40)
4	0.87 (0.73–1.04)	0.94 (0.77–1.14)	0.92 (0.73–1.15)	0.63 (0.36–1.11)
5 (most)	0.92 (0.77–1.09)	0.93 (0.77–1.13)	1.01 (0.80–1.26)	0.84 (0.54–1.31)
Crime and disorder				
1 (least)	1	1	1	1
2	0.92 (0.76–1.12)	0.90 (0.74–1.10)	1.01 (0.80–1.28)	0.95 (0.36–2.50)
3	1.19 (0.99–1.43)	1.07 (0.88–1.30)	1.23 (0.98–1.54)	1.76 (0.75–4.17)
4	1.20 (1.001–1.44)	1.17 (0.96–1.41)	1.32 (1.05–1.65)	2.21 (0.99–4.93)
5 (most)	1.20 (1.003–1.44)	1.09 (0.90–1.33)	1.43 (1.14–1.79)	2.53 (1.16–5.51)
Living environment				
1 (least)	1	1	1	1
2	1.02 (0.84–1.24)	1.00 (0.82–1.22)	0.96 (0.76–1.21)	1.73 (0.83–3.64)
3	1.11 (0.92–1.34)	1.09 (0.90–1.33)	1.05 (0.84–1.32)	1.22 (0.56–2.66)
4	1.28 (1.07–1.54)	1.24 (1.02–1.50)	1.32 (1.06–1.65)	1.90 (0.95–3.82)
5 (most)	1.21 (1.01–1.45)	1.04 (0.86–1.27)	1.12 (0.88–1.42)	2.71 (1.44–5.11)

[a] Calculated at the local authority rather than the lower super output area (LSOA) level.

averages of deprivation measures) and quintiles recalculated to allow analysis at the larger local authority level.

Estimates of the incidence of listeriosis relative to increasing deprivation were obtained by fitting generalised linear models with a count of cases per LSOA or local authority per year as the outcome variable. Incidence in each quintile relative to the lowest quintile of deprivation (least deprived) was calculated. Four sets of analyses were undertaken: all cases, all non pregnancy-associated cases, non pregnancy-associated cases aged 60 years or older and pregnancy-associated cases. In each, a log-link function was included to control for the underlying population (all people, people aged 60 years or older and all live births as appropriate) in each LSOA or local authority in each year. Chi-square tests and chi-square tests for trend, performed in Epi Info version 6.04d [34], were used to assess simple comparisons of proportions or trend in proportions respectively.

Analysis 2. Food purchasing comparison

To inform further on the findings of the incidence calculations, patients' food purchasing patterns were examined in relation to commercial denominator data. The standardised epidemiological questionnaire includes questions on various retail premises where cases had recently purchased food. These data, available from 2005 to 2007, were interrogated to obtain the number of cases reporting food shopping in different types of retailer. Commercial denominator data for the same time period and population were obtained from the Worldpanel Purchase database from the market research company Taylor Nelson Sofres (TNS, London). This database is the largest continuous consumer panel in Great Britain, capturing purchasing behaviour for 48,000 individuals in 25,000 households, and is used extensively by major retailers and manufacturers in the UK to understand consumer behaviour. Participants, chosen to be representative of Great Britain as a whole in terms of age, social class and region, record retail purchases by various means (e.g. bar code scanners, online surveys, till receipt scanning, etc.) and report to TNS fortnightly. Crude data were obtained from the database for the total number of individuals and the

TABLE 3

Characteristics of listeriosis cases, according to receipt of epidemiological questionnaires, England, 2005–2007 (n=566)

| Parameter | Epidemiological questionnaire received | |
	Yes (n=231) Number (%)[a]	No (n=335) Number (%)[a]
Patient type		
Pregnancy-associated	39 (17)	38 (11)
Non pregnancy-associated	192 (83)	297 (89)
Year		
2005	37 (21)[b]	142 (79)[b]
2006	50 (28)[b]	126 (72)[b]
2007	144 (68)[b]	67 (32)[b]
Gender		
Male	121 (52)	165 (49)
Female	110 (48)	168 (50)
Unknown	0 (0)	2 (1)
Age		
Median	65 years	68 years
Interquartile range	42–76 years	55–79 years
Quintile of increasing deprivation[c]		
1 (least)	44 (19.0)	59 (18)
2	35 (15.2)	79 (24)
3	41 (17.7)	54 (16)
4	48 (20.8)	72 (21)
5 (most)	62 (26.8)	67 (20)
Unknown	1 (0.4)	4 (1)
Mortality		
Died	62 (27)	111 (33)
Did not die	167 (72)	128 (38)
Unknown	2 (1)	96 (29)

[a] Column percentage, unless stated otherwise.
[b] Row percentage.
[c] Indices of multiple deprivation.

total number of individuals aged 60 years or older, and the food purchasing habits of both groups from various supermarkets, discount supermarkets, convenience stores (typically small retail stores selling limited produce over extended periods) and local services (corner shops, local butchers, bakers, greengrocers and fishmongers). Reported places for food shopping among cases and the general population were compared in Microsoft Excel 2007. Odds ratios (OR) and 95% CIs were calculated.

Analysis 3. Food purchasing, storage and consumption in relation to quintiles of multiple deprivation

Finally, the quintiles of the index of multiple deprivation calculated in analysis 1 above were combined with the standardised food purchasing, storage and consumption data from analysis 2 and data were stratified by quintiles of increasing neighbourhood deprivation. Changes in the upwards or downwards trend in relation to increasing deprivation were assessed using the chi-square test for trend.

Results
Study population
Between 2001 and 2007, 1,242 cases of human listeriosis were reported; of these, 1,084 (87%) were non pregnancy-associated and 158 (13%) were pregnancy-associated. Where patient age was available for non pregnancy-associated cases (n=1,072), 810 (76%) of cases were aged 60 years or older. Patients' home postcodes were available for 1,179 (95%) cases and all matched to an LSOA (Table 1). Postcode availability increased significantly over the surveillance period (chi-square test for trend P<0.001), but postcodes were more likely to be unavailable for patients aged under 60 years (chi-square test p=0.001) or for those defined as ethnic on the basis of their names (chi-square test p=0.04) (Table 1).

Incidence by quintiles of deprivation
The incidence of listeriosis increased with increasing relative neighbourhood deprivation (Table 2), with 38% (95% CI: 16 to 65) higher incidence in the most deprived quintile compared with the least. Incidence was positively correlated with all of the dimensions of deprivation (reflecting their intracorrelation and their

TABLE 4

Food purchase patterns for listeriosis cases (n=171) compared with those of the general population (n=60,415), England, 2005–2007

Premises	Food shopping by premises					
	All cases n (%)	Population[a] n (%)	OR (95% CI)	Cases aged ≥60 years n (%)	Population aged ≥60 years[a] n (%)	OR (95% CI)
Supermarkets						
Chain B	85 (49.7)	47,811 (79.1)	0.26 (0.19–0.35)	44 (42.3)	11,383 (75.2)	0.24 (0.16–0.36)
Chain G	63 (36.8)	37,238 (61.6)	0.36 (0.27–0.50]	35 (33.7)	8,063 (53.2)	0.45 (0.30–0.67)
Chain J	63 (36.8)	35,475 (58.7)	0.41 (0.30–0.56)	34 (32.7)	9,315 (61.5)	0.30 (0.20–0.46)
Chain A	55 (32.2)	30,596 (50.6)	0.46 (0.34–0.64)	35 (33.7)	8,000 (52.8)	0.45 (0.30–0.68)
Chain D	48 (28.1)	24,225 (40.1)	0.58 (0.42–0.81)	32 (30.8)	8,050 (53.2)	0.39 (0.26–0.59)
Chain K	27 (15.8)	19,935 (33.0)	0.38 (0.25–0.57)	13 (12.5)	5,259 (34.7)	0.27 (0.15–0.48)
Chain U	24 (14.0)	18,993 (31.4)	0.36 (0.23–0.55)	15 (14.4)	5,579 (36.8)	0.29 (0.17–0.50)
Chain P	15 (8.8)	10,025 (16.6)	0.48 (0.28–0.82)	7 (6.7)	3,372 (22.3)	0.25 (0.12–0.54)
Discount supermarkets						
Chain X	15 (8.8)	15,568 (25.8)	0.28 (0.16–0.47)	7 (6.7)	5,032 (33.2)	0.15 (0.07–0.31)
Chain Q	16 (9.4)	14,500 (24.0)	0.33 (0.20–0.55)	8 (7.7)	4,279 (28.3)	0.21 (0.10–0.44)
Chain C	7 (4.1)	7,605 (12.6)	0.30 (0.14–0.63)	4 (3.8)	2,004 (13.2)	0.26 (0.10–0.71)
Chain E	9 (5.3)	5,594 (9.3)	0.54 (0.28–1.07)	7 (6.7)	1,715 (11.3)	0.57 (0.26–1.22)
Convenience stores						
Chain H	4 (2.3)	3,534 (5.8)	0.39 (0.14–1.04)	1 (1.0)	1,184 (7.8)	0.11 (0.02–0.82)
Chain L	10 (5.8)	3,846 (6.4)	0.91 (0.48–1.73)	5 (4.8)	1,013 (6.7)	0.70 (0.29–1.73)
Chain M	26 (15.2)	1,952 (3.2)	5.37 (3.53–8.17)	17 (16.3)	668 (4.4)	4.23 (2.50–7.16)
Local services						
Corner shops	44 (25.7)	13,864 (22.9)	1.16 (0.83–1.64)	15 (14.4)	4,241 (28.0)	0.43 (0.25–0.75)
Butchers	35 (20.5)	8,300 (13.7)	1.62 (1.11–2.34)	17 (16.3)	3,510 (23.2)	0.65 (0.38–1.09)
Green grocers	35 (20.5)	7,155 (11.8)	1.92 (1.32–2.78)	16 (15.4)	3,148 (20.8)	0.69 (0.41–1.18)
Bakers	40 (23.4)	4,973 (8.2)	3.40 (2.39–4.86)	23 (22.1)	2,140 (14.1)	1.73 (1.08–2.75)
Fishmongers	21 (12.3)	1,631 (2.7)	5.05 (3.19–7.99)	11 (10.6)	938 (6.2)	1.79 (0.96–3.36)

CI: confidence interval; OR: odds ratio.
[a] Source: commercial market research data.

contribution to the overall index of multiple depriva-
tion) except 'education, skills and training' and 'bar-
riers to housing and services' domains. Incidence in
non pregnancy-associated cases generally followed
that for all cases and was more marked for those cases
aged 60 years or older. The incidence of pregnancy-
associated listeriosis showed a more marked associa-
tion with increasing neighbourhood deprivation, with
the strongest associations observed with the 'income',
'employment' and 'health deprivation and disability'
domains.

Standardised patient exposure
data (2005–2007)

Between 1 January 2005 and 31 December 2007, 231
epidemiological questionnaires were received for the
566 reported cases in England (response rate 41%),
with the response rate increasing significantly over the
surveillance period (chi-square test for trend p<0.001)
(Table 3). Surveillance questionnaire receipt was inde-
pendent of case type (chi-square test p=0.06), age
(chi-square test p=0.09), sex (chi-square test p=0.5)
and level of deprivation (chi-square test p=0.09), but
not mortality (chi-square test p<0.001) (Table 3). A total
of 20 non-standard and 40 partially completed ques-
tionnaires were excluded, leaving 171 for analysis.

Of the 32 cases classed as ethnic on the basis of their
name, 29 described their ethnicity as something other
than 'white British', compared with 16 of 138 cases
classed as non-ethnic (positive predictive value: 90.6%
(95% CI: 86.2 to 95.0); negative predictive value:
88.4% (95% CI: 83.6 to 93.2). One case classed as
non-ethnic on the basis of their name did not describe
their own ethnicity.

Food purchasing patterns in relation to
the general population (2005–2007)

The use of supermarkets and discount supermarkets
was underrepresented among cases of listeriosis when
compared with the general population, while the use
of national convenience store chain M, and most local
services, was overrepresented (Table 4). This relation-
ship was observed to a lesser extent for cases aged 60
years or older, but could not be determined for preg-
nancy-associated cases due to a lack of denominator
data. Cases who reported food shopping at national
convenience store chain M were equally distributed
across all quintiles of deprivation (chi-square for trend
test p=0.38), were infected with nine different *L. mono-
cytogenes* subtypes and food shopping at this store
was overrepresented in each study year: OR: 6.00
(95% CI: 1.75 to 20.56) in 2005; OR: 6.16 (95% CI: 2.72
to 13.91) in 2006; OR: 4.67 (95% CI: 2.7 to 7.97) in 2007,
suggesting that this association did not represent a
single outbreak due to a single or restricted range of
L. monocytogenes strains.

Food purchasing, storage and consumption
in relation to quintiles of multiple
deprivation (2005–2007; data not shown)

As quintiles of neighbourhood deprivation increased,
cases (n=171) were more likely to describe their ethnic-
ity as something other than white British (chi-square
test for trend p=0.01) and were more likely to report:

- avoiding soft blue cheese (chi-square test for trend
  p=0.04)
- avoiding pâté (chi-square test for trend p=0.01).

They were more likely to report eating:

- liver sausage (chi-square test for trend p=0.04)
- cold roast turkey (chi-square test for trend p=0.045)
- pre-packed cold turkey (chi-square test for
  trend p=0.048).

They were less likely to report eating:

- food from hotels (chi-square test for trend p=0.01)
- food from restaurants serving British cuisine (chi-
  square test for trend p=0.04)
- duck liver pâté (chi-square test for trend p=0.049)
- oysters (chi-square test for trend p=0.03)
- watercress (chi-square test for trend p=0.03).

They were more likely to report recent food shopping
in:

- national supermarket chain G (chi-square test for
  trend p=0.001)
- national supermarket chain K (chi-square test for
  trend p=0.006)
- national discount supermarket chain X (chi-square
  test for trend p=0.004)
- local bakers (chi-square test for trend p=0.02)
- fishmongers (chi-square test for trend p=0.03)
- greengrocers (chi-square test for trend p<0.001).

They were no more likely to have acute or long-standing
medical conditions (chi-square test for trend p=0.22).

Discussion and conclusion

Laboratory-based surveillance of human *L. mono-
cytogenes* infection in England between 2001 and
2007 revealed that incidence was highest in the most
deprived areas of the country. Additional analyses
demonstrated that cases of listeriosis were more likely
than the general population to purchase foods from
convenience stores or from local services, and that
among cases, food purchasing and consumption pat-
terns changed with increasing deprivation. While cases
of listeriosis form the numerator in each of the three
analyses presented, the denominators are either differ-
ent or are absent, and therefore the findings of each
are not necessarily comparable.

Cases in this study comprise laboratory-confirmed
cases reported to national surveillance. Reporting
will be affected by disease severity, health-seeking
behaviour and reporting artefacts, all of which will

have a bearing on incidence estimates. Infection with *L. monocytogenes* results in a range of symptoms, and laboratory surveillance will undoubtedly underascertain milder forms of the disease. Disease severity relates largely to the degree of exposure and susceptibility of the host, and both might be driven by socio-economic factors (income-related food consumption leading to a greater or lesser exposure; known associations between certain underlying conditions (e.g. cancer [35], general poor health [36,37], diabetes [38]) and socio-economic status). By using laboratory-confirmed cases we might therefore be biasing our estimates for certain socio-economic groups. Community-based studies would be prohibitively expensive for a disease as rare as listeriosis, however, and without undertaking such studies it is impossible to measure the extent or direction of this bias in our study.

Healthcare usage also differs by socio-economic status for patients in England with infectious intestinal disease. Tam *et al*. demonstrated that individuals in lower socio-economic groups (as defined by age at leaving full-time education and housing) were more likely to present with infectious intestinal disease to a general practice than community controls were [39]. This might explain some of the observed difference in incidence by socio-economic status in our study. Tam's study included all causes of infectious intestinal disease, however, and it is not possible to determine how this differential presentation might relate to listeriosis, which differs markedly from most gastrointestinal infections in terms of severity, symptoms and population at risk.

National surveillance of listeriosis in England and Wales is passive, hence our estimates might be affected if clinicians' reporting practices differ depending on their patients' socio-economic status. In their study of listeriosis in Bristol, Jones *et al*. noted that the incidence in 1988 (1.2 cases per 100,000 population) was higher than the national average (0.58 cases per 100,000 population), suggesting that not all cases were reported to national surveillance and thus creating the opportunity for this form of selection bias [25]. The confidence intervals surrounding the above estimates overlap (0.58 to 2.24 per 100,000 population for Bristol; 0.5799 to 0.5801 per 100,000 population for England and Wales), however, suggesting no actual difference between incidence at the local and national level, and that the majority of cases confirmed at the local level are reported nationally.

We applied 2007 indices of deprivation to surveillance data from 2001 to 2007, meaning that areas that hypothetically experienced extreme social change during this time might not be adequately represented by these indices for part of the surveillance period. Such changes will be exceptional over such a short period, so most of the data will be unaffected by this generalisation, and any effect will be minimised further by arranging the data in quintiles.

By assigning cases to socio-economic groups on the basis of their home postcode, the effect of socio-economic status at the individual level is masked and individuals take on the socio-economic characteristics of their local environment [13]. While the merits of assigning social class to individuals by postcode is debatable [40,41] and the potential for ecological fallacy is increased, this method is advantageous in that it does not rely on high response rates to questionnaires (a particular problem for a severe disease such as listeriosis) or to potentially sensitive questions required for establishing socio-economic status (e.g. on income). Furthermore, the opportunity for misclassification through the direct derivation of socioeconomic status, based on occupation, for example [23], is minimised.

With these caveats in mind, the association between listeriosis and increasing deprivation reported in this study differs from other studies on the socio-economic determinants of gastrointestinal infections, where incidence was often positively associated with increased socio-economic status [17-24]. With pâté and soft mould-ripened cheese historically considered high-risk foods for listeriosis in the UK, our *a priori* hypothesis was that listeriosis would be a disease of affluence. The breakdowns in food safety that give rise to listeriosis differ from other food-borne pathogens, however, and these could impact on the demographics of the population at risk. While inadequate cooking of and/or cross-contamination from contaminated raw poultry meat increases the risk of campylobacteriosis, and inappropriate storage of uncooked or undercooked egg-based products over short time periods can lead to salmonellosis, the risk of listeriosis increases with the growth of *L. monocytogenes* to hazardous levels in refrigerated long shelf-life products [42]. It is possible that such conditions arise more frequently with increased deprivation where refrigeration may be inadequate or unavailable. Additionally, financial pressures may encourage individuals to store food for longer than the food product's safe shelf-life. Alternatively, as general poor health and certain chronic conditions such as cancers and diabetes are associated with lower socio-economic status [35-38] it is therefore intuitive that *Listeria* incidence would be higher in poorer areas.

Home postcodes were available less often for ethnic patients, hence the observed association with increasing neighbourhood deprivation might be underestimated, as ethnic groups reside more frequently in more deprived areas of England [43]. As neighbourhood deprivation increased, cases were also more likely to report their ethnicity as something other than white British, suggesting that at least part of the overall association may be due to an increased risk of infection in ethnic minorities. Currently, specific UK Government food safety advice on minimising the risk of listeriosis is delivered passively (via a website [44]) and is targeted preferentially at pregnant women. Our study suggests that advice should be communicated proactively and effectively to all patient groups at risk

of listeriosis, especially where language barriers exist, or where access to the Internet is limited [45]. Advice should be extended to include information on safe use and storage of foods in the home to avoid listeriosis (e.g. refrigerate once opened, consume within the shelf life of the product, etc.).

Several factors should be considered while interpreting our comparisons of cases' exposures in relation to increasing neighbourhood deprivation, and their food purchasing patterns with that observed in the general population. Firstly, routine surveillance of listeriosis is problematic due to the severity of the disease and the population at risk. For this reason, the response rate to our epidemiological questionnaire, while improving, is lower than for other active surveillance systems for gastrointestinal infections in England, e.g. 77% for verocytotoxin-producing *Escherichia coli* infection in England (Health Protection Agency, unpublished data) and is better for patients who survive their infection. It is possible that certain exposures will be underrepresented in our surveillance dataset if those exposures are linked to increased mortality, e.g. foods containing higher concentrations of *L. monocytogenes* or certain subtypes, or those consumed more often by the most vulnerable. To date, studies of *L. monocytogenes* mortality [6,7,11] have focussed on host factors, making quantification of this potential bias impossible.

Secondly, the population at risk of listeriosis in England is not the same as the population of England, as listeriosis patients are often individuals predisposed to opportunistic infections due to suppression of their T-cell-mediated immunity [46], and the conditions that give rise to this immunological state might alter their behaviour, including food purchasing patterns. People tend to keep the same shopping habits though, and while they might avoid some foods due to certain underlying conditions (or their treatments), they are less likely to change their favoured supermarkets or shops. Finally, individuals participating in surveys of any kind will differ systematically from the general population by virtue of their willingness to participate, and this bias might be more profound for market research surveys where participation is often rewarded financially. Market research data are used extensively by many business sectors, however, and therefore there is an economic pressure on market research companies for their study participants to be as representative as possible, and the denominator data used matched closely to the British population with regard to age and social class. This could be detrimental to our food purchasing comparison, as the numerator (listeriosis cases in England, skewed towards increased deprivation) differs from the denominator (commercial data, representative in terms of social class), and this might explain some or all of the observed differences in food

FIGURE

Non-seasonally adjusted product price index for food products (excluding beverages), United Kingdom, January 1991 – July 2009[a]
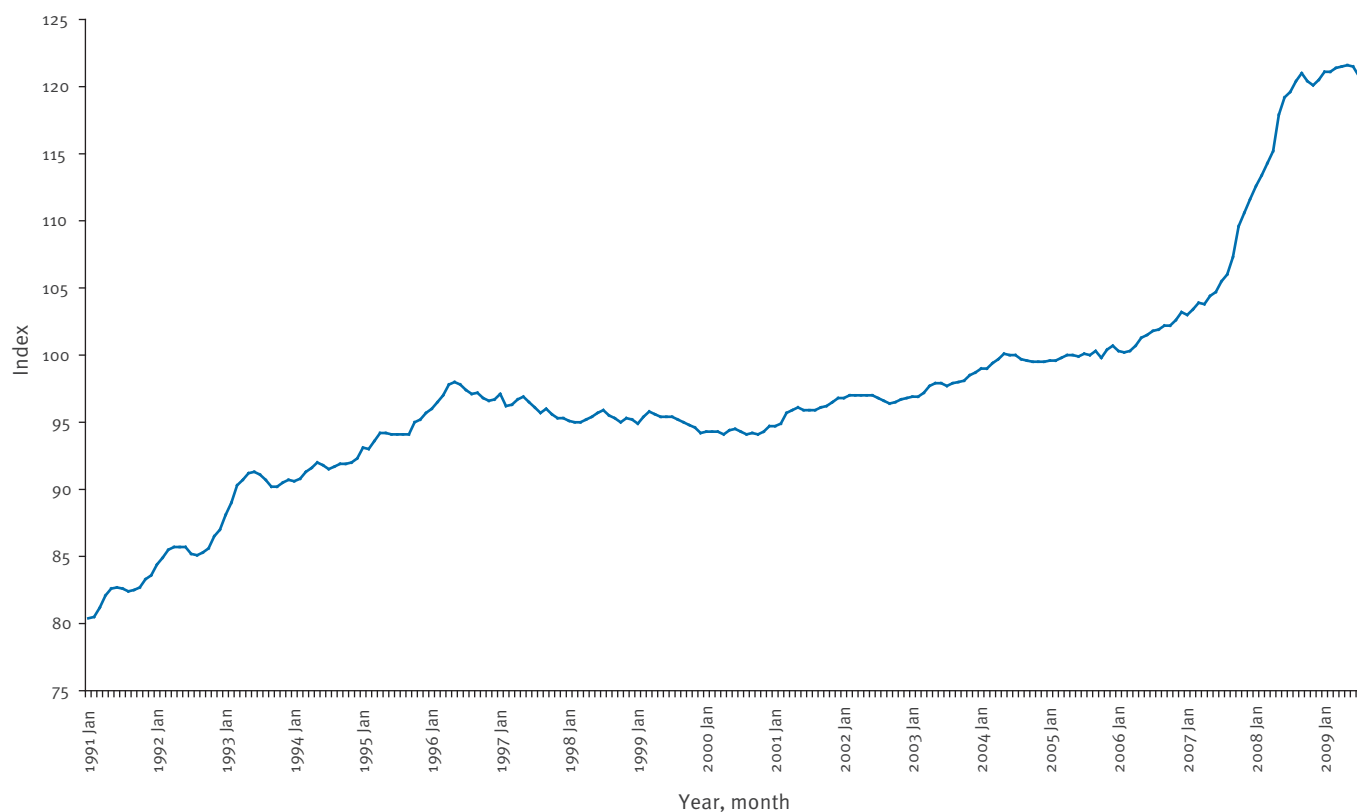
[a] Index set at 100 for 2005.
Source: [52].

purchasing. Further work could address this shortcoming by examining the food purchasing patterns of cases in relation to deprivation-matched population groups, but the provision of such detailed denominator data was prohibitively expensive for this unfunded study. Discussions of the findings from this study are still warranted, however, as shopping for food at several of the 'over-indexed' types of premises (those reported more often by cases than by the general population) also increased among listeriosis cases as neighbourhood deprivation increased.

The apparent overuse of national convenience store chain M by listeriosis cases may represent differential misclassification, as this chain is colloquially synonymous with small convenience stores in the UK, and therefore patients may report shopping there when they are in fact referring to any convenience store. Commercial data, on the other hand, will be ascribed correctly to the appropriate premises type, based on the comprehensive collection methods described previously. Similarly, the associations with local services might reflect the fact that, on average, a shopper would visit several shop types among their local services to purchase the variety of items that would be available in a single supermarket and therefore the numerator is inflated. Alternatively, residents in poorer areas may be limited to shopping locally due to poorer access to transportation. Convenience stores and local services generally represent the smaller end of the market in terms of business size, and this feature has been frequently linked to lower microbiological quality of foods in a number of surveys undertaken in England and Wales since 1994 [47]. Small businesses do not have access to the same level of food safety expertise [48] as larger retail companies do, and these food control deficiencies might increase the food safety risk for consumers. The 2006 'Safer food better business' initiative by the UK Government [49], designed to help small food businesses implement hazard-based control systems and to comply with food hygiene regulations, was therefore timely. Food safety management systems employed to satisfy legislation will only fully meet legal obligations, however, when they account for all relevant hazards and risks. Clearly *L. monocytogenes* and its associated food safety storage issues, which are different from those of other food-poisoning bacteria, must be considered carefully in food manufacturing and retail operations, particularly for foods sold to vulnerable individuals [50].

In conclusion, our study demonstrates that *L. monocytogenes* incidence was highest in the most deprived areas of England when compared with the most affluent, that cases were more likely to purchase foods from convenience stores or from local services than the general population were, and that patients' risk profile changed with increasing neighbourhood deprivation. Increasing 'healthy life expectancy' in the UK does not follow increasing life expectancy, meaning that in future, individuals may spend a greater part of their retirement in poor health [51]. With poor health in later life allied to increasing deprivation and recent rises in food prices (Figure [52]) predicted to continue, food poverty could become an increasingly important driver for listeriosis. While UK Government policy should continue to focus on small food businesses to ensure sufficient levels of food hygiene expertise, tailored and targeted food safety advice on the avoidance of listeriosis is required for all vulnerable groups within the community. Failure to do so will enhance health inequality across socio-economic groups.

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Emergence of pregnancy-related listeriosis amongst ethnic minorities in England and Wales

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Listeriosis is a rare but severe food-borne disease that predominantly affects pregnant women, the unborn, newborns, the elderly and immunocompromised people. Following a large outbreak in the 1980s, specific food safety advice was provided to pregnant women and the immunocompromised in the United Kingdom. Following two coincident yet unconnected cases of pregnancy-related listeriosis in eastern European women in 2008, a review of the role of ethnicity in pregnancy-related listeriosis in England and Wales was undertaken in 2009. Cases reported to the national listeriosis surveillance scheme were classified as 'ethnic', belonging to an ethnic minority, or 'non-ethnic' based on their name, and trends were examined. Between 2001 and 2008, 1,510 cases of listeriosis were reported in England and Wales and, of these, 12% were pregnancy-related cases. The proportion of pregnancy-related cases classified as ethnic increased significantly from 16.7% to 57.9% (chi-square test for trend p=0.002).The reported incidence among the ethnic population was higher than that among the non-ethnic population in 2006, 2007 and 2008 (Relative Risk: 2.38, 95% confidence interval: 1.07 to 5.29; 3.82, 1.82 to 8.03; 4.33, 1.74 to 10.77, respectively). This effect was also shown when analysing data from January to September 2009, using extrapolated live births as denominator. Increased immigration and/or economic migration in recent years appear to have altered the population at risk of pregnancy-related listeriosis in England and Wales. These changes need to be taken into account in order to target risk communication strategies appropriately.

Introduction

Listeriosis is a rare but severe bacterial disease that predominantly affects pregnant women, the unborn, newborns, the elderly and immunocompromised individuals. In newborns, the elderly and immunocompromised individuals, the disease usually manifests as meningitis and/or septicaemia, with high mortality rates reported amongst these risk groups. Listeriosis is mainly transmitted via the consumption of foods contaminated with *Listeria monocytogenes* and recent estimates suggest that listeriosis is the greatest cause of food-related deaths in the United Kingdom (UK) [1]. It has been reported that pregnant women have a 12-fold increased risk of developing disease after the consumption of contaminated food when compared with the general population [2], indicating that pregnancy may constitute a disposition to acquiring listeriosis. Pregnant women rarely have central nervous system infection [3] but may experience fever, miscarriage, premature delivery or stillbirth. Pregnant women infected with *L. monocytogenes* may also be asymptomatic.

While most pregnancy-related infections are detected during the third trimester, listeriosis can develop at any time during pregnancy and, in some instances, asymptomatic pregnant women may still pass on infection to the fetus. Pregnancy-related cases of listeriosis are divided into early and late onset. An early onset case is defined as a newborn with symptoms at birth or within 48 hours of birth resulting from *in utero* infection from the mother. The term late onset is applied when a newborn develops symptoms more than 48 hours after birth and such infections are thought to be predominantly the result of infection during passage through the birth canal. While rare, there have also been reports of late onset cases being a consequence of nosocomial transmission via indirect contact with early onset cases, for example through common birthing staff or equipment [4,5]. Newborns born with listeriosis and who survive may have complications that include physical retardation and granulomatosis infantiseptica (pyogenic nodules distributed systemically).

Between 1985 and 1989, the number of cases of listeriosis in England, Wales and Northern Ireland nearly doubled before rapidly declining in 1990 [6].This upsurge in cases was, however, mainly caused by an outbreak which disproportionately affected pregnant women, and was related with consumption of pâté produced by a single manufacturer [7]. The suspension of sales of pâté from this manufacturer, whose pâté was highly contaminated with subtypes of *L. monocytogenes* indistinguishable from those isolated from cases, coincided with the dissemination of two government health warnings in 1989: one with regards to

the general risk of listeriosis and pâté [8] and a second one specifically targeted at vulnerable groups, which were defined at the time as pregnant women and people with impaired resistance to infection [9]. The aforementioned rapid decline in cases followed the second of these warnings.

The outbreak highlighted the risk to pregnant women of developing listeriosis after consuming pâté and reiterations of the health advice with regards to pâté and other high-risk foods still target this group [10]. Following two coincident but unconnected cases of pregnancy-related listeriosis in women of eastern European nationality during 2008, a review of pregnancy-related cases of listeriosis between 2001 and 2008 was undertaken using national surveillance data for England and Wales, to assess the role of ethnicity in this population and examine trends. A provisional investigation of cases between January and September 2009 was also carried out.

Methods

The Health Protection Agency Centre for Infections coordinates the surveillance of listeriosis in England and Wales. Cases are ascertained by the voluntary electronic reporting of laboratory-diagnosed cases and/or the referral of cultures for identification and subtyping. Epidemiological and microbiological data reported by these systems are combined, de-duplicated, and stored in a bespoke Microsoft Access 2003 database. Since 2005, supplementary clinical data are sought routinely from the consultant medical microbiologist responsible for the case, including onset date, date of hospital admission, principal listeria illness, clinical outcome, antibiotics and other drugs administered and symptoms [11]. In addition, exposure data with regards to travel, food consumption and food retailers are sought from the case or a relative of the case by environmental health officers in liaison with local health protection staff, using a standard exposure questionnaire [11]. Postcode data are employed to estimate socio-economic status using quintiles [12] of established indices of multiple deprivation [13].

A case of listeriosis is defined as an individual presenting with clinically compatible illness and from whom *L. monocytogenes* was isolated from a normally sterile site. Cases are classified as either non-pregnancy-related in individuals over four weeks old, or pregnancy-related where a mother and/or fetus/newborn of less than four weeks old are affected. An affected mother and newborn are classified as one pregnancy-related case. Pregnancy-related cases that involve a live birth are routinely stratified further into early and late onset cases, as described above.

All cases of listeriosis are routinely classified as either 'ethnic' (belonging to an ethnic minority) or 'non-ethnic' (not belonging to an ethnic minority) based on their first name and surname, where available. This classification is in addition to case-reported ethnicity, reported via the standard exposure questionnaire since

2005 and based on the 2001 UK census classification [14]. Name-based classification was used throughout the study period from 2001 to 2008, and used in analyses, while case-reported ethnicity data, were used to validate the name-based approach only. The numbers of live births, recorded in England and Wales from 2001 to 2008 and stratified by country of birth of mother, were obtained from the Office for National Statistics [15] and used as denominator data. The number of live births (i.e. not including stillbirths, miscarriages and abortions) to mothers who were born outside of the UK was used for comparative analyses with the number of pregnancy-related cases that were classified as ethnic, using the name-based approach. Similarly, the number of live births to mothers born in the UK was used for comparative analyses with the number of pregnancy-related cases that were classified as non-ethnic. Both denominator datasets included live births to mothers whose usual residence was outside of the UK, accounting for 1.1% of live births to mothers who were born outside the UK and 0.2% of live births to mothers born in the UK.

Statistical analyses were carried out using Stata version 10 and Epi Info. Trends in proportions were investigated using the chi-square test for trend while differences in proportions employed the chi-square test and Fisher's exact test as appropriate. Relative risks (RR) and corresponding 95% confidence intervals (CI) were calculated. Poisson regression was employed for multivariable analysis: incidence in pregnancy-related cases belonging to an ethnic minority, relative to pregnancy-related cases not belonging to an ethnic minority, were calculated whilst controlling for trend over the surveillance period. A log-link function was included to control for differences in the underlying population-live births to mothers born outside and inside the UK respectively in each year.

Linear regression models were fitted to live births to mothers born outside and inside the UK data for January to September, 2001 to 2008, and predictions (with corresponding 95% prediction intervals) for this denominator population were obtained for 2009 based on the linear trend of the previous years. For 2009, the RR was estimated using the number of provisional cases between January and September and estimated denominator predictions for this period. An uncertainty interval around the RR was calculated based on the CIs calculated for the upper and lower prediction intervals.

Results
Study population

Between 2001 and 2008, 1,510 cases of listeriosis were reported in England and Wales and, of these, 12% were pregnancy-related. The proportion of cases that were pregnancy-related did not change during the study period (chi-square test for trend p=0.866; Figure). Of all cases reported, 12.3% were classified as ethnic cases, 86.7% as non-ethnic cases and the remaining 1% could not be classified as ethnic or non-ethnic by

their name. Of the 181 pregnancy-related cases, 36.5% had ethnic names while 63% did not. One case in 2005 did not have a recorded name and, hence, ethnicity could not be established. This case was therefore not considered in these analyses. The proportion of pregnancy-related cases classified as having ethnic names over the whole study period was greater than that for non pregnancy-related cases (37% vs. 9% respectively; chi-square test p<0.001).

Incidence

Amongst pregnancy-related cases, there was a significant increase in the proportion of cases classified as ethnic, from 16.7% to 57.9% (chi-square test for trend P=0.002), during the study period (Figure). This change in proportion was not observed for non-pregnancy-related cases (chi-square test for trend p=0.124). The increasing proportion of pregnancy-related cases classified as ethnic was most noticeable in 2006, 2007 and 2008, during which years the reported incidences of ethnic cases were higher than that expected in the underlying population (RR: 2.38, 95%CI: 1.07 to 5.29; 3.82, 1.82 to 8.03; 4.33, 1.74 to 10.77; respectively) (Table 1). Poisson regression indicated that there was

a significant increase in incidence of ethnic cases after adjusting for the trend observed over the study period (RR: 2.25, 95%CI: 1.66 to 3.05).

Pregnancy-related cases classified as ethnic and reported between 2006 and 2008 (the years with an observed significant increase) were distributed across eight of nine regions in England and in Wales. A greater proportion of these pregnancy-related cases classified as ethnic were reported in London (47.2% of all ethnic cases in England and Wales vs. 11.1% of all non-ethnic cases) when compared with elsewhere (52.7% vs. 88.9%; chi-square test p<0.001). This level was above that expected, based on the number of live births in London during this period (RR: 3.66, 95%CI: 1.23 to 10.89). Based on provisional case data for January to September 2009 (16 ethnic cases and 10 non-ethnic cases) and extrapolated live births denominator data for the same period (425,495 live births to mothers born within the UK and 128,148 live births to mothers born outside of the UK), there remains an increased risk associated with ethnic minorities for this period (RR: 5.31, 95% uncertainty interval: 2.33 to 12.20). All subsequent analyses relate to pregnancy-related cases, henceforth referred to as 'cases'.

Total number of listeriosis cases (n=1,510), proportion of cases that are pregnant and proportion of pregnant cases classified as ethnic[a], England and Wales, 2001-2008
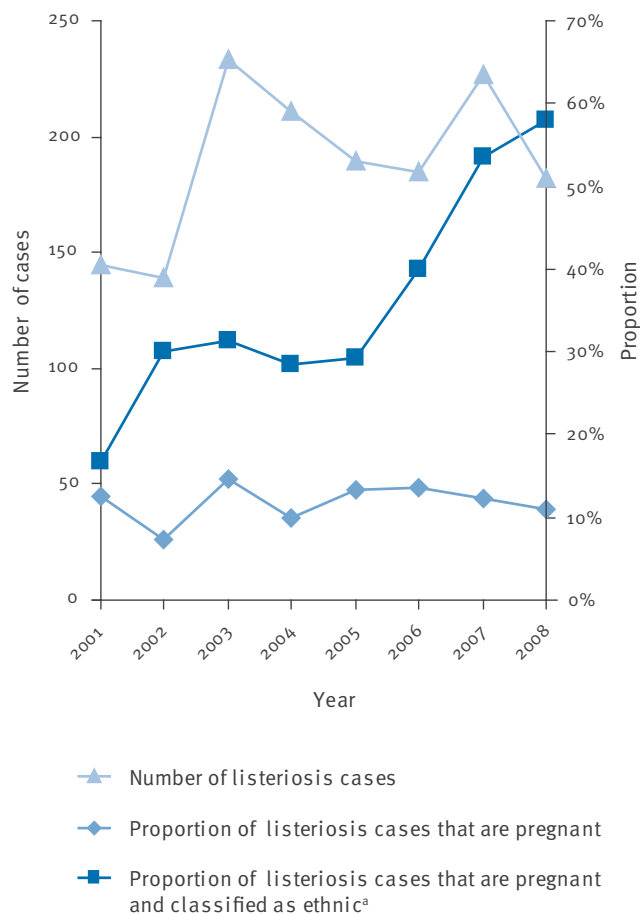
Clinical data

There was no significant difference in the proportion of clinical questionnaires returned for ethnic and non-ethnic cases (91% vs. 94% respectively; Fisher's exact test p=0.553). There was also no difference in the proportion of infecting serotypes that were 1/2 compared with 4 between ethnic and non-ethnic cases (31% vs. 24% respectively; chi-square test p=0.390). When characteristics of ethnic and non-ethnic cases with a returned clinical questionnaire were compared, there was no significant difference in the recorded outcome of pregnancy, newborn survival, the stage of onset of symptoms in the newborn (early vs. late onset) or presentation with either meningitis or septicaemia in the newborn (Table 2). However, newborns born to ethnic mothers were more likely to present with symptoms of listeriosis at birth (chi-square test p=0.039) and these cases were more likely to come from more deprived areas (chi-square test for trend p<0.001), with almost half of the ethnic cases belonging to the most deprived group (Table 3).

Exposure data

There was no significant difference in the proportion of exposure questionnaires returned for ethnic and non-ethnic cases (58% vs. 47% respectively; chi-square test p=0.285). Of the 37 cases for which exposure and clinical data were available, 18 were classed as ethnic on the basis of their name. The cases defined as ethnic were more likely to describe their own ethnicity as 'non-white British', i.e. as something other than white British, compared with all cases (positive predictive value 94.4% and negative predictive value 68.4%)(Table 3). No single country or group of countries (e.g. countries within the Indian sub-continent)

[a] Cases were classified as either ethnic or non-ethnic based on their name.

predominated for cases who described themselves as non-white British (Table 4).

Cases defined as ethnic on the basis of their name were significantly more likely to consume pâté, cabbage or dill. In addition, they were more likely to shop in two national supermarket chains A and B or green grocers but less likely to shop in local bakeries (Table 5).

Discussion
We report a sustained increase in the incidence of pregnancy-related cases of listeriosis from ethnic

Pregnancy-related listeriosis cases by name-based ethnicity classification[a] (n=180), number of live births to mothers born outside (n=1,055,827) and within the United Kingdom (n=4,110,279) and related relative risks, England and Wales, 2001-2008

Year	Number of ethnic[a] pregnancy-related listeriosis cases	Number of live births to mothers born outside the UK	Number of non-ethnic[a] pregnancy-related listeriosis cases	Number of live births to mothers born in the UK	Relative Risk (95% confidence intervals)
2001	3	98,115	15	496,519	1.01 (0.29-3.5)
2002	3	105,514	7	490,608	1.99 (0.52-7.71)
2003	11	115,593	24	505,876	2.01 (0.98-4.09)
2004	6	124,746	15	514,975	1.65 (0.64-4.26)
2005	7	134,334	17	511,501	1.57 (0.65-3.78)
2006	10	146,643	15	522,958	2.38 (1.07-5.29)
2007	15	160,083	13	529,930	3.82 (1.82-8.03)
2008	11	170,799	8	537,912	4.33 (1.74-10.77)
Total	66	1,055,827	114	4,110,279	

UK: United Kingdom.

[a] Cases were classified as either ethnic or non-ethnic based on their name.

Characteristics of pregnancy-related listeriosis cases with a returned clinical questionnaire by name-based ethnicity classification[a], England and Wales, 2001-2008 (n=167)

Factor	Ethnicity of pregnancy-related listeriosis cases[a]	
	Ethnic	Non-ethnic
	(N=60)	(N=107)
Death related with pregnancy (miscarriage, stillbirth, or death)		
Yes	15/49	22/81
No	34/49	59/81
Pregnancy Outcome		
Live birth	47/57	71/91
Miscarriage	6 /57	16 /91
Stillbirth	2 /57	3 /91
Still pregnant	2 /57	1/91
Survival of live births		
Survived	32 /39	53/56
Died	7 /39	3 /56
Onset type of live births		
Early Onset (≤48 hrs)	28/38	30/43
Late Onset (>48hrs)	10/38	13/43
Symptoms of listeriosis in newborns		
Yes	38/45	40/60
No	7 /45	20/60
Meningitis in newborns		
Yes	11/16	3/6
No	5/16	3/6
Septicaemia in newborns		
Yes	14/17	12/15
No	3/17	3/15

[a] Cases were classified as either ethnic or non-ethnic based on their name, 'unknowns' were excluded in these analyses.

minexies in England and Wales between 2006 and 2008, with provisional case data suggesting that this increase continued into 2009 when compared with estimated population data. This increase was not observed amongst non pregnancy-related cases. An increase in pregnancy-related listeriosis in women born outside of the country was reported in Ireland in late 2007 [16]. Listeriosis has also been reported as

TABLE 3

Socio-economic status of pregnancy-related listeriosis cases with a returned clinical questionnaire by name-based ethnicity classification[a], England and Wales, 2001-2008 (n=161)

Socio-economic status	Ethnic[a] pregnancy-related listeriosis cases N=59	%	Non-ethnic[a] of pregnancy-related listeriosis cases N=102	%
IMD 1 (least deprived)	4/59	7	19/102	19
IMD 2	4/59	7	26/102	25
IMD 3	8/59	14	6/102	6
IMD 4	15/59	25	24/102	24
IMD5 (most deprived)	28/59	47	27/102	26

IMD: Indices of Multiple Deprivation [12].
[a]Cases were classified as either ethnic or non-ethnic based on their name, 'unknowns' were excluded in these analyses.

TABLE 4

Case-reported ethnicity data (as per 2001 census classification system) of pregnancy-related listeriosis cases by name-based ethnicity classification[a], England and Wales, 2005-2008 (n=37)

Case-reported ethnicity	Name-based ethnicity	
	Ethnic[a] (N=18)	Non-ethnic[a] (N=19)
White (British)	1/18	13/19
White (Non-British)	5 /18	2/19
Black African	2/18	1/19
White/Black Caribbean	0/18	1/19
Indian	4/18	1/19
Pakistani	1/18	0/19
Chinese	1/18	0/19
Other Asian	2/18	1/19
Other Ethnic	2/18	0/19
Total (other than white British)	17/18	6 /19

[a] Cases were classified as either ethnic or non-ethnic based on their name, 'unknowns' were excluded in these analyses.

TABLE 5

Food history of pregnancy-related listeriosis cases by name-based ethnicity classification[a], England and Wales, 2005-2008 (n=37)

Food history	Ethnic[a] pregnancy-related listeriosis cases (n=18)	Non-ethnic[a] pregnancy-related listeriosis cases (n=19)	p-value
Consumption of pâté	5/18	0/19	0.020[b]
Consumption of cabbage	8/16	1/19	0.005[b]
Consumption dill	5/16	0/18	0.016[b]
Shopped in national supermarket chain A	4/18	0/19	0.046[b]
Shopped in national supermarket chain B	8/18	1/19	0.008[b]
Shopped at green grocers	7/18	0/19	0.003[b]
Shopped at local bakeries	3/18	9/19	0.046[c]

[a]Cases were classified as either ethnic or non-ethnic based on their name, 'unknowns' were excluded in these analyses.
[b] Fisher's exact test.
[c] Chi-square test.

disproportionately affecting pregnant Hispanic women in the United States [17,18] and pregnant women living in a household where a language other than English was spoken in Australia [19]. To the authors' knowledge, the sustained increase reported in this study has not been previously described elsewhere. Pregnancy-related listeriosis cases comprise the minority of what is already a rare disease, and by this very nature any changes in incidence trends within this population will only become evident after a number of years.

Differences in health seeking behaviour and access to healthcare between ethnic minorities and the general population may impact on our incidence estimates, but this is difficult to assess. It is reasonable to assume that new migrants to the UK may find it more difficult to access the existing healthcare services than UK residents.

There appears to be no differential ascertainment of clinical and exposure data between ethnic and non-ethnic cases which minimises the likelihood of this form of bias affecting our findings. Analyses performed on those cases with a completed clinical questionnaire returned indicate that, compared to non-ethnic cases, ethnic cases were more likely to be from more deprived areas and newborns more often displayed symptoms of listeriosis at birth. It has previously been established that ethnic minorities reside disproportionately in more deprived areas [20] and this would explain the distribution of these pregnancy-related cases. Differential symptom presentation at birth may reflect differences in gestational age at time of infection (i.e. trimester) or route of infection (*in utero* or during passage through the birth canal) between ethnic and non-ethnic cases but this needs further investigation. Furthermore, we could not assess any differences in terms of clinical characteristics and exposures amongst those that did not have a completed clinical or exposure questionnaire returned in our analyses.

Cases' own description of their ethnic background was used to validate the name-based classification method of ethnicity employed in this study. The negative predictive value for this approach indicates that approximately 30% of cases defined as non-ethnic report their own ethnicity as something other than white British. Consequently, the number of pregnancy-related cases defined by their name as ethnic seems to underestimate the number of those belonging to an ethnic group other than white British. Therefore, the risk of pregnancy-related listeriosis associated with ethnic minorities is likely to be greater than that reported here. Regardless, any misclassification is likely to be non-differential over the study period and would therefore not affect the observed increase in pregnancy-related listeriosis in the ethnic group.

The reporting of certain foods and retail exposures differed between ethnic pregnancy-related cases and non-ethnic pregnancy-related cases. However, it is important to note that comparisons are not being made with controls without illness and hence, findings should not be considered as risk factors for infection [21]. Furthermore, such case-case comparisons would not indicate the magnitude or direction of risk among pregnancy-related cases and should only be used for hypothesis generation, which then need to be tested by alternative methodologies. If exposures were common to both ethnic and non-ethnic groups, they would have been underestimated or, indeed, would have remained unidentified using this method. It is important to bear in mind that ethnic minorities are a heterogeneous group who likely vary in their food preferences and behaviours. The sample size of this study did not allow for analyses of strata within this group. Nevertheless, the consumption of pâté was reported more commonly by ethnic than non-ethnic pregnancy-related cases, suggesting that food safety advice issued by the UK government is not reaching this at-risk population or is not being followed.

Incidence was calculated by comparing cases classed as ethnic or non-ethnic with the numbers of live births by country of origin of mother (non-UK born and UK born respectively). Differences between the numerator and the denominator may have affected the accuracy of our risk estimates. Firstly, live birth data will exclude instances of stillbirth or miscarriage – these are both included in the numerator - and, consequently, the risk of listeriosis will be over estimated. The denominator data employed in the analyses also included mothers whose usual country of residence was outside of the UK, while cases living outside the UK are not reported to this surveillance scheme and would not be represented in this numerator. While these mothers represent only a small proportion of the total, inflation of the denominator will lead to some underestimation of risk. The final, and perhaps most important, consideration is that the numerator refers to cases (mothers/newborns/both) stratified by ethnicity whereas the denominator refers to live births to mothers stratified by country of birth. A mother could, however, be born in the UK and belong to an ethnic minority but this was the best available proxy for ethnicity of mothers of live births. While there are limitations to using live birth data by country of origin of mother, there was a need to assess the observed increasing trend in the context of population change, and our study suggests that the increase in incidence is over and above what would be expected.

Conclusions

Increased immigration and/or economic migration in recent years appear to have altered the population most at risk of pregnancy-related listeriosis in England and Wales. The increase in the number of pregnancy-related cases belonging to an ethnic minority has disproportionately affected London, where migration has directly increased the number of new births in some local authorities [22]. Passive food safety messages, which highlight high-risk foods, appear not to be

reaching pregnant women from ethnic minorities or are not being followed by this emerging at-risk population. More specific and targeted routes of communication and materials, which should be both culturally-relevant and in a range of appropriate languages, are needed. Our findings should be considered by those targeting risk communication strategies to vulnerable groups. Studies to identify which ethnic minorities are most at risk would provide further valuable information on how to more effectively tailor communication strategies.

Acknowledgements

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Human activities predominate in determining changing incidence of tick-borne encephalitis in Europe

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Explanations for the dynamics of tick-borne disease systems usually focus on changes in the transmission potential in natural enzootic cycles. These are undoubtedly important, but recent analyses reveal that they may not be quantitatively the most significant side of the interaction between infected ticks and humans. Variation in human activities that may impact inadvertently but positively on both the enzootic cycles and the degree of human exposure to those cycles, provide more robust explanations for recent upsurges in tick-borne encephalitis in Europe. This can account for long-term increases in incidence that coincided with post-soviet political independence, for small-scales spatial variation in incidence within a country, and for short-scale fluctuations such as annual spikes in incidence. The patterns of relevant human activities, typically those related to the use of forest resources, are evidently driven and/or constrained by the cultural and socio-economic circumstances of each population, resulting in contrasting national epidemiological outcomes.

Introduction

The incidence of infection with vector-borne zoonoses is inherently dynamic in space and time because transmission cycles depend on interactions between pathogens, arthropod vectors and vertebrate hosts, many of which are responsive to changing environmental conditions. Furthermore, the risk of human infection varies not only with the abundance of infected vectors, but also with the amount of human exposure to that hazard, either one of which may change independently. The relative contributions of these various factors can be dissected for one of the most significant vector-borne diseases in Europe, tick-borne encephalitis (TBE), because of the reliable long-term records and a well-quantified understanding of the underlying biology, ecology and human risk factors [1-5] (and see below). One obvious environmental change concerns the climate, which has been much debated in the past and will not form part of this review that is focused specifically on socio-economic determinants. Furthermore, hitherto, a convincing explanation for an increase in enzootic transmission potential to match an observed upsurge in TBE cases has been found only in some parts of western Europe and does not involve climate change. In north-east Italy, land and wildlife management practices have improved habitat suitability for rodents, the transmission hosts for the TBE flavivirus, and for enhanced populations of deer, the most important host for the vector, the tick *Ixodes ricinus* [6], concomitant with a steady increase in TBE cases over the past decade. In Sweden, prior to the first doubling in TBE incidence in 1984 an epidemic of sarcoptic mange had knocked the fox population down, allowing a sharp increase in numbers of deer as predation on fawns was reduced [7,8]. Although causality has not been tested, this could have resulted in increased tick densities, as tick abundance and tick-borne disease incidence are correlated temporally and spatially with deer densities [9,10]. This, however, accounts for neither the second doubling in Sweden in 2000, nor the continuing steady increase since the disease became notifiable there in 2004.

In most central and eastern European (CEE) countries, where TBE has been a notifiable disease since at least the 1970s [11], national mean incidences increased between 2- and 30-fold abruptly in 1993, with marked heterogeneity in degree and timing at finer spatial scales. Within any one country, upsurges did not occur everywhere that the virus is known to circulate, but when they did the degree of increase varied by an order of magnitude and the timing of onset varied between 1990 and 1998 (see Figure 1 for an example from Slovakia).

No single factor is likely to cause such a pattern. Instead, a nexus of interacting, independent but synergistic, biotic, abiotic and socio-economic impacts on all four partners within the system (virus, vector, vertebrate wildlife and human) has been proposed and supported by comparative data from five diverse countries (Slovenia, Czech Republic and the three Baltic countries) [12-14]. The conclusion from analyses of extensive datasets on past and present events is that local human activities can and have shifted suddenly to alter the degree of contact between people and infected

ticks, while human-induced environmental changes that may enhance enzootic cycles generally take effect more gradually. This is consistent at different time- and space-scales, from long-term political reorganisation, through small-scale changes in land use and ownership, to short-term responses to weather conditions. At each scale, socio-economic conditions and cultural practices appear to have driven and/or constrained the relevant human activities. The same ideas can be applied to the more gradual emergence of TBE in western Europe, but data on potential causal factors relating to humans have not yet been compiled and analysed to identify specific effects.

Long-term impacts from political independence

Political independence in CEE in the early 1990s was unexpectedly accompanied by a dramatic upsurge in TBE incidence in most countries (Hungary and Croatia were notable exceptions). Detailed analyses of primary data have suggested a causal linkage [13] that can be summarised as follows: to varying degrees in each country, agricultural reorganisation left much arable land fallow and much grassland un-grazed, and therefore subject to gradual re-colonisation by natural vegetation suitable for rodents and ticks. At the same time, significantly reduced pesticide usage (documented for the Baltic countries and Slovenia [13]) and higher densities of deer in all countries may account for the marked increase in tick (*I. ricinus*) abundance, as shown by rare long-term systematic records from a forest close to Riga, Latvia [13]. Alongside much reduced industrial activity, the reduced collective agricultural activity also contributed to an abrupt rise in unemployment, driving many people back to their small farmsteads for a more subsistence way of life on land closer to tick-infested forested areas and using virtually no pesticides; this could have brought them into closer contact with ticks. With the polarisation of society, measured by an increasing Gini coefficient (an index of household economic inequality), other fractions of the populations benefited from increased wealth in

FIGURE 1

Annual numbers of tick-borne encephalitis cases since 1970 in all Slovakia (inset) and each kraj (region), showing the typical spatial and temporal heterogeneity in incidence within one country
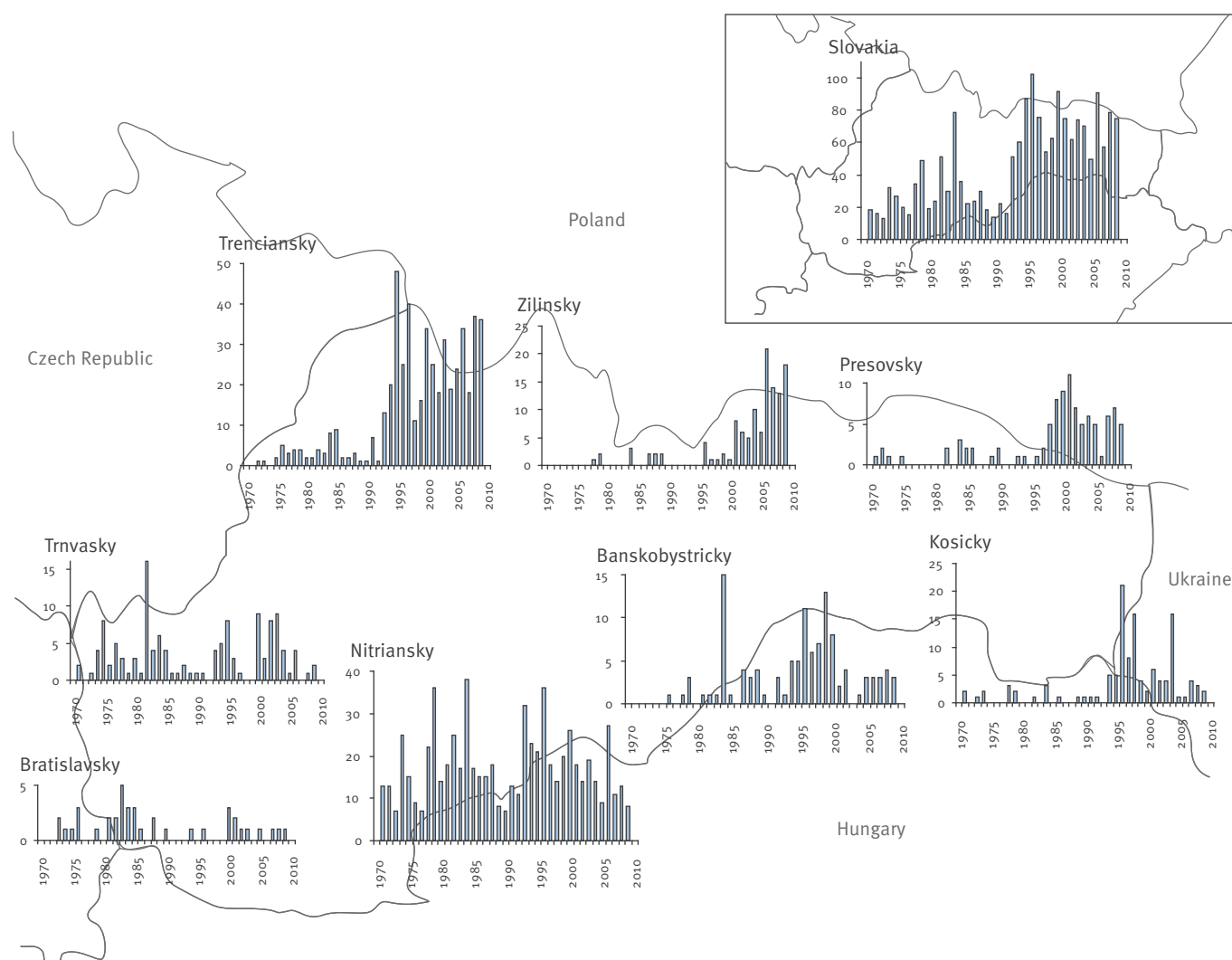
Source: Public Health Authority of the Slovak Republic.

the new market economy. The traditional practice of harvesting berries and mushrooms from forests was enforced both by poverty, when this free food necessarily augmented family diets, and by greater wealth, leisure time and individual travel. Furthermore, new markets for wild mushrooms opened up in western Europe, where city market stalls and delicatessens are now commonly supplied from Poland and Lithuania. Data from a survey in 2000 in Latvia [15] reveal that the activity of mushroom gathering is unfortunately, but not surprisingly, associated with a much higher risk of tick bite than is simple recreational use of forests [16]. With different democratisation processes during the early 1990s, the degree of socio-economic transition and its impact on human exposure to TBE virus evidently varied markedly between countries, with the Czech Republic amongst the least affected while Lithuania, Latvia and northeast Poland were hardest hit. This is reflected in a remarkable correlation between the degree of TBE upsurge (doubling in the Czech Republic, but 4- to 30-fold increases in the Baltic States) and the percentage of household expenditure spent on food across eight CEE countries (R²=0.716)

[13], which suggests that activities related to the conditions of everyday life are a significant factor in TBE incidence.

As a potential alternative explanation, changes in public health activities, particularly those related to surveillance and diagnosis, could have caused an artificial increase in recorded TBE incidence. The impact of these activities on recorded incidence is difficult to assess, especially as surveillance practices vary between countries, there is no standardised case definition, and diagnostic protocols are improved periodically [11]. While these problems might reduce the precision of the quantitative associations described here, longterm familiarity with this infection amongst local medical practitioners confirmed by personal interviews, and detailed analyses of the timing of improved diagnosis relative to the geographically heterogeneous patterns of TBE upsurge, provide convincing evidence that much of the upsurge was real and not purely a product of public health changes [17]. After all, similar changes in public health practices also occurred in western Europe without causing such a massive abrupt

FIGURE 2

Numbers of *Ixodes ricinus* ticks (A) and numbers of people self-reporting tick bites (B), by 10-day period, Riga county, Latvia, January 2002–December 2003
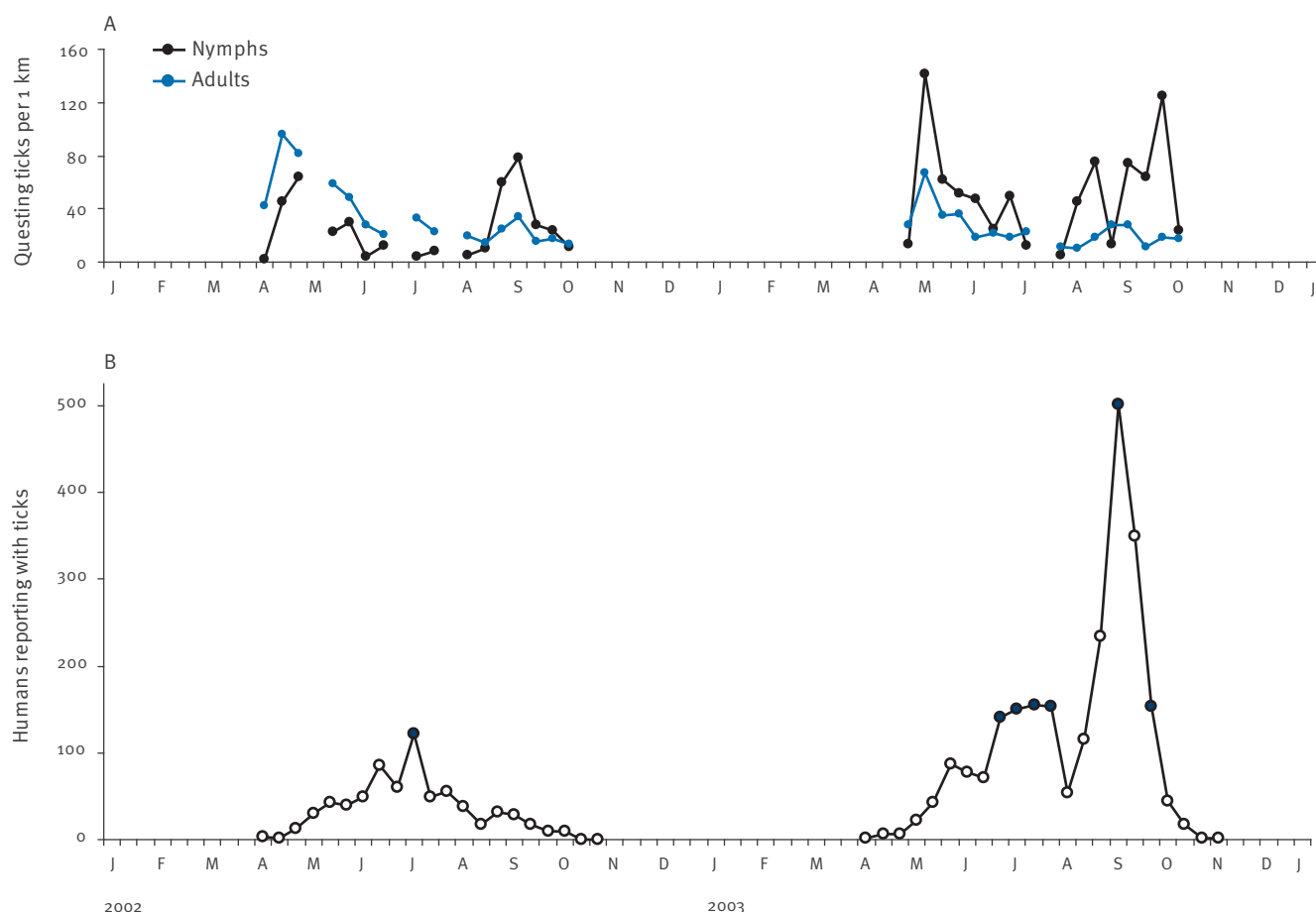

A. Ticks (nymphs: black; adults: blue) were counted by standardised flagging methods at the Tireli monitoring site.

B. Self-reporting of tick bites was to the State Public Health Agency in Riga. Dark blue dots mark periods that included rain-free weekends with mean maximum air temperatures above 15oC and heavy rainfall in the preceding week.

Reproduced from [16].

FIGURE 3

Examples of contrasting patterns of the relative seasonal profiles of monthly TBE cases and questing nymphal ticks expressed as percentages of annual totals for the mean of 2000–2005, 2006 and 2007
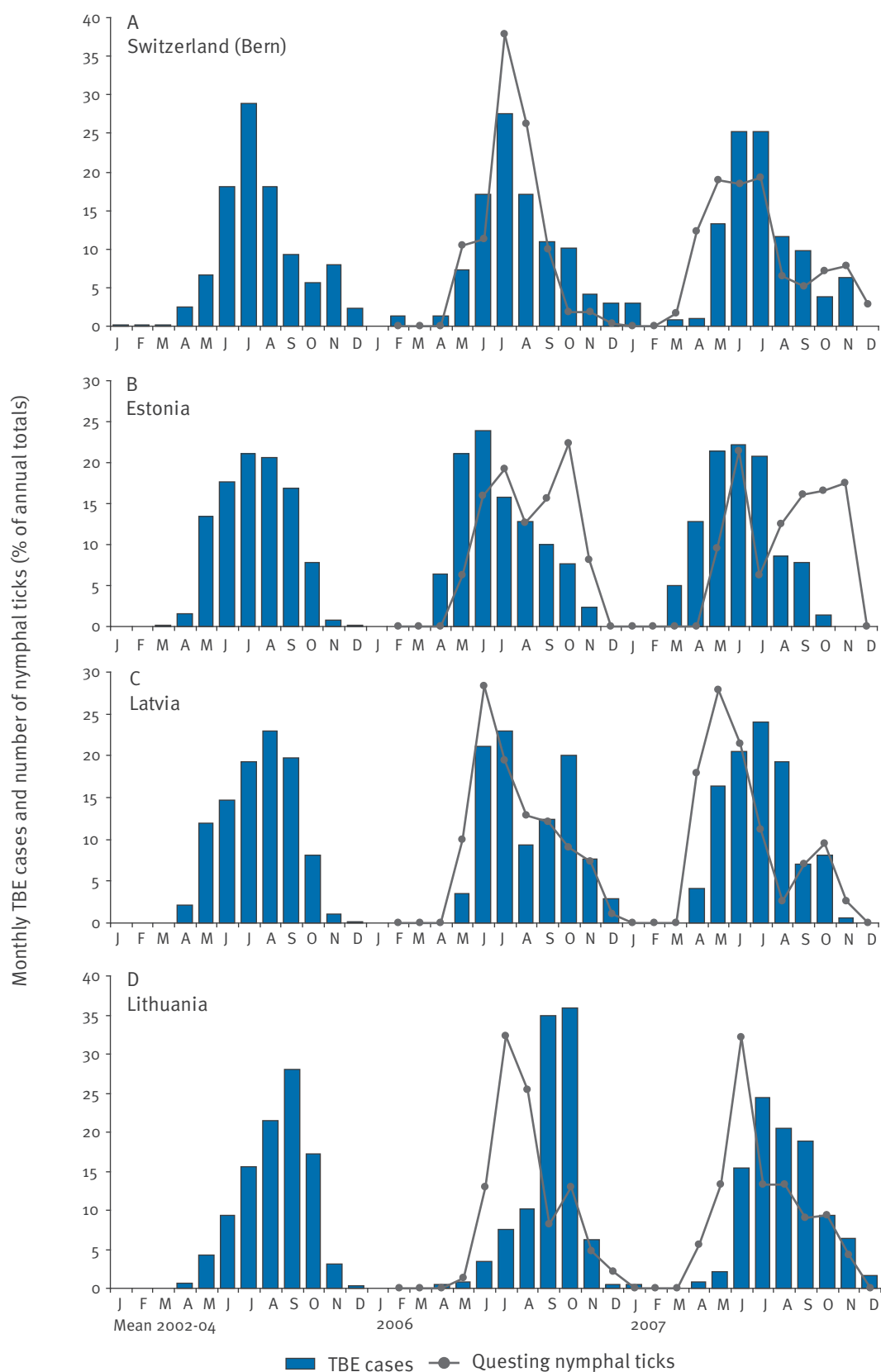
TBE: tick-borne encephalitis.

The tick data are lagged by one month to accommodate the average delay between tick bites and TBE reporting.

For information on tick monitoring sites, see [21].

upsurge. In no country does the date when TBE became a notifiable disease [11 and Table1 therein] coincide with any increase in incidence, apart from Sweden in 2004. Furthermore, some changes would be expected to reduce the incidence, particularly any campaign to promote self-protection through awareness and avoidance of risk, and the use of the highly effective anti-TBE vaccine [18]. Vaccination coverage did indeed increase in Slovenia and all three Baltic States from two years after the TBE upsurge, fluctuated thereafter in step with TBE incidence two years previously, and was highest in those Baltic counties that had the greatest TBE incidence [16]. These observations suggest a response to perceived risk. Moreover, TBE incidence in Latvia decreased markedly from 1999, but the degree of this decrease far exceeded that which could be explained by vaccination and was greatest where the previous incidence had been highest, again indicating human avoidance of ticks in response to perceived risk. The Latvian survey [15] reported a change in behaviour, with people going to forests less often after 1999 than before. Nevertheless, both vaccination and reduced use of high-risk forests were least common amongst the poorest sector of the population [16], pointing to an economic constraint. Finally, there was no correspondence between these epidemiological patterns and the presence of the second tick species, *I. persulcatus*, which occurs only in eastern Estonia and Latvia.

Hungary is an interesting case where there was no increase in TBE incidence in the early 1990s, but a sudden decline in TBE incidence in 1997, which may have been due to changes in public health services leading to under-reporting. Since that time, diagnosis has had to be paid for by the individual hospitals, and financial constraints mean that this is now requested only in the special situations of milk-borne outbreaks of TBE or where there are problems with differential diagnosis. As West Nile virus also circulates in Hungary, expensive virus neutralisation tests are needed to distinguish between this and TBE virus, while physicians gain little from an accurate diagnosis in their medical care of patients (limited to symptomatic treatment) (Emôke Ferenczi, personal communication, September 2009). Irrespective of any differential medical care, correct diagnosis is, of course, vital for establishing the epidemiology of these two infections.

Small-scale impacts of land cover, land use and land tenure

The significance of human activities constrained by socio-economic factors in driving the dynamics of TBE incidence, as inferred from the above gross-scaled epidemiological patterns, is also apparent from a finer-scaled analysis within a single country. The spatially variable incidence of reported TBE cases from 1999 to 2003 in rural parishes (i.e. municipalities) in Latvia can best be explained and predicted by three aspects of landscape that include human as well as physical factors: land cover, that determines the suitability of the habitat for ticks and tick-host populations, land use,

that determines whether the local human population is likely to enter the forest on a regular basis, and land-ownership, that determines how these two aspects may intersect through access rules [19]. In this analysis, land use (i.e. the purpose for which people enter forests) was inferred indirectly from socio-economic markers known from analysis of the Latvian survey data [15] to be associated principally with either recreational use of forests or collection of wild foods from forests [16]. Thus, although people in all socio-economic brackets visit forests regularly, those with lower income and lower education do so more frequently, and more commonly with the purpose of collecting wild food, in contrast to those in the middle and upper socio-economic classes who are more likely to visit the forest for recreation.

At the Latvian national scale, a multi-factorial negative binomial regression model, including the auto-correlated spatial factor of infection in neighbouring parishes, revealed a higher risk of TBE where a higher percentage of forest had been felled in 2000 (probably reflecting high exposure of forest workers), where a smaller percentage of the population had an economic activity and where more of each parish was occupied by state-owned forest to which the public has right of access [19]. Within the more homogenously rural northeastern region of Latvia, Vidzeme, a complementary range of similar predictor variables was identified: TBE risk was greater in parishes with more forest that had not been clear-cut, less cultivated land, proportionately fewer people with higher education, and proportionately more pensioners. Similar effects of forest clearance on tick abundance has been recorded for the Czech Republic, but persisting only for two years after clearing until regeneration of the natural vegetation restored favourable conditions for *I. ricinus* ticks [20].

Thus the evidence supports the intuitive expectation that the spatially variable risk of TBE within a small country is determined by a combination of landscape structure, much of it shaped by human agency, and people's socio-economic status that may direct the way they use tick-infested forests.

Short-term responses to weather conditions

In addition to these inferences, more direct evidence for the importance of human activities in determining exposure to infection can be gleaned from short-term temporal patterns. One example comes from comparing regular records of questing tick abundance in the Tireli forest just outside Riga, Latvia with the numbers of tick bites reported to the Public Health Agency in Riga in the years 2002 and 2003 [16]. Within each annual tick activity season (spring to autumn), there was considerable variation in abundance of *I. ricinus* ticks recorded at 10-day intervals (Figure 2A, reproduced from [16]). High tick numbers, however, were not matched by high numbers of reported tick bites. Rather, tick bites peaked on rain-free weekends with mean maximum air temperatures above 15 °C following

heavy rainfall during the preceding week (marked by dark blue dots in Figure 2B, reproduced from [16]). As mushrooms are thought to be most abundant after rainfall followed by warm weather, and as people prefer outdoor activity in dry weather, these mismatching temporal patterns suggest that exposure to tick bites is determined more by human foraging activities than tick questing activities.

Furthermore, against the background of longer-term shifts in TBE incidence, there are occasional sudden spikes in annual incidence, which must reflect the natural variability in environmental conditions for enzootic transmission and/or human exposure. The year 2006 was particularly valuable in throwing light on such short-term phenomena because unusually high spikes occurred in synchrony in several western and central European countries, and by great good fortune these spikes coincided with monthly sampling of ticks during the period 2006 to 2008 at a total of 81 sites in 13 countries across Europe as part of the EU-FP6 Emerging Diseases in a Changing European Environment (EDEN) project (http://www.eden-fp6project.net/). Detailed analyses of meteorological records (daily maximum temperature and precipitation), monthly numbers of *I. ricinus* nymphs and monthly cases of TBE for eight countries (Switzerland, Germany, Slovenia and the Czech Republic that showed exceptional spikes in 2006, north-east Poland and Lithuania where incidence was high in 2006 but not exceptionally so, and Estonia and Latvia that showed no change in 2006) revealed that the variable spikes in TBE case numbers were related to a specific combination of weather over 2006, but independent of variable tick abundance, suggesting that human responses to weather were more important [21]. In all these countries, but least marked in Estonia and Latvia, relative to other years in the period between 1970 and 2008, an unusually cold January to March 2006 was followed by unusually warm and dry July to December 2006, punctuated by a cold wet August, and warm January to June 2007. Ticks started their seasonal activity about one month earlier in the warm spring of 2007 compared with 2006, but the annual total number counted in 2007 was not consistently higher than in 2006 (higher only at 11 of the 41 sites), as expected if each new cohort of unfed ticks emerges after moulting only in the autumn [22]. More importantly, the spike of TBE cases in 2006 did not coincide consistently with a greater abundance of ticks in 2006 than in 2007 (more ticks at only eight of the 41 sites), nor was the earlier onset of tick activity in 2007 matched by more than a very small number of earlier cases of TBE that year.

All the evidence indicates that seasonal and annual patterns of TBE incidence are not simple reflections of tick abundance, but due in large part to changing human activity. The testable prediction, therefore, is that the degree of mismatch in the seasonal profiles of questing tick abundance and TBE incidence should vary according to cultural and socio-economic constraints, which is indeed observed (Figure 3).

Consistently from 2000 to 2007, case numbers of TBE in Germany, Slovenia and Switzerland peaked between June and August, more or less matching the seasonal profile of tick abundance (lagged by one month to accommodate the delay between tick bites and TBE reporting), but with virtually no change in response to the earlier tick season in 2007 (Figure 3A, Switzerland shown as an example of a pattern consistent for these three countries). This suggests that TBE risk mirrors people's summer (recreational) outdoor activity, which, unfortunately, coincides with maximum seasonal tick challenge in these countries. Numbers of summer visitors to a major national park in Slovenia confirm the obvious supposition that 90% of such activity occurs between May and September, and is encouraged by unusually warm dry weather (in July, September, October, but not August, 2006) [21]. The situation in Estonia also points to human summer activity as the determinant of risk, as TBE cases decline after August even though tick activity persists more or less undiminished through September and October (Figure 3B). A different pattern is seen in the Czech Republic and Latvia, where high incidence of TBE persists later in the summer and autumn (exaggerated in 2006) after tick activity has declined markedly from its spring peak (Figure 3C), which is thought to reflect disproportional exposure to ticks during the harvest of autumnal forest foods [23]. A differently skewed mismatch occurs in Lithuania and north-east Poland, where disproportionately few TBE cases occur before July when ticks are most abundant, as if people rarely enter forests at this time, but many more TBE cases occur after August, despite much reduced tick activity after midsummer (Figure 3D). Given the importance of mushrooms as an exported cash crop in these last two countries [24], it is reasonable to suppose that people may make additional efforts to secure a good harvest for their living when the crop is poor, with less potential for opportunistic recreational foragers to respond to good years. This could explain the sporadic autumnal spikes in TBE incidence rather than an exceptional spike in 2006. In summary, these extensive and intensive data all indicate that the spikes in TBE cases in 2006, and possibly other less dramatic fluctuations in incidence, were due to exceptional weather conditions affecting people's behaviour, which had a differential impact depending on socio-economic and cultural factors.

Discussion

Human activities of all sorts are commonly directed to a greater or lesser extent by geographically and temporally variable socio-economic constraints, with consequences for health (both non-communicable ill-health and directly transmitted infectious diseases) and reciprocal impacts of health on wealth, even within Europe [25-29]. For vector-borne zoonoses, human-induced environmental change (climatic, landscape, biotic) may affect the transmission potential of wildlife cycles,

whereas human activities per se predominate in determining, and thereby potentially avoiding, contact with those cycles and so the risk of infection. This adds complexity and instability to the spatio-temporal dynamics of these disease systems. The analyses described here are based on correlational studies, which are by no means ideal for attributing causality to epidemiological patterns. They have, nevertheless, advanced our thinking significantly by identifying a range of new factors that need to be considered in future, more purpose-built, empirical studies. In the specific case of TBE in central and eastern Europe, many of the recent human-induced environmental changes originated in the socio-economic effects of political transition, and appear to have had an impact on the living conditions of all partners within this disease system - virus, ticks, wildlife and humans. Because of the biology of ticks as vectors, with their long generation time and slow pace of pathogen transmission due to the long interval between feeds, changes in transmission potential operate on a longer time scale than do changes in human exposure to infected ticks. The evidence presented in this review indicates that this latter effect can occur rapidly and thereafter may endure for variable periods, from a few months of extra recreation to many years of a new life-style. The fluidity with which people respond to new opportunities depends not only on current socio-economic conditions but also on their cultural traditions and expectations. The traditional exploitation of forests for food, apparently expanded either for export or for private enterprise in local markets or to enhance diets out of necessity or pleasure, has been quantified as a major risk factor for TBE [15,16]. Greater wealth, leisure and consequent potential for outdoor recreation brings similar risks. As soon as more than one causal factor is introduced, each operating with differential force and eliciting variable human responses, a spatially and/or temporally heterogeneous outcome is to be expected. Although many of these conclusions arise from detailed analyses of data from the Baltic States, because of the quality of data available there, entirely consistent patterns are seen where comparable information has been examined for other countries, notably Slovenia and the Czech Republic. This is striking, because these latter countries fall at opposite ends of both the geographical range of CEE countries and the spectrum of socio-economic impacts of the political reform of the early 1990s.

Elsewhere in Europe, where socio-economic conditions have been more stable (pace the recent economic crises), the more gradual emergence of TBE may prove to be due more to enhanced enzootic cycles. In northeast Italy, the geographically defined appearance of TBE over the past two decades has been attributed to changes in forest structure, specifically a decreased ratio of coppice to high stand forest that has improved habitat suitability for rodents and deer [6]. As these authors point out, these changes in land and wildlife management practices are part of a shift from the pre-19th century concept of a forest as a wood-producer

to the modern concept of a complex ecosystem highly connected with the territory where it is located, with cultural and aesthetic landscape values, and the functions of protecting hydrogeology, soil and biodiversity. Once again, human purposes, operating within a philosophy permitted by relative socio-economic wellbeing, are instrumental in driving TBE emergence.

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Strategies to intervene on social determinants of infectious diseases

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Systematic health inequalities exist in all European countries today. Individuals with lower socio-economic status suffer disproportionally from adverse health outcomes. While this is widely accepted for chronic diseases, a literature review covering the years 1999-2010 reveals that infectious diseases are also distributed unevenly throughout society, with vulnerable groups bearing a disproportionate burden. This burden is not restricted to a few 'signature infections of social determinants' such as tuberculosis or human immunodeficiency virus (HIV) infections, but also a wide array of other infectious diseases. Tremendous advances in public health over the last century have reduced the absolute magnitude of inequalities but relative differences remain. In order to explore the underlying reasons for such persistent inequalities in Europe, I examined interventions targeting social determinants of infectious diseases: interventions on social determinants tend to focus on chronic diseases rather than infectious diseases, and interventions for these mainly focus on HIV/AIDS or other sexually transmitted infections. Thus, there seems to be a need to intervene on inequalities in infectious diseases but ideally with a comprehensive public health approach. Three intervention strategies are discussed: population-at-risk, population, and vulnerable population approaches. Strengths and weaknesses of these options are illustrated.

Introduction

Social circumstances determine prospects in life. They differ throughout society and can manifest themselves for example through conditions in early childhood, education, employment, living conditions. Two types of contextual drivers can be differentiated [1]: (i) structural determinants of health, the social, political, cultural, and economic context give rise to the distribution of income, education, etc. as defined by specific social, gender, or race/ethnicity norms that set the process of social stratification in motion; (ii) intermediary determinants of health, crowded living and working conditions, inadequate food availability, high-risk sexual behaviour, etc. shape differences in exposure and vulnerability. As a result, socio-economic status determines health conditions [2]. For example, educational attainment determines mortality in different groups, with the highest mortality rates found in groups with lowest educational levels [3]. This mortality difference was observed throughout Europe, although less in some some urban, relatively prosperous southern European populations, and more in most eastern European countries and Baltic region such as Lithuania and Estonia [4]. The absolute differences between these health indicators (e.g. mortality or morbidity) for low compared with high socio-economic classes have decreased over the last decades [5]. However, relative differences between these two groups have remained stable in western European countries, if not increased, with individuals in a lower socio-economic class suffering from worse health outcomes [6]. In fact, income-related health inequalities expanded, the longer they persisted based on a longitudinal analysis of European survey data [7]. These findings suggest that a declining income over time is associated with growing health limitations when compared with a rising income. Because differences in health and socio-economic status persist over time they are a policy priority in Europe [4,8,9].

However, intervening on these health discrepancies is intricate at best [10] and a number of open questions remain. What specific infectious diseases in which groups should be targeted for effective control, and how? Moreover, interrupting transmission in certain subpopulations has proven to be remarkably resilient to public health interventions. Interventions on individual health behaviour changes, to prevent HIV infection (e.g. condom use) or for early cancer detection (e.g. cervical cancer screening with the Papanicolaou test) for example, often yield lower participation rates in marginalised groups [11,12]. Prevalence and incidence rates of many health endpoints tend to be elevated in these populations while response rates are generally lower for health promotion and health education interventions [13]. The purpose of this paper is to assess the range of infectious diseases in Europe that are determined by socio-economic factors, to examine respective interventions with a focus on infectious diseases and finally to discuss a theoretical framework for interventions on inequalities in infectious diseases.

In addition to micro-interventions focusing solely on behaviour change, other strategies should be considered such as (i) the populations-at-risk approach, (ii) the population approach, or (iii) the vulnerable population approach. Advantages and disadvantages of these three strategies for infectious disease control are discussed.

Footprint of social inequalities on infectious disease in Europe

Original research articles addressing socio-economic determinants of infectious diseases in Europe were retrieved from Medline (PubMed) and ScienceDirect bibliographic databases. The search strategies submitted were: ("socioeconomic factors"[MeSH Terms] OR "inequality"[All Fields]) AND ("infectious diseases"[MeSH Terms] OR "infectious"[All Fields]) AND ("Europe"[MeSH Terms] OR "Europe"[All Fields]); the search was expanded with a number of other terms

Pathogen	Health endpoint	Socio-economic determinants and site of study
Campylobacter spp.	Intestinal disease	Pakistani community at greater risk of infection than 'white'[a] community in England [36] [a] Classified according to the 1991 census, England.
Clostridium botulinum	Progressive bulbar palsy, diplopia, dysarthria	Injecting heroin drug users at risk, Dublin, Ireland [37]
Common childhood pathogens	Infectious/parasitic diseases	High infection rates found in children in an area characterised by lower socio-economic status in Romania (Moldova) [38]
Cytomegalovirus (CMV)	Infectious mononucleosis, with fever, mild hepatitis, congenital abnormalities	Low socio-economic status and social environment as risk factor for CMV seroprevalence and congenital CMV infection in Helsinki, Finland [39]
Bacillus anthracis	Inflammation or abscesses related to sites of heroin injection, death	Outbreak among (predominantly) intravenous drug users in Scotland [40]
Pathogens associated with injecting drug use	Numerous major health consequences	Risks from injecting drug use, sex, unhygienic living and injecting conditions in marginalised (Roma or homeless) intravenous drug users, Budapest, Hungary [41]
Flaviviridae (Arbovirus) transmitted by ticks	Tick-borne encephalitis (TBE)	Transmission of TBE in Central and Eastern European countries influenced by socio-economic factors [42]
Herpes simplex virus type 1 (HSV1) and 2 (HSV2)	Significant morbidity, Herpes simplex virus type 1 (HSV1) considered a risk factor for HIV transmission	Increase of HSV1 seroprevalence with age among people of Turkish and Moroccan origin, homosexual men, and individuals with low educational level in Amsterdam, the Netherlands [43]
Listeria. monocytogenes	Listeriosis	Incidence associated with neighbourhood deprivation in England [44]
Neisseria meningitidis (meningococcus)	Meningococcal disease	Parental smoking and unfavourable socio-economic circumstances among children in the Czech Republic [45]
Rubella virus	Congenital rubella syndrome (CRS)	Low socio-economic status associated with low rubella seropositivity in Dogankent Health Center, Turkey [46]
Gardnerella vaginalis, Mobiluncus, Bacteroides, Mycoplasma	Bacterial vaginosis	Increased risk for bacterial vaginosis in women who have daily coitus, are single, smokers, with a previous sexually transmitted disease, or with high alcohol consumption in pregnancy, Denmark [47]
Hepatitis A virus	Acute infectious disease of the liver	Outbreak in Lomnička, a village in the eastern part of Slovakia, among the Roma population associated with low socio-economic conditions [48]
Hepatitis B virus	Malignant and non-malignant liver disease	Significant higher prevalence rates in immigrant women in Greece [49]
Hepatitis C virus	Malignant and non-malignant liver disease	Prevalence of anti-HCV antibodies in underprivileged individuals without social insurance in France, much higher than in the general population [50]
Helicobacter pylori	Peptic ulcer disease, gastric cancer	Poor socio-economic status as an important risk factor for peptic ulcer disease in Denmark [51]
Influenza virus	Vaccine coverage	Lower vaccine uptake in socio-economically deprived populations in Britain [52]
Methicillin-resistant *Staphylococcus aureus* (MRSA)	Postoperative infection	Patients from the most deprived areas at higher infection risk than those from the least deprived areas in England [53]
Sexually transmitted pathogens (STI)	Sexually transmitted diseases (STD)	High-risk sexual behaviour among immigrant groups in Amsterdam, the Netherlands [54]
Toxoplasmosis	Encephalitis and congenital malformations	Incorrect monitoring for toxoplasmosis during pregnancy among migrants in northern Italy, precluding timely application of preventive measures [55]
Trichomonas vaginalis	Sexually transmitted diseases (STD)	High prevalence of *T. vaginalis* and multiple infections with other STDs among female inmates in Lisbon, Portugal [56]
Puumala virus (PUUV)	Nephropathia epidemica, a mild form of haemorrhagic fever with renal syndrome (HFRS)	PUUV infection risk higher among low-income populations in remote forest areas with low level of urbanisation, Belgium [57]

such as inequity, ethnicity, race, homeless, vulnerable, marginalised, prison, or drug use. Key words were used in the search strategies for papers in all languages with an English abstract, published between January 1999 and July 2010. Retrieved citations were screened by title and abstract review. Inclusion criteria were defined widely, in order to retrieve a broad range of articles. Papers that did not address infectious diseases and articles that did not pertain to Europe were excluded from further analysis. Selected articles underwent data extraction using a standardised form to capture infectious pathogens, health endpoints, social determinants, epidemiologic findings and geographic location covered in the studies (Table 1).

The majority of research on socio-economic determinants of health focused on chronic diseases, because infectious diseases only represent 9% of the total burden of diseases in Europe [14]. The review revealed vulnerable or marginalised groups to carry a disproportionate proportion of this infectious diseases burden (Table 1). The socio-economic gradient has been well established for human immunodeficiency virus (HIV) infections and tuberculosis with a large number of articles documenting this discrepancy; for example, in an ecologic analysis of European countries, tuberculosis notification rates increased with rising wealth inequality [15]. In addition to these 'signature infections of socio-economic determinants' a number of other infections were also indentified in this literature search (Table 1). They included not only minor infections with relatively benign health outcomes but also

a number of infections with potentially serious health consequences: a discrepancy between socio-economic groups was found for the prevalence of human papillomavirus and *Heliobacter pylori* infections, which have been associated with cervical or gastric cancer, respectively [16,17]. Moreover, health endpoints associated with social determinants included infectious disease incidence, prevalence, mortality or vaccination coverage. Crowded living conditions, migration status, incarceration, substandard education, low income, or other socio-economic factors were associated with a disproportionate burden of infectious diseases in studies from every European Union (EU) Member State [18]. It is apparent that infectious diseases in Europe remain not only a serious public health threat to vulnerable populations but potentially also to the population at large. Since, as documented here, infectious disease incidence and prevalence are not distributed evenly throughout society, concentration of infections and risk factors can hasten the spread of communicable diseases. Vulnerable populations are at greater risk due to environmental or behavioural risk factors; moreover, these groups tend to lack access to healthcare to prevent further dissemination and adverse consequences of disease.

European interventions on inequalities in infections

Interventions addressing health inequalities, used in infectious disease prevention or management were identified from national websites (Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany,

TABLE 2

Selected examples of interventions on inequalities in infectious diseases in Europe, 1999–2009

Country	Outcome	Target groups	Intervention
Czech Republic	HIV, AIDS, sex education	Adolescents and adults from lower socio-economic status groups, including Roma and Sinti	Gradual improvement of knowledge, opinions and attitudes in the population, especially adolescents, with free, open and responsible patterns of behaviour and decision making [58]
Estonia	HIV, AIDS	Ethnic minorities (e.g. Sinti, Roma) and substance abusers	Improving access to quality services offered to HIV-positive pregnant women and their infants in East Viru County and reducing the risk of mother-to-child transmission of HIV during pregnancy and delivery [59]
Germany	HIV, AIDS, prevention	Asylum seekers, refugees, undocumented immigrants, migrants	Prevention of sexually transmitted infections [60]
Latvia	HIV, AIDS, counselling, testing, prevention, support, needle exchange	People living with HIV/AIDS and those at risk of developing HIV/AIDS (at risk youth, intravenous drug users, commercial sex workers, gay men, etc.), stakeholders interested/involved and the healthcare community	Operating a low threshold drop-in centre that provides support, counselling and information to people with HIV/AIDS and other relevant parties and to advocate for their interests [61]
the Netherlands	Sexually transmitted diseases, prevention, education	Migrants from the Dutch Antilles aged between 15 and 50 years	Promoting safe sex practices [62]
Spain	HIV, AIDS, sex education	(Ex)prisoners	Health promotion among the prison population [63]
United Kingdom	HIV, AIDS, sex education	11 - 25 year-olds, with difficult access to regular sex education (e.g. those with learning disabilities, deaf adolescents, homeless, excluded from education, autistic spectrum children)	Reducing the incidence of sexually transmitted infections and HIV in vulnerable young people [64]

AIDS: acquired immune deficiency syndrome; HIV: human immunodeficiency virus.

Greece, Hungary, Iceland, Ireland, Italy, Latvia, the Netherlands, Norway, Poland, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, United Kingdom) and The Good Practice Directory of the European Health Inequalities portal [19] with the following English search terms: infection, infectious, infectious, best practice, inequity, and inequality. Interventions were searched that set the reduction of health inequalities as a clear aim and target individuals or groups in a social disadvantage concerning education, occupational status or income, neighbourhood or ethnicity, etc. Three databases were identified from European Portal for Action on Health Equity [19] with relevant information (i) Closing the Gap, (ii) Health Promotion for Marginalised Groups (Gesundheitsförderung bei sozial Benachteiligten), (iii) and the QUI-database (health promotion and prevention).

The majority of interventions were designed for chronic diseases but only very few for infectious diseases. The paucity of examples in Table 2 may also reflect the lack of accessible information on existing programmes. Table 2 is unlikely a comprehensive list of all existing interventions in this field, since other programs might not be available on the internet or are only listed in their national language. Nevertheless, all infectious disease interventions identified specifically targeted sexually transmitted infections and/or HIV infection (Table 2). The narrow focus of these interventions on a specific transmission pathway and specific infections suggests that most interventions on social determinants of diseases target intermediary determinants, as discussed above. However, interventions could target both structural and intermediary determinants, to assure highest possible impact.

Intervening on inequalities in infections
Population-at-risk approach
This intervention entry point targets the population with the highest level of risk [20]. In this context, the population-at-risk can be defined as a group or groups with elevated risk for a specific infectious disease, irrespective of socio-economic status. All examples listed in Table 2 adhere to this approach since they focus on specific health endpoints in high-risk populations. Such a targeted approach can be highly efficacious in lowering the incidence of infectious diseases because it can effectively interrupt transmission. For example, in low tuberculosis prevalence countries, selective Bacillus Calmette-Guérin (BCG) vaccination of high-risk groups can be more cost-effective than a universal BCG programme [21]. In the hypothetical example illustrated in Figure 1A, assuming a normal distribution of risk, the curve is shifted to the left after the interventions, with clearly measurable benefits. Intervening on a single intermediary determinant of health is particularly efficacious when the high-risk group represents a small proportion of the population. Moreover, timely interventions targeting populations-at-risk could attenuate immediate health threats from exposure to infectious pathogens.

Limitations
Population-at-risk interventions can reduce the health threat for a specific infection singled out by the intervention. However, underlying structural determinants of health such as poverty, are not targeted with this approach [22]. Other risk factors or drivers of transmission for food, water, or vector-borne diseases might not be captured by the population-at-risk intervention (e.g. polio vaccination campaign) and thus new food, water, or vector-borne infections continue to occur. Consequently, overall health in the population-at-risk may not necessarily improve in the long run [23]. The shape of the population distribution with the overall level of risk is not altered either, with individuals remaining in the high-risk tail of the distribution in Figure 1A [24]. Even if disease transmission is interrupted, other infectious diseases continue to occur under the same contextual conditions.

The population approach
The population approach targets intermediary determinants of health through broad regulatory, environmental or health promotion measures [24]. Rather than intervening on specific populations-at-risk, this approach intervenes on the entire population. It has proven to be exceptionally successful in many settings by shifting the distribution of risk in a population to the left (Figure 1B). As a result a widespread impact in the general population can be measured. Some of these sweeping structural interventions include building codes (occupancy limits, building safety, etc.) or drinking water regulations, but also food hygiene, safe sex education or cervical cancer screening.

Limitations
This approach is based on the assumption that all groups have the same risk and same response rate to interventions, regardless of their socio-economic background. In other words, it assumes normality of the risk distribution and that individuals on the continuum of risk distribution respond equally well to the intervention, regardless if they are at the high-end of the distribution or the low end. Unfortunately, this is not necessarily the case. Populations low on the socio-economic scale tend not to respond equally well to health promotion campaigns compared with the general population [13]. For example, high-income women are more likely to take advantage of cervical cancer screening programmes compared with low-income women [12]. Therefore, the variance of the risk distribution can increase as illustrated in Figure 1C with wider tails. Moreover, the increased variance can be asymmetrical with a disproportional impact of the intervention on the left part of the distribution. Thus, those with lower risk derive more benefits from the intervention than those with greater risk and ironically, population approaches generate health inequalities.

Vulnerable population approach
In contrast to the population-at-risk approach, which targets just one risk factor, the vulnerable population

approach addresses structural determinants of health. Thus, a subset of the population, vulnerable to infections, is pursued. Several examples of marginalised populations can be found in Table 2. They include: migrants, asylum seekers, refugees, prisoners, Roma, etc. However, based on the information provided in Table 2, the interventions do not address structural determinants but rather focus on health education and health promotion for a specific health outcome (e.g. HIV infection, or acquired immune deficiency syndrome (AIDS)).

The vulnerable population approach targets underlying drivers that place individuals at 'risk for other risk factors' [25]. Rather than vaccinating against a specific infectious disease the vulnerable population approach aims at changing the social, political, cultural, or economic context that exposes marginalised populations to a number of infectious diseases. This strategy aims to lift individuals that share the same social characteristics out of a vulnerable position in society associated with a number of health threats (Figure 1D). By implementing interventions such as education

and occupational training programmes for vulnerable groups their social position can be improved with tangible health benefits [26,27]. Specifically, moving children out of poverty, or childhood interventions with early childhood education, can shape the experiences of the developing child with benefits for the entire life course [28,29]. Thus, it empowers individuals to abandon the 'fundamental causes' of disease, the risk of being at risk, which are linked to the social position of vulnerable individuals within society [30]. The goal is to alter the life trajectory for vulnerable populations which concentrate risk factors for a range of outcomes.

Limitations
The urgency of infectious disease control in many instances calls for rapid interruption of disease transmission; thus, large scale, macro-social interventions with a long-term timeframe cannot do justice to immediate personal or public health needs [31]. Moreover, high exposure prevalence in vulnerable populations justifies swift interventions among high-risk individuals to minimise exposure. Thus, certain conditions are not amenable to a long-term vulnerable population
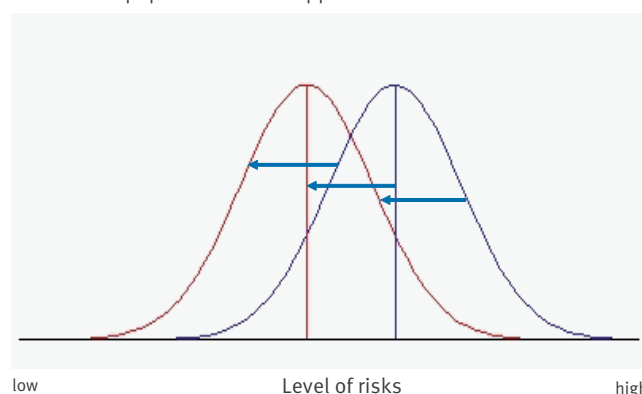
FIGURE

A-D. Hypothetical distribution of infectious diseases risk in a population and impact of selected interventions*
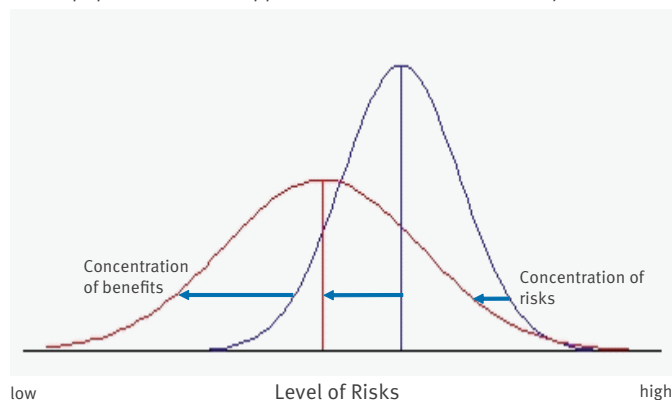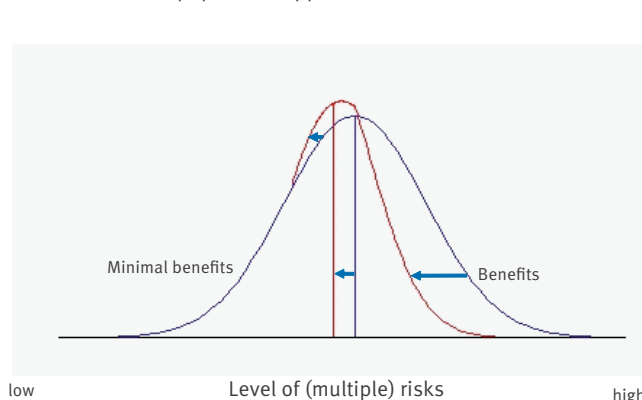

A. The population-at-risk approach
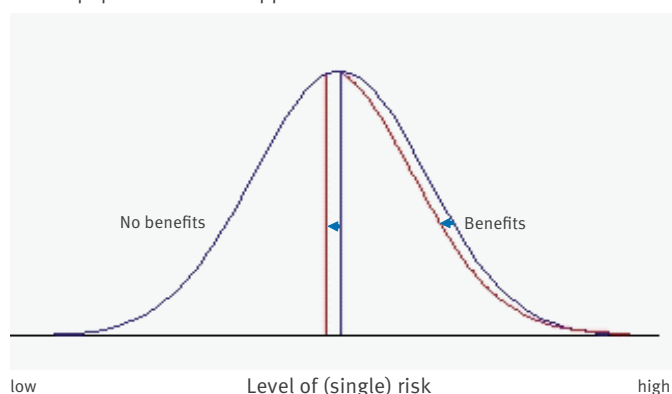
B. The ideal population-based approach

C. The population-based approach with unintended consequences

D. The vulnerable population approach

■ Before intervention   ■ After Intervention   ← Mean effect

y-axis: population.

approach and might require interventions on a single risk factor.

Conclusion

This analysis calls for flexible and dynamic infectious disease control in Europe. No strategy fits all; rather a complementary approach is warranted. Different intervention strategies might have to be put in place simultaneously [32]. Vulnerable population interventions implemented in conjunction with population-at-risk and population interventions could lead to a substantial cost-effectiveness of such a programme. Currently, however, the interventions on inequality in infections identified in this study follow the population-at-risk approach. Potentially promising elements of these interventions were identified, such as improvements in knowledge and decision making, health promotion and health education. Nevertheless, macro-social or vulnerable population interventions were not found in this search. These complementary interventions are interdisciplinary in nature and difficult to implement. Public health is a societal enterprise and interventions aimed at improving the health of population groups ought to integrate a variety of different sectors, besides the health sector, to assure a comprehensive approach by drawing from civil engineering, urban planning, education, non-governmental organisations and other stakeholders. Interventions also need to consider the socio-political context and alter project goals accordingly. Each European country has specific socio-political circumstances requiring special attention and adjustment. Interventions should be evidence-based and prioritised according to their probability of success. Clear, measurable goals should be defined prior to project implementation and monitored for efficacy. Community participation in the intervention with collective decision making increases buy-in of vulnerable/marginalised groups and helps to advance social capital [33].

In light of the inequality in infectious diseases discussed above, interventions should simultaneously consider the population-at-risk approach, the population approach, and the vulnerable population approach. Fiscal and regulatory incentives must simultaneously and sustainably support behavioural change for interventions to succeed. In practical terms, this means that the healthiest behaviour option should also be the cheapest and easiest preference.

This analysis assumes a normal risk distribution which is clearly a simplification. Many infectious diseases show a bimodal distribution of risk but for the purpose of this 'thought experiment' a normal distribution is assumed that might apply to more common infectious diseases. Nevertheless, the scenarios presented illustrate intervention options available to the public health practitioners in Europe. With these options in the tool box, public health can strive towards effective infectious disease control and prevention and even elimination of certain infectious diseases.

Considerable challenges remain to reduce inequalities in health linked to social, economic and environmental factors, as recognised by the new EU Health Strategy [34]. In light of changing demographics in Europe, the policy debate on 'Health and Migration in the EU' encourages stakeholders to build partnerships and engage in cross-sectorial work, to achieve knowledge improvements, innovation and more effective interventions [35]. Effective interventions will assure fair treatment of all segments of society with an impartial share of society's benefits. Health is fundamental to the integration of vulnerable groups into a productive, diverse and fair society.

*Erratum: In this figure, the colours in the legend were inverted. The mistake was corrected after publication of the article, on 9 July 2010.

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