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Temporal trends and demographic risk factors for hospital admissions due to carbon monoxide poisoning in England

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Abstract

Unintentional non-fire related (UNFR) carbon monoxide (CO) poisoning is a preventable cause of morbidity and mortality. Epidemiological data on UNFR CO poisoning can help monitor changes in the magnitude of this burden, particularly through comparisons of multiple countries, and to identify vulnerable sub-groups of the population which may be more at risk. Here, we collected data on age- and sex- specific number of hospital admissions with a primary diagnosis of UNFR CO poisoning in England (2002-2016), aggregated to small areas, alongside area-level charactersitcs (i.e. deprivation, rurality and ethnicity). We analysed temporal trends using piecewise log-linear models and compared them to analogous data obtained for Canada, France, Spain and the US. We estimated age-standardized rates per 100,000 inhabitants by area-level characteristics using the WHO standard population (2000-2025). We then fitted the Besag York Mollie (BYM) model, a Bayesian hierarchical spatial model, to assess the independent effect of each area-level characteristic on the standardized risk of hospitalization. Temporal trends showed significant decreases after 2010. Decreasing trends were also observed across all countries studied, yet France had a 5-fold higher risk. Based on 3,399 UNFR CO poisoning hospitalizations, we found an increased risk in areas classified as rural (0.69, 95% CrI: 0.67; 0.80), highly deprived (1.77, 95% CrI: 1.66; 2.10) or with the largest proportion of Asian (1.15, 95% CrI: 1.03; 1.49) or Black population (1.35, 95% CrI: 1.20; 1.80). Our multivariate approach provides strong evidence for the identification of vulnerable populations which can inform prevention policies and targeted interventions.

Keywords

Hospital Episode Statistics; carbon monoxide; International comparison; ethnicity; sociodemographic status; prevention policies; age standardisation; incidence risk ratio; epidemiology.

Introduction

Carbon monoxide (CO) is an odourless, tasteless and colourless gas which can rapidly reach life-threatening levels indoors following the incomplete combustion of carbon-based fuel products including those burned in heating and cooking appliances [1]. Most unintentional exposures are preventable through appropriate ventilation, maintenance of burning appliances and the use of CO detectors. Nevertheless, a high proportion of household appliances are often identified as unsafe [2–4], suggesting that more prevention could be done.

Unintentional CO poisoning remains an important cause of preventable morbidity and mortality worldwide [5–12]. The Global Burden of Disease (GBD) added CO poisoning estimates in 2017 and reported 35,500 (95% CI: 25,700–38,800) deaths and 1,462.4 (95% CI: 1,073,000; 1,613,600) disability-adjusted life years, globally for that year[13]. In addition to lethal exposures, CO poisoning can have substantial short- or long-term health implications depending on concentrations inhaled, duration of exposure and physical condition [1,2,14]. Morbidity studies are scarce and often limited to one small geographical area [6,12,15–17], with only a limited number reporting national estimates [5,8,18]. The health and economic burden of CO poisoning are therefore likely to be underestimates.

In England, unintentional non-fire related (UNFR) is the most common cause of CO poisiong, with an average of 25 deaths per year being reported between 2015 and 2016 by the Office of National Statistics (ONS) [19,20] and a hospitalization rate of 0.49/100,000 between 2001 and 2010 [17,18,21]. Risks of UNFR CO poisoning vary across countries [22], over time [23,24] and by population characteristics [25]. Although monitoring temporal trends and comparing countries can provide valuable information about risk factors and the efficacy of interventions, few epidemiological studies have addressed these questions. Ghosh *et al* conducted a spatial-temporal analysis of hospital admissions due to UNFR CO poisoning in England only[18]. Braubach and colleagues compared mortality data across 28 of the MemberStates of the WHO European Region between 1980 and 2008 [9], excluding UK.

Finally, there is some evidence that specific sub-groups of the population are at higher risk than the general population [25,26]. A pilot study funded by the Gas Safety Trust (GST), a UK gas safety research charity, on low-income households across England and Wales, identified the elderly and those living in rural areas and under fuel poverty as those at higher risk of living with unsafe CO levels in their households [26], yet this has not been explored thoroughly using nationally representative routine health data. Identifying vulnerable population sub-groups can help inform public health strategies, including awareness campaigns, prevention plans or budget allocation.

Herein, we analysed 15 years (2002-2016) of small-area hospital admission data for England to: i) describe temporal trends in England, and compare them with those reported in other high-income countries including France, Spain, the United States (US) and Canada, ii) describe spatial patterns, and iii) identify vulnerable population sub-groups for UNFR CO poisoning.

Material and Methods

Data sources

Hospital admission data

We extracted data on all non-elective CO poisoning hospital admissions registered in England between 2002 and 2016 from the Hospital Episode Statistics (HES) inpatient dataset [27]. HES contains detailed information on any admission at a National Health Service (NHS) hospital – i.e. public hospital— in England, including private patients treated in NHS hospitals. Hospital stays are broken down in periods of care under different consultants, referred to as 'episodes'. The order of episodes reflects the relevance of events in relation to the reason of hospitalization. Each episode contains a primary diagnosis and up to 19 secondary diagnostic fields, coded based on the International Classification of Disease 10th edition (ICD-10) [28]. We included hospital records with any mention of unintentional toxic effects of CO (ICD-10: T58 + X47), excluding fire-related hospital admission (ICD-10: X00-X09; T20-T32 or Y26). Nonetheless, other causes of CO poisoning (*Appendix Methods A1* & *Table A1*) were examined for context (*Table 1*). We considered both primary and secondary diagnostic fields of a first episode. Multiple admissions by the same patient were retained as exposure to the same emission source is plausible. Data on UNFR CO poisoning admissions were obtained from other high-income countries for which data could be accessed freely online (Canada) or through collaborations (US, France and Spain) (*Table A2*).

Individual and area-level indicators of risk

Individual characteristics including sex, age, place of residence (postcode) and date of diagnosis were obtained from the HES hospital records. Individual hospital records were spatially assigned to Middle Layer Super Output Areas (MSOA, 1,500 population average), based on the residential postcode at diagnosis. MSOAs are administrative area units for England defined by ONS [29]. We considered them to represent the optimum compromise between spatial resolution and statistical power for the presented analyses. Forty-three hospital records had missing information on residential postcode and thus, were excluded from the spatial analysis.

Area-level indicators included: deprivation, rural-urban classification and ethnic composition. For deprivation, we chose the Carstairs Index as it provides a small-area composite measure based on four deprivation indicators: unemployment, household overcrowding, no car ownership and social class [30]. Carstairs scores were computed using 2011 census data, standardized at MSOA level and categorised into quintiles for the analysis. For rurality, MSOAs were classified as urban if their constituent Census Output Areas (COA), the smallest statistical area units available for England (29) were predominantly classed as urban (>10,000 people) based on the ONS Rural/Urban Classification 2011 [31]. Ethnic composition was defined as the proportions of Asians and Blacks below or equal to: i) the national average; ii) 2-fold the national average; and iii) 6-fold the national average (*Appendix Methods A2*). Data on overall non-white population (i.e. Asian, Black, mixed ethnic groups and other ethnic groups) were also used for a sub-analysis with a similar approach for the cut-offs, here derived from the national non-white population proportion.

Mid-year population estimates stratified by sex, age group, year and geography were obtained from the ONS [32].

Statistical analyses

Temporal trends

Age-standardized rate (ASR) trends were studied using joinpoint analysis, which identify change points in trends and estimates the regression function for the segments[33]. We modelled the ASRs as log-linear piece-wise functions of time where the slope of each of the segment is the annual percentage change (APC). Significance was set at $p<0.05$ and tested using the Monte Carlo Permutation method. We tested up to three joinpoints and assessed the model fit and the numbers of joinpoints with the Bayesian Information Criterion (BIC). We also analysed temporal trends for Crude Rates (CR) using sex-specific hospital admission counts per year modelled as log-linear piece-wise functions of time with Poisson variance and a log-population offset [34]. All joinpoint analyses were conducted using the Joinpoint Trend Analysis Software Version 4.6.0 of the Surveillance Research Program of the National Cancer Institute [33]. Results for England were compared to those in Canada, France, Spain and the US. All country-specific rates were age-standardized using the Canadian 1991 standard population. Data collected extended from 1995 to 2016, with the range of available years varying for each country (*Table A3*).

Spatial variability

To evaluate spatial variability at the regional level, we estimated ASRs for the nine Government Office Region (GOF) across England: East Midlands, East of England, Greater London, North East England, North West England, South East England, South West England, West Midlands and Yorkshire and the Humber [10], based on their postcode at diagnosis. In addition, small-area spatial patterns of relative risk (RR) were analysed using the Besag, York and Mollié (BYM) model[35] which is a generalized linear mixed effects model that accounts for both spatially unstructured and spatially structured random effects, the latter modelled by an intrinsic conditional auto-regressive (CAR) prior.

Sub-groups at risk

Overall and sex-specific crude rates (CRs), and ASRs, using the WHO standard population, 2000-2025 [36], were estimate for each area-level indicator category. The ASR 95% confidence intervals (95% CI) were estimated according to the method proposed by Tiwari and colleagues [37]. Age-specific rates were also estimated by broad age groups (i.e. <10; 10-24; 25-39; 40-54; 55-69; 70-84, and ≥85 years old). All rates are given per 100,000 inhabitants.

To evaluate the independent effect of each area-level indicator on the age- and sex-standardized risk of UNFR CO poisoning hospitalization, we fitted a multivariate Poisson regression with random structured and unstructured random effects, following the BYM model [35] with a spatial unstructured and spatial structured random effects. Results are reported as posterior smoothed residual relative risk (RR) estimates for each covariate category and its correspondent 95% credible intervals (95% CrI). Integrated nested Laplace approximations (INLAs) were applied as a tool for Bayesian inference using the *R*-INLA package [38]. The proportion of non-whites was used, instead of the proportion of Asians and Blacks, in a sensitivity analysis (*Table A3*).

Results

We identified 6,643 hospital admissions for CO poisoning in England between 2002 and 2016, excluding fire-related cases (n=408; 5.9%) (*Fig. A1*). Of these, 1,782 (52.5%) were unintentional, which represented 47.5% (n=1,617) and 52.5% (n=1,782) of female and male hospitalizations, respectively (p=0.091) (*Table 1*). Overall, this is equivalent on average to 227 UNFR CO poisoning hospital admissions per year (min_{2013}= 166; max_{2010} = 326) (*Table 1*).

Temporal trends

There was clear seasonality in the admissions, with the largest proportion of hospitalisations occurring during winter months (November to February) (*Fig. 1*). The average annual ASR was 0.44 for males and 0.37 for females, with a peak in 2010 (males: 0.65, females: 0.51) which coincided with the inflection point detected by the Joinpoint analysis (*Fig. 2*). The trend analysis only suggested a statistically significant decrease for both male and females (-8.0% and -9.0%, respectively) beyond that inflection. Similar results were observed for CR (*Fig. A2*).

A comparison of rates and temporal trends for the five countries considered is presented in *Fig. 3*. Rates in Spain (2000-2015), which suggested a slightly negative trend overall, were similar to those found in England. . US rates, which remained unchanged between 2003 and 2013, were slightly lower than those reported in England. Canadian rates were consistently lower than those reported in the other countries considered. In France (2010-2015), there was no clear trend and rates were three- to four-fold higher than in England.

Spatial variability

Across the nine GORs, the highest ASRs were found in the North East (ASR=0.55, 95% CI: 0.47; 0.63) and Yorkshire and the Humber (ASR=0.48; 95% CI: 0.43; 0.53) and the lowest in the East (ASR=0.32; 95% CI: 0.28; 0.36) and the South East of England (ASR=0.33, 95% CI: 0.30;0.37) (*Table 2, Fig. 5*). Rates were lower among females, with the exception of the Greater London Authority and the South East where higher rates were found among females (*Fig. 4*). The unadjusted small area analysis with spatial smoothing (*Fig. 5.1a*) had an increased risk between 1.05 and 1.5 across all England with the exception of the Greater London Authority and surrounding areas, yet those associated to low confidence (*Fig. 5.1b*). Our maps also highlighted high-risk pockets across the South West, and in the coastline across the South East, East Midlands and North East of England. Spatial patterns appeared more fragmented after adjustments for area-level deprivation, rurality and ethnic composition (Fig. 5.2a and 5.2b).

Sub-groups at risk

The highest age-specific CRs were found among those aged over 85 years (1.61, *Table 2*). CRs among children aged less than 10 years old were slightly higher (0.51) than those found in older children, 10 to 24 years old (0.32) and young adult groups, 25 to 29 years old (0.41). We found higher ASRs in rural areas (0.46) compared to urban ares (0.39). Rates in areas with the largest proportion of Blacks and Asians were higher (0.57 and 0.61, respectively) than in those with a lower proportion than the national average (0.42 and 0.42, respectively). The most deprived areas had a 45% increased rate as compared to the least deprived (0.51 and 0.35, respectively). These patterns were observed both overall and by gender. ASRs were slightly higher among males than females, 0.44 and 0.37, respectively.

In our multivariate model (*Table 3*), we found a reduced risk of UNFR CO poisoning hospitalization in urban areas (RR=0.69, 95% CrI: 0.67; 0.80). We observed an association between risk and area-level deprivation, with the most deprived areas showing a 1.7-fold increase (RR: 1.76, 95% CrI: 1.66; 2.10). in relation to ethnicity, areas with the highest proportion of Asians had the highest risk (RR=1.15, 95% CrI: 1.04; 1.50). Areas with >21% of Blacks had a 1.35 (95% CrI: 1.20; 1.80) increased risk compared to areas with <3.5% (average England). When the model was fitted using the proportion of non-Whites (*Table A3*)**,** the effects of rurality and deprivation remained, although no effect was seen for areas with a higher proportion of non-White population (1.04; 95% CrI: 0.96; 1.29).

Discussion

Our study combined 15-years of nationally representative health data on UNFR CO poisoning hospitalizations with a range of individual and area-level characteristics, to provide detailed spatio-temporal epidemiological evidence for England, and to identify sub-groups at higher risk to guide future public health interventions.

Temporal trends

As in previously published studies [6,8,17,39,40], our data indicated a clear seasonality of CO poisoning, with admissions being more common during colder months. Lower temperatures and especially extreme conditions are strongly associated with higher consumption of gas and electricity, increased heating appliances usage and more time spent indoors [41,42]. This is also reflected in temporal trends observed over our study period. The highest rates of UNFR CO poisoning hospitalizations in England in 2010 coincided with the coldest winter recorded since 1979 with a mean winter temperature 2°C lower than the average temperature recorded during 1971-2000 [43]. This correlated with a peak in energy consumption for home heating [44], which is associated with an increased likelihood of CO poisoning [45,46].

Our joinpoint analysis indicated an inflexion point around 2010 in the ASR of UNFR CO poisoning hospitalizations both for females and males. Although this shift in the trends could have been driven by the 2010's cold winter, it seems more likely to reflect the impact of a new regulation, implemented in 2010, making the installation of a CO detector mandatory in all new buildings with solid fuel appliances [47]. This legislation, together with a gradual increase in the awareness, prevention campaigns and/or media coverage of CO poisoning fatal cases may have contributed to the observed decreasing trends. This regulation was extended to private sector rental properties in 2015 [48], but our study period did not allow to assess whether this legislation had further impact.

Our international comparison showed substantial variation between countries, with the lowest rates across the reporting periods observed in Canada and the highest in France and the US. This international variability has previously been reported for both CO-related hospital admissions and deaths across different countries in Europe [22]. Multiple factors including climate, data recording differences, socio-demographic characteristics, housing stock characteristics, energy efficiency, and legislation, to mention a few, may have contributed. Standardized regulations, such as those implemented across the European Union, could help facilitating such comparisons.

Spatial variability

We found substantial regional variations across England. According to Energy Performance Certificate (EPC) data, areas in the South West and North of England have a higher percentage of oil- and wood-fired primary heating appliances[49]. After adjusting for rurality, deprivation and ethnicity, the spatial patterns became more inconsistent with more pockets of high and low risk across England, which suggests that the spatial variation of UNFR CO poisoning hospital admissions is substantially influenced by the distribution of area-level characteristics considered. Cluster analyses may help identify areas which are particularly at risk.

Sub-groups at risk

Our study found males, children and the elderly, and individuals living in rural, deprived or ethnically diverse areas to be at a higher risk of UNFR CO poisoning hospital admission. Higher rates of UNFR CO poisoning hospitalizations observed in males are consistent with previous studies on CO poisoning [8,50] or poisoning in general [51]. Although reasons behind these differences remain unclear, it has been suggested that this could be related to the use of fuel-burning appliances[23,52], occupational exposure [53], time spent at home [8,50,54,55], or the likelihood of being hospitalized [39,52]. The observed bi-modal distribution across age (<10 and >85 years old), similar to that reported elswehere [20], could be explained by the greater susceptibility of the elderly and children to the manifestation of CO poisoning symptoms [2,53]. Therefore, children and the elderly could be acting as early indicators of CO exposure in the home. In addition, the elderly spend greater amount of time spent at home [8,50,54,56], and they tend to reside in old households with heating appliances less likely to be regularly checked [22,53].

Rural areas had an excess risk compared to urban areas, which remained even after adjusting for area deprivation and ethnic composition. Similar results have been reported in the US [50,55] and Romania [57]. According to data from the English Housing Survey and EPC, solid, oil and electric fuel appliances are more common in English rural areas whereas other fuel types (gas or electric) are often used in apartments, the most common building type in urban areas. Furthermore, in a pilot study assessing low income households in England, rural households with non-gas appliances were found to be linked to older and riskier boiler types [26].

Areas with a high prevalence of Asians and Blacks have an increased risk of UNFR CO poisoning hospitalization, independently of socio-economic status. The lack of effect observed when using the proportion of non-Whites instead, seems to suggest the existence of cultural practices (e.g. choice of cooking and/or heating appliance type) rooted in the Asian and Black communitie may influence their exposure to CO. An earlier study in the US reported an increased prevalence of indoor burning of charcoal briquettes among Asian populations [25]. More research is needed to confirm these results and provide a more detailed insight in its drivers.

Our results in relation to deprivation contrasts with earlier evidence for England (1988 – 1994)[17] and (2001- 2010) [18] where no linear relations were observed. However, these studies considered deprivation alone as opposed to our multivariate model which included ethinicty composition, rural/urban classification, age and sex as well asspatial structure. A widening in the health inequality gap between 2001 and 2016 [58] could also explain these differences. The increasing risk of UNFR CO poisoning hospitalization by area-level deprivation quintile could be related to a higher prevalence of smoking, poor housing conditions and poor maintenance of heating and cooking appliances. Previous studies have reported that home exposures and malfunctioning heating systems represent the majority of UNFR CO poisoning cases [2,3,49,54,59]. According to a UK survey, 40% of low-income respondents stated that they faced the choice between ‘heating or eating’ dilemma [60]. This may lead to risk behaviours including reduction of ventilation, lack of maintenance of appliances, and use of old, poorer quality supplementary heating appliances to reduce their central heating costs [61]. According to a report produced by the National Energy Action in 2017, households reporting stress and anxiety about energy affordability were more likely to have peaks of CO levels greater than 10ppm and for these to be longer [26]. Furthermore, a vulnerability differential is plausible as multiple risk factors tend to cluster in low socioeconomic groups [62–64], which may trigger biological synergism between existing conditions and the effects of CO exposure. Such clustering of risk factors in deprived groups has been widely studied for some diseases such as cardiovascular disease and diabetes [65,66].

Study strengths and limitations

This analysis of the risk of UNFR CO poisoning hospitalization in various population sub-groups in England is based on a nationally representative number of cases of CO poisoning, combined with a wide range of individual and area-level characteristics. However, our study only reflects severe cases that require hospitaliation; which may be affected by misdiagnosis, a prevalent issue in CO poisoning [21] that contributes to its underestimation, and although our approach provides valuable insights into regional and local differences, it is subject to the ecological bias as the differences in risk shown apply to populations rather than individuals.

Public health implications

Our study provides robust evidence that CO poisoning remains as neglected preventable cause of morbidity in England despite their consistent decrease since 2010. Our comparison with other countries suggested that further reductions in morbidity and mortality of CO poisoning should be possible. This is relevant as the economic burden of UNFR CO poisoning from direct care costs, long-term reductions on the earning potential of the population or death, can be substantial [67,68].

Finally, the evidence provided here on sub-groups at risk should be considered when planning and implementing targeted preventive measures, such as designing information/awareness campaigns targeted to sub-groups at risk, distributing free CO alarms, and implementing improvements in the housing sector to alleviate fuel poverty and to reduce the risk of CO poisoning among deprived populations.

Conclusion

This study highlights the urgent need to address the inequalities in the risk of CO poisoning and provides information on population groups at risk which can be used to develop more adequate and targeted measures.

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Disclosure of potential conflicts of interest

The authors declare that they have no conflict of interest.

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Tables

Table 1. Number of CO-related hospital admissions in England between 2002 and 2016 by sex and cause of poisoning. Fire-related cases were excluded.

CO poisoning type	Male		Female		Total	
	n (%)	**Annual average (n/year)[¥]**	**n (%)**	**Annual average (n/year)[¥]**	**n (%)**	**Annual average (n/year)[¥]**
Unintentional (UNFR)	1,782(52.5)	118.8/year	1,617(47.5)	107.8/year	3,399(100)	226.6/year
Intentional	2,169(80.9)	144.6/year	515(19.1)	34.3/year	2,684(100)	178.9/year
Unknown	332 (57.3)	22.1/year	228(42.7)	15.2/year	556(100)	37.1/year
Total	4,283 (64.5)	285.5/year	2,360 (35.5)	157.3/year	6,643 (100)	442.9/year

¥: number of cases per year calculated as follows: $N_{2002\text{-}2016}/15_{years}$

Table 2. Crude (CR) and age-standardized (ASR) rates of ANFR hospital admissions in England (2002-2016) by population characteristics. CI: confidence interval.

	Total				Male				Female			
	N	**CR**	**ASR**	**(95% CI)**	**N**	**CR**	**ASR**	**(95% CI)**	**N**	**CR**	**ASR**	**(95% CI)**
Total	3,399	0.43	0.41	(0.39;0.42)	1,782	0.46	0.44	(0.42;0.46)	1,617	0.41	0.37	(0.35;0.39)
Age groups (years old)												
<10	476	0.51	-		253	0.53	-		223	0.49	-	
10 to 24	476	0.32	-		237	0.32	-		239	0.33	-	
25 to 39	670	0.41	-		379	0.47	-		291	0.36	-	
40 to 54	600	0.37	-		346	0.43	-		254	0.31	-	
55 to 69	419	0.33	-		236	0.38	-		183	0.28	-	
70 to 84	486	0.65	-		218	0.65	-		268	0.65	-	
>85	272	1.61	-		113	2.09	-		159	1.38	-	
Governmental Official Regions*												
East of England	313	0.35	0.32	(0.28;0.36)	185	0.43	0.40	(0.34;0.46)	128	0.28	0.25	(0.20;0.30)
East midlands	288	0.42	0.39	(0.34;0.44)	169	0.51	0.48	(0.41;0.57)	119	0.34	0.29	(0.23;0.36)
London	513	0.42	0.41	(0.37;0.45)	236	0.40	0.40	(0.34;0.45)	277	0.43	0.43	(0.38;0.49)
North east	193	0.49	0.55	(0.47;0.63)	102	0.54	0.58	(0.47;0.71)	91	0.44	0.53	(0.42;0.66)
North west	483	0.45	0.42	(0.38;0.46)	246	0.48	0.46	(0.40;0.52)	237	0.43	0.38	(0.33;0.44)
South east	471	0.36	0.33	(0.30;0.37)	209	0.33	0.31	(0.27;0.36)	262	0.39	0.36	(0.32;0.42)
South west	336	0.42	0.38	(0.34;0.43)	189	0.49	0.47	(0.40;0.54)	147	0.35	0.31	(0.25;0.37)
West midlands	362	0.43	0.42	(0.37;0.46)	193	0.47	0.47	(0.41;0.55)	169	0.39	0.36	(0.30;0.42)
Yorkshire and the Humber	385	0.48	0.48	(0.43;0.53)	216	0.56	0.56	(0.49;0.64)	169	0.41	0.41	(0.34;0.48)
Rural/Urban Classification*												
Rural	640	0.48	0.46	(0.42;0.50)	364	0.55	0.51	(0.46;0.58)	276	0.41	0.41	(0.35;0.47)
Urban	2704	0.41	0.39	(0.37;0.40)	1381	0.43	0.41	(0.39;0.43)	1323	0.39	0.36	(0.34;0.38)
Carstairs Index*												
Q1 - Least deprived	565	0.35	0.33	(0.30;0.36)	302	0.38	0.35	(0.31;0.40)	263	0.32	0.30	(0.26;0.35)
Q2	537	0.34	0.30	(0.27;0.33)	283	0.36	0.33	(0.29;0.38)	254	0.31	0.27	(0.23;0.31)
Q3	664	0.43	0.40	(0.37;0.43)	342	0.46	0.44	(0.39;0.49)	322	0.41	0.36	(0.32;0.41)
Q4	696	0.47	0.44	(0.41;0.48)	353	0.48	0.47	(0.42;0.53)	343	0.45	0.41	(0.37;0.46)
Q5 - Most deprived	882	0.51	0.50	(0.47;0.54)	465	0.55	0.54	(0.49;0.59)	417	0.48	0.47	(0.42;0.51)

*43 hospital admissions excluded due to missing geographical information.

Table 2 (continuation). Crude and age-standardized rates of ANFR hospital admissions in England (2002-2016) by population characteristics

	Total				**Male**				**Female**			
	N	**CR**	**ASR**	**(95% CI)**	**N**	**CR**	**ASR**	**(95% CI)**	**N**	**CR**	**ASR**	**(95% CI)**
Black population (%)*												
<3.5%	2567	0.42	0.40	(0.38;0.42)	1368	0.46	0.44	(0.42;0.47)	1199	0.39	0.36	(0.33;0.38)
3.5-7%	237	0.32	0.30	(0.26;0.34)	112	0.30	0.29	(0.24;0.36)	125	0.33	0.30	(0.24;0.36)
7-21%	376	0.44	0.44	(0.39;0.49)	186	0.43	0.44	(0.38;0.51)	190	0.44	0.44	(0.38;0.51)
>21%	164	0.56	0.57	(0.48;0.67)	79	0.55	0.56	(0.44;0.70)	85	0.58	0.58	(0.46;0.72)
Asian population (%)*												
<7.8%	2483	0.42	0.40	(0.38;0.42)	1316	0.46	0.44	(0.41;0.46)	1167	0.39	0.36	(0.34;0.39)
7.8-15%	378	0.36	0.33	(0.30;0.37)	195	0.38	0.37	(0.31;0.42)	183	0.35	0.30	(0.25;0.35)
15-47%	337	0.42	0.41	(0.37;0.46)	157	0.39	0.39	(0.33;0.46)	180	0.45	0.43	(0.37;0.50)
>47%	146	0.59	0.61	(0.51;0.71)	77	0.62	0.64	(0.50;0.80)	69	0.57	0.57	(0.44;0.73)

*43 hospital admissions excluded due to missing geographical information.

Table 3. Estimates (relative risk, RR) of the fully adjusted model for ANFR CO poisoning hospital admission in England, 2002-2016*. The model used age and sex standardized rates

	RR	**(95% CrI)**
Rural/Urban Classification		
Rural	1	
Urban	0.69	(0.67; 0.80)
Carstairs Index		
Q1 - Least deprived	1	
Q2	0.98	(0.93;1.13)
Q3	1.35	(1.28;1.56)
Q4	1.55	(1.46;1.81)
Q5 - Most deprived	1.77	(1.66;2.10)
Asian population (%)		
<7.8%	1	
7.8-15%	0.93	(0.89;1.09)
15-47%	0.94	(0.89;1.13)
>47%	1.15	(1.03;1.49)
Black population (%)		
<3.5%	1	
3.5-7%	0.76	(0.71;0.91)
7-21%	1.00	(0.92;1.21)
>21%	1.35	(1.20;1.80)

RR, Relative Risk; 95% CrI, 95% Credible Intervals

*43 hospital admissions excluded due to missing geographical information.

Figures

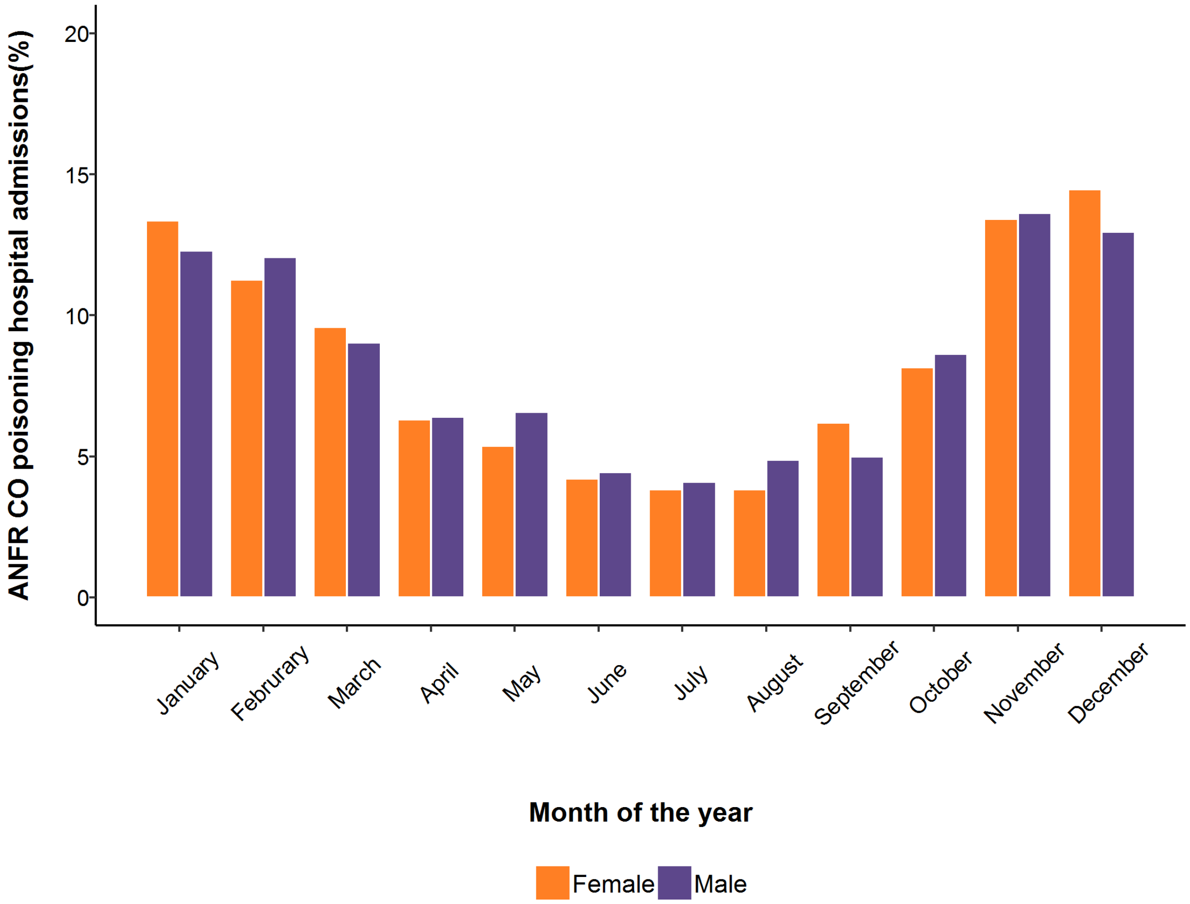

Fig. 1. Percentage of ANFR CO poisoning hospital admissions among males (purple) and females (orange) by calendar month, England, 2002-2016.

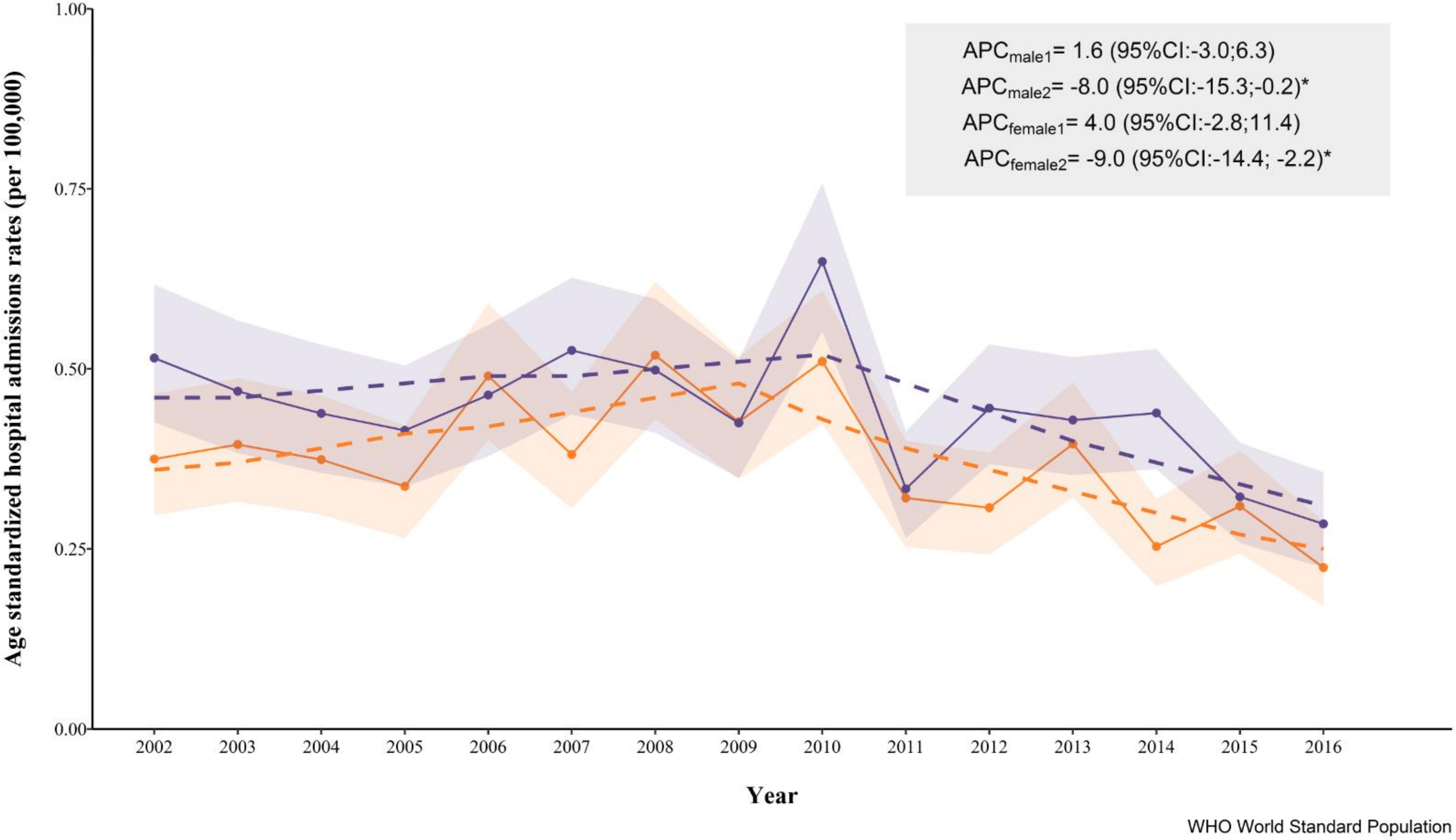

Fig. 2. Age-standardized rates (per 100,000 inhab.) of ANFR CO poisoning among male (purple) and females (orange) in England (2002-2016), shadowed areas showing the 95% confidence intervals. In dashed lines, the fitted piecewise linear regression with a joinpoint for females in 2010 and males 2009. The average percentage of change (APC) for each segment with its 95% confidence intervals (CI) is also provided. Rates were age-standardized using the WHO standard population 2000-2025.

(a)

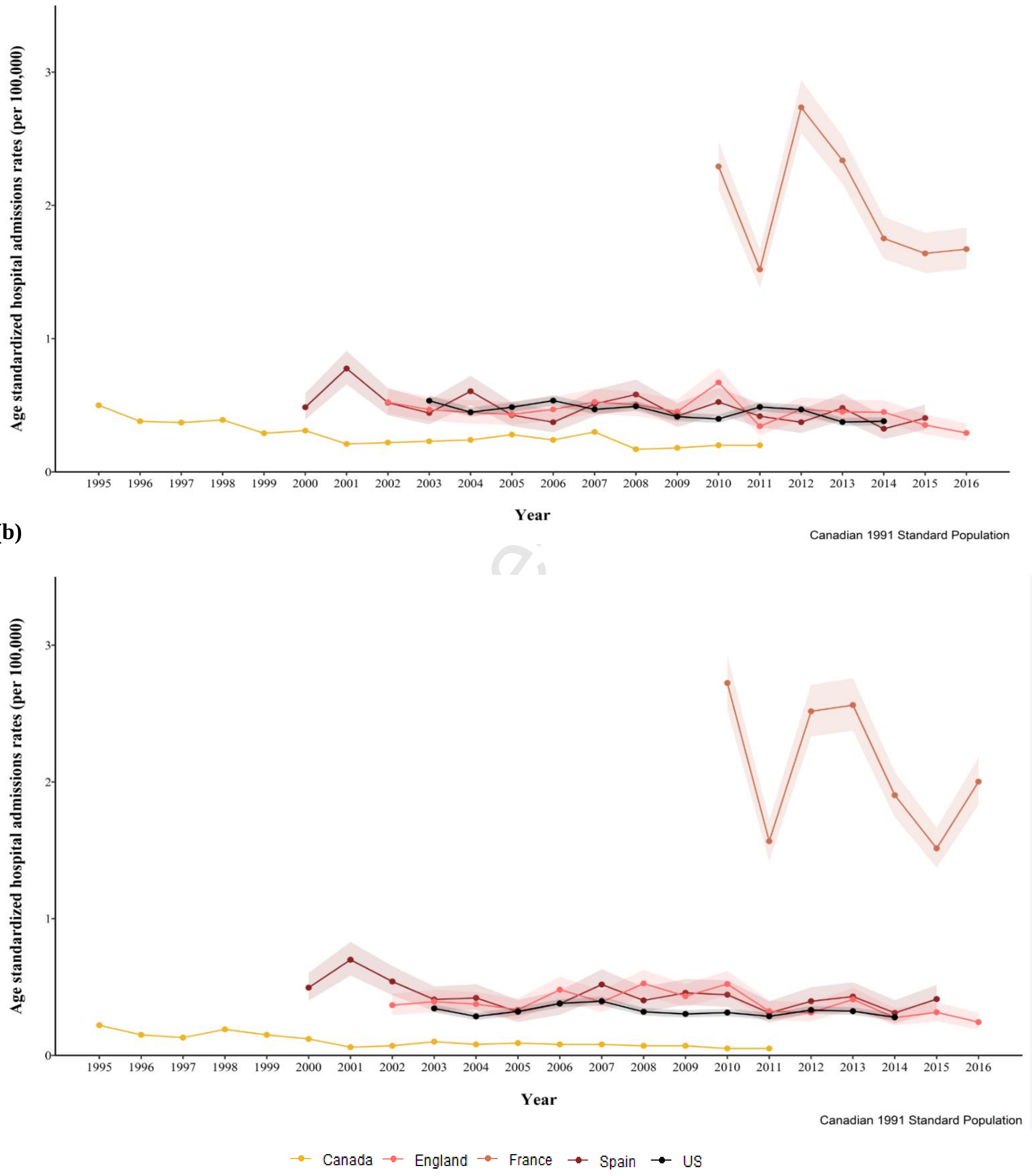

Fig. 3. Age-standardized rates of ANFR CO poisoning hospital admissions (per 100,000 inhab.) in England (light pink), France (dark orange), US (black) and Canada (yellow) and Spain (maroon) for (a) males and (b) females. Rates age-standardized using the Canadian 1991 standard population.

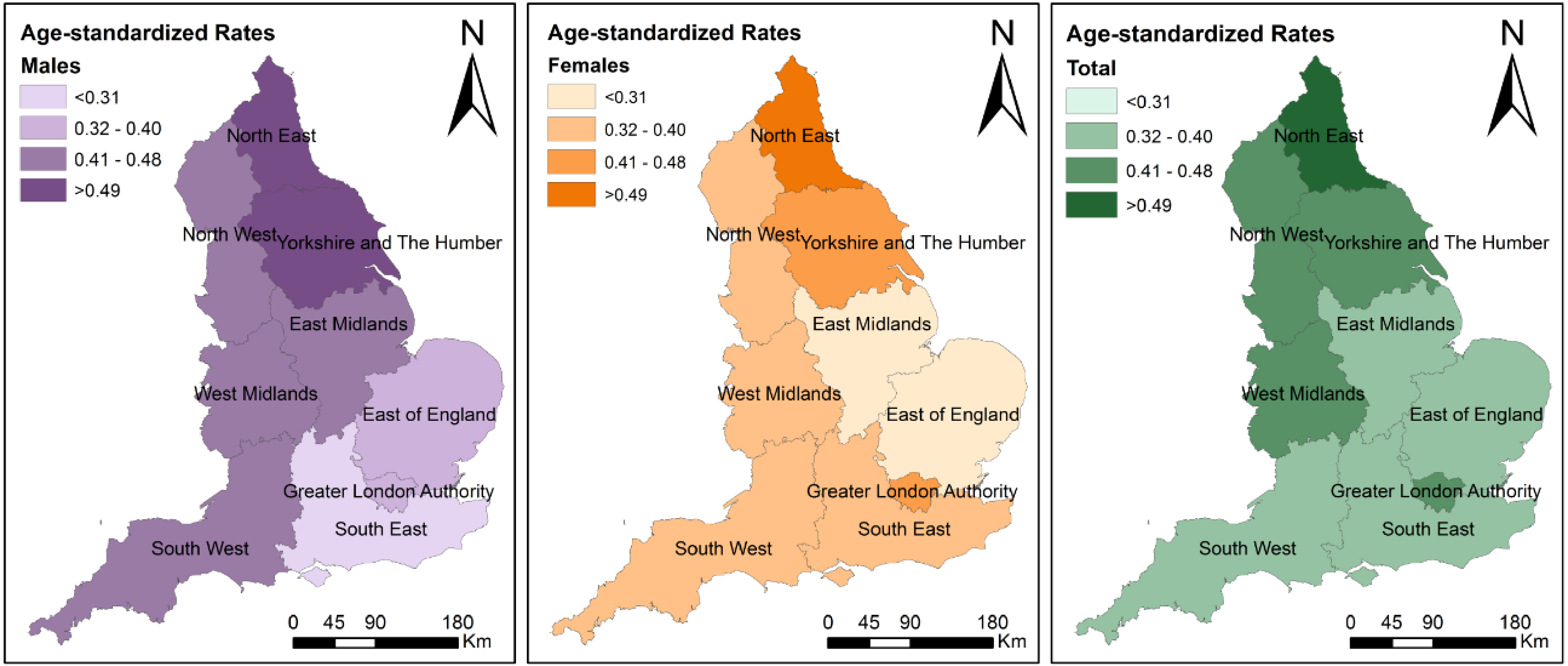

Fig. 4. Age-standardized rates per 100,000 population per Governmental Official Region for males (left), females (middle), and total (right).

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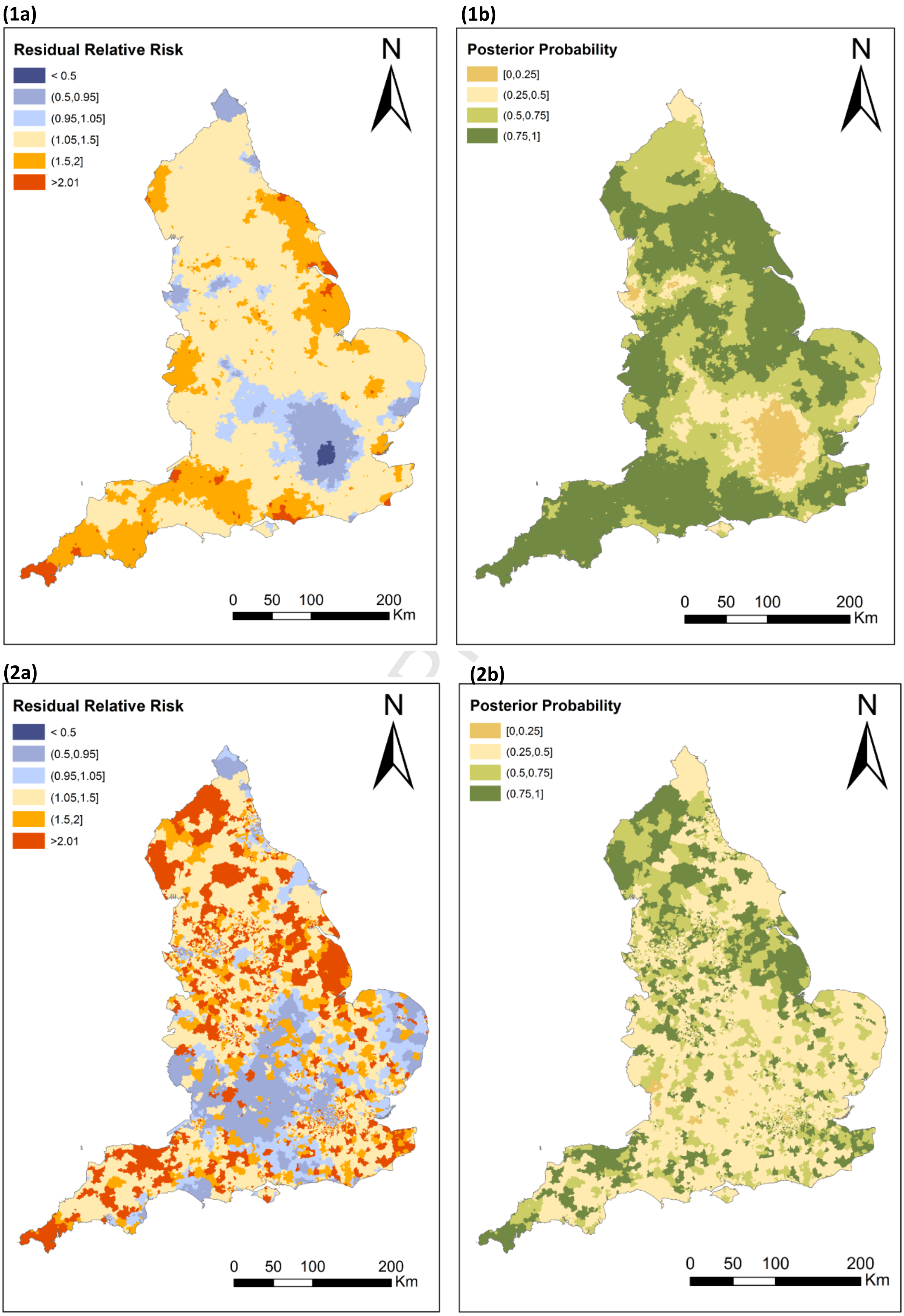


Fig. 5. (1) Unadjusted and (2) adjusted estimates of the (a) smoothed residual relative risk and (b) posterior probability of UNFR CO poisoning hospital admission in England, 2002-2016. The model used age and sex standardized rates.

Appendix Methods

A1. Classification of CO poisoning

Admissions were classified based on the reported intention as being (i) unintentional (ICD-10: T58 + X47); (ii) intentional (ICD-10: T58 + X67) or, (iii) of unknown intent (ICD-10: T58 + Y17 and admissions where no causal code was specified). All fire-related hospital admission (ICD-10: X00-X09; T20-T32 or Y26) were excluded. Only UNFR CO poisoning hospital admissions are reported here. Results of a parallel analysis of intentional UNFR admissions will be reported separately. *Supplementary Table A1* summarizes the included ICD-10 codes and their descriptions.

A2. Ethnicity indicator

MSOA-level ethnic composition was defined as the proportion of Asian (census term "Asian or Asian British," which includes "Indian," "Pakistani," "Bangladeshi", "Chinese" and "Other Asian") and Black population (census term "Black or Black British," which includes "Black Caribbean," "Black African," and "Other Black") per MSOA, which are the two major non-white ethnic groups in England. We used the following cut-off points: the national average (%) of Asian and Black population for England at MSOA level (7.8%, 3.5%), 2-fold the national average (15%, 7%), and 6-fold the national average (47%, 21%), respectively. We used those areas where the proportion was less than or equal to the national average (%) as the reference category. Furthermore, we explored the overall non-white population composition which included Asian and Black populations, as well as mixed ethnic groups (census term "Mixed/Multiple ethnic groups", which includes "White and Black Caribbean", "White and Black African", "White and Asian" and "Any other Mixed/Multiple ethnic backgrounds") and other ethnic group populations (census term "Other ethnic group", which includes "Arab" and "Any other ethnic group"). We classified them using the following cut-off points: 15% (the national average), 30% (2-fold the national average), 50% (majority of non-white ethnicities).

A3. Model description

To evaluate the independent effect of area-level deprivation, ethnic composition and rural-urban classification on the age and sex standardized risk of UNFR CO poisoning hospitalization, we fitted a Poisson regression with random structured and unstructured effects as conditional autoregressive spatial model, as developed by Besag, York and Mollié (BYM) [35]. The model included two random effects terms: (i) a structured component, to capture spatial dependency due to shared characteristics with neighbouring areas (i.e. areas nearby are more similar than those far apart), and (ii) an unstructured component (heterogeneity), which is explained by unobserved variables. The neighbouring structure was defined by adjacency of MSOA boundaries. The model equation is presented below (Eq. A1).

Eq. A1. Bayesian conditional autoregressive spatial equation for the fully adjusted main model for UNFR CO poisoning hospital admissions.

$$Obs_i \sim Poisson(Exp_i \, \lambda_i)$$

$$\log(\lambda_i) = \alpha + \beta_1 Carstairs_i + \beta_2 Asian_i + \beta_3 Black_i + \beta_4 Rural/Urban_i + h_i + b_i$$

Where:

Obs_i is the number of hospital admissions in MSOAi

Po is Poisson distribution

Exp_i are the expected number of UNFR CO poisoning hospital admissions

λ_i is the relative risk in MSOAi

α is the intercept

$\beta_1 Carstairs_i$ is the regression coefficient for the Carstairs quintile for $MSOA_i$

$\beta_2 Asian_i$ is the regression coefficient for the Asian composition at $MSOA_i$

$\beta_3 Black_i$ is the regression coefficient for the Black composition at $MSOA_i$

$\beta_4 Rural/Urban_i$ is the regression coefficient for the rural/urban classification for $MSOA_i$

h_i is the MSOA heterogeneity term (unstructured component)

b_i is the spatial term (structured component).

Appendix - Tables

Table A1. Included ICD-10 codes and description.

ICD-10 code	Description
T58.X	Toxic effect of carbon monoxide
CO poisoning by cause	
T58 + X47	Unintentional poisoning by and exposure to other gases and vapours
T58 + X67	Intentional self-poisoning by and exposure to organic solvents and halogenated hydrocarbons and their vapours
T58 + Y17	Poisoning by and exposure to other gases and vapours, undetermined intent
Fire-related exposures	
X00-X09	Exposure to smoke, fire and flames
T20-T32	Burns and corrosions
Y26	Exposure to smoke, fire and flames, undetermined intent

Table A2. Summary information on published and obtained data for ANFR CO poisoning hospital admissions by country. Rates have been standardized using the Canadian 1991 standard population unless otherwise specified.

Country		Reporting period	Reporting years	Total hosp. admissions	Average annual rates*	Lowest admission rate *(year)*	Highest admission rate *(year)*
England[a]	*Male*	2001-2010	9	1,617	0.41	0.33 *(2016)*	0.68 *(2010)*
	Female			1,782	0.46	0.28 *(2016)*	0.55 *(2010)*
	Total			3,399	0.43	0.30 *(2016)*	0.62 *(2010)*
Canada [b]	*Male*	1995-2011	16	1441	0.28	0.17 *(2008)*	0.50 *(1995)*
	Female			543	0.10	0.05 *(2010)*	0.22 *(1995)*
	Total			1984	0.39	-	-
France[c]	*Male*	2010-2016	6	4,155	1.92	1.50 *(2011)*	2.62 *(2012)*
	Female			4,464	1.94	1.43 *(2015)*	2.51 *(2010)*
	Total			8,619	1.94	1.47 *(2011)*	2.49 *(2012)*
Spain[d]	*Male*	2000-2016	16	1,670	0.47	0.30 *(2014)*	0.72 *(2001)*
	Female			1,552	0.42	0.30 *(2014)*	0.63 *(2001)*
	Total			3,222	0.44	0.30 *(2014)*	0.68 *(2001)*
US[e]	*Male*	2003-2014	12	8,025	0.48	0.41 *(2013)*	0.53 *(2003)*
	Female			6,273	0.36	0.30 *(2004)*	0.37 *(2010)*
	Total			14,298	0.43	0.38 *(2004)*	0.48 *(2006)*

*Rates given per 100,000 per year
¥ Reported period specific for each study.
¥ ¥ Average computed based on rates for 2010 and 2011 which are the common reported period across all studies
[a] Ghosh R et al. (2015)
[b] ASR directly obtained from Lavigne E et al. (2014)
[c] Counts provided by the Subdireccion General de Informacion Sanitaria y Evaluacion, Ministerio de Sanidad, Servicios Sociales e Igualdad, Spain.
[d] Counts provided by the Agence Nationale de Sante Publique, France.
[e] Counts provided by the National Environmental Public Health Tracking, Centers for Disease Control and Prevention (CDC), USA.

Table A3. Estimates of the relative risk of ANFR CO poisoning hospital admission in England, 2002-2016*, in a fully adjusted model. The model used age and sex standardized rates.

	RR	(95% CrI)
Rural/Urban Classification		
Rural	1	
Urban	0.70	(0.66; 0.79)
Carstairs Index		
Q1 - Least deprived	1	
Q2	0.98	(0.93;1.13)
Q3	1.34	(1.27;1.55)
Q4	1.55	(1.46;1.80)
Q5 - Most deprived	1.81	(1.70;2.15)
Non-white population (%)		
<3.5%	1	
3.5-7%	0.84	(0.79;0.97)
7-21%	0.88	(0.82;1.07)
>21%	1.04	(0.96;1.29)

RR, Relative Risk; 95% CrI, 95% Credible Intervals

*43 hospital admissions excluded due to missing geographical information.

Appendix- Figures

Fig. A1. Flowchart illustrating the selection criteria used to classify carbon monoxide poisoning hospital admission data for England (2002-2016). NFR, non-fire related.

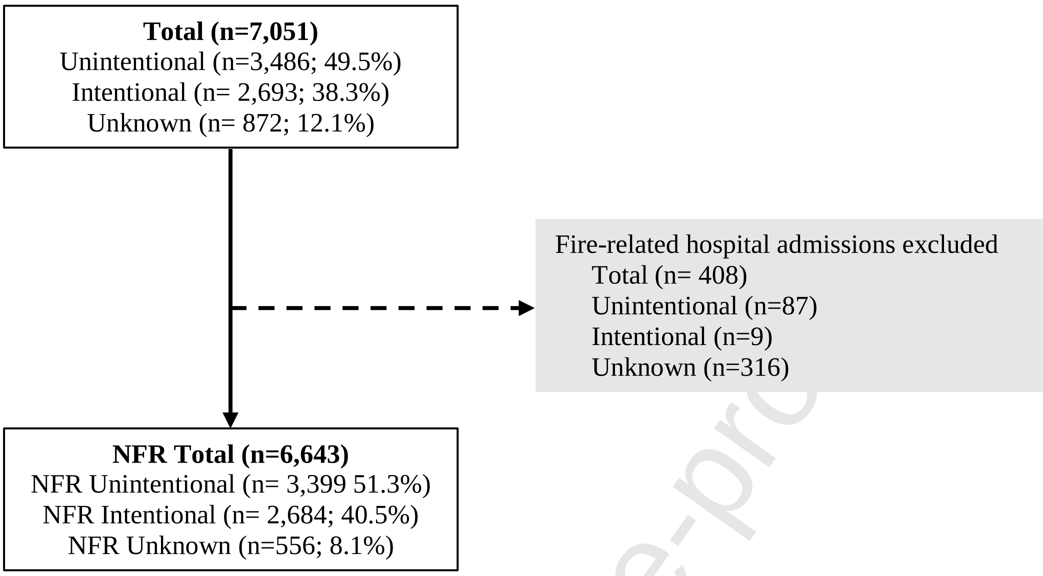
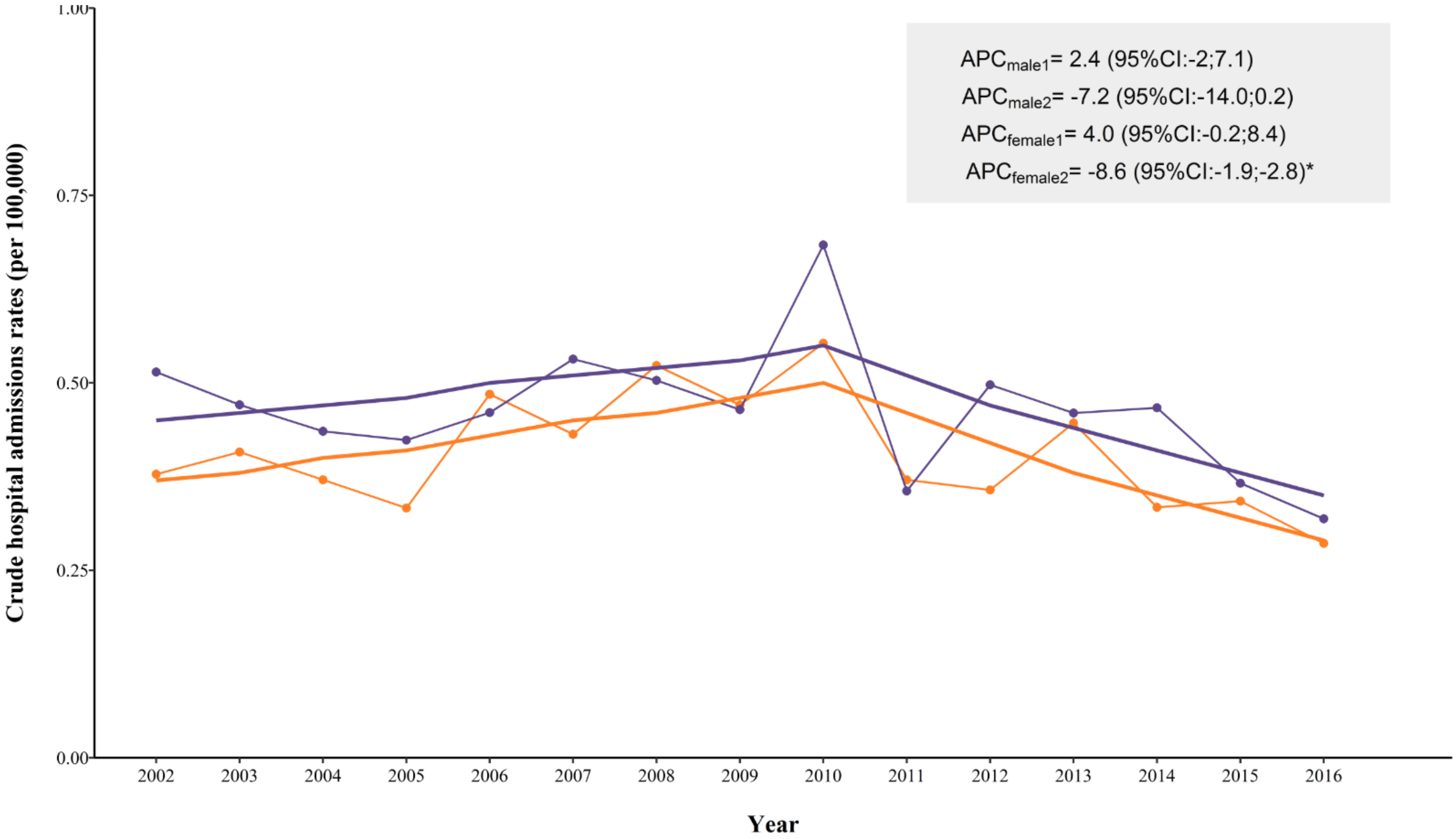


Fig. A2. Crude rates of ANFR hospital admissions among males (purple) and females (orange) by sex in England, 2002-2016. Solid lines show the piecewise linear regression with a joinpoint in 2010.



Temporal trends and demographic risk factors for hospital admissions due to carbon monoxide poisoning in England

Highlights

- **Hospital admissions for carbon monoxide (CO) poisoning have decreased in England and other high-income countries.**
- **Striking differences in age-standardized rates per 100,000 inhabitants were observed within Europe.**
- **In England, the risk of UNFR CO poisoning is higher in rural areas, deprived areas, and ethnically diverse areas.**
- **A better understanding of national, regional and local risk factors can help informing future prevention policies.**

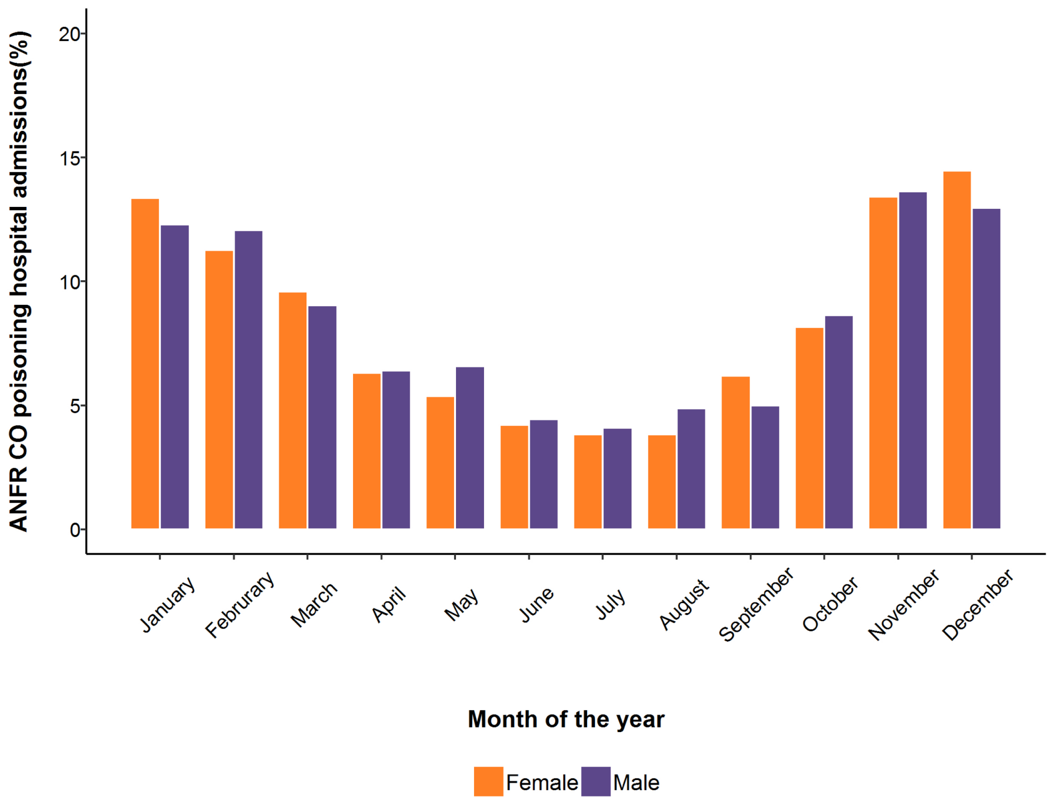

ANFR CO poisoning hospital admissions(%)
20
15
10
5
0
January
Februrary
March
April
May
June
July
August
September
October
November
December
Month of the year
Female
Male

Figure 1

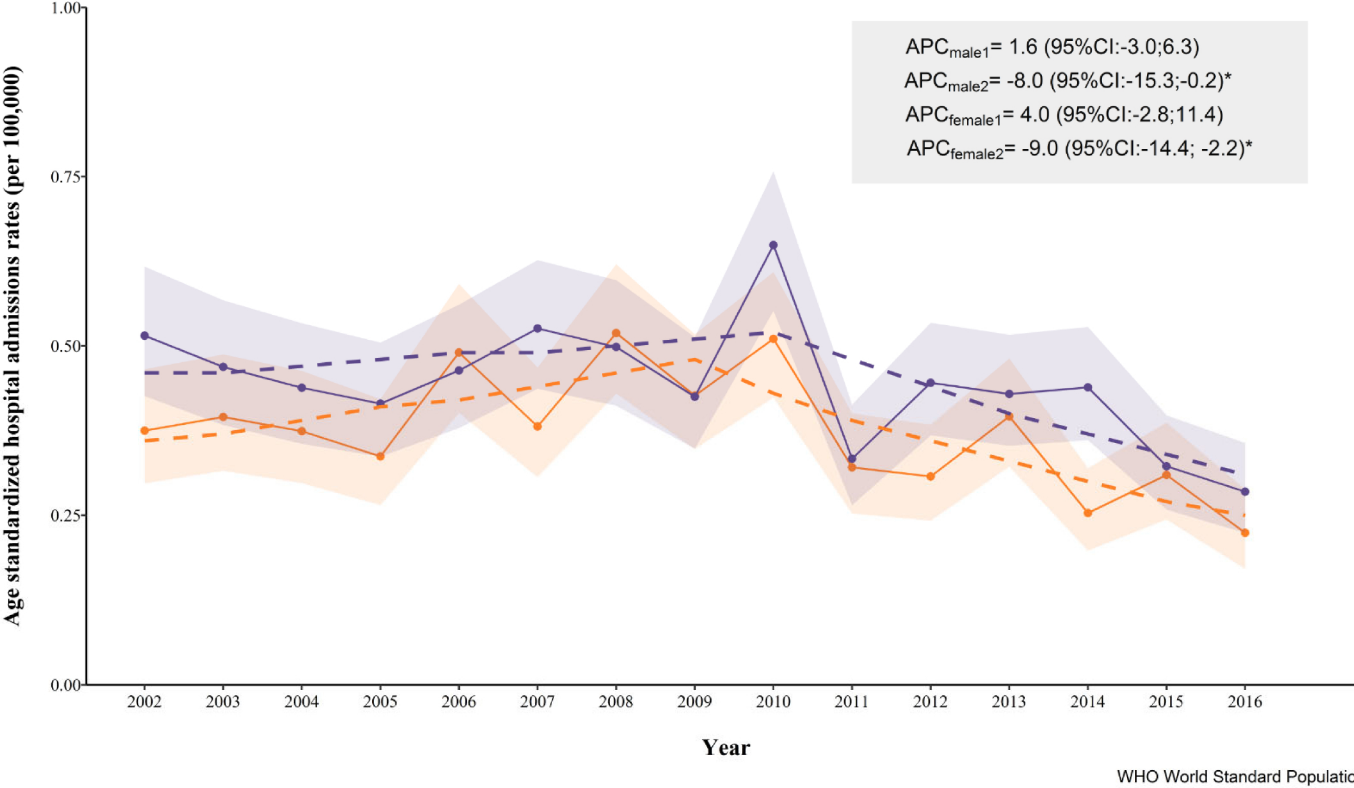

APCmale1= 1.6 (95%CI:-3.0;6.3)
APCmale2= -8.0 (95%CI:-15.3;-0.2)*
APCfemale1= 4.0 (95%CI:-2.8;11.4)
APCfemale2= -9.0 (95%CI:-14.4; -2.2)*
Age standardized hospital admissions rates (per 100,000)
1.00
0.75
0.50
0.25
0.00
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
Year
WHO World Standard Population

Figure 2

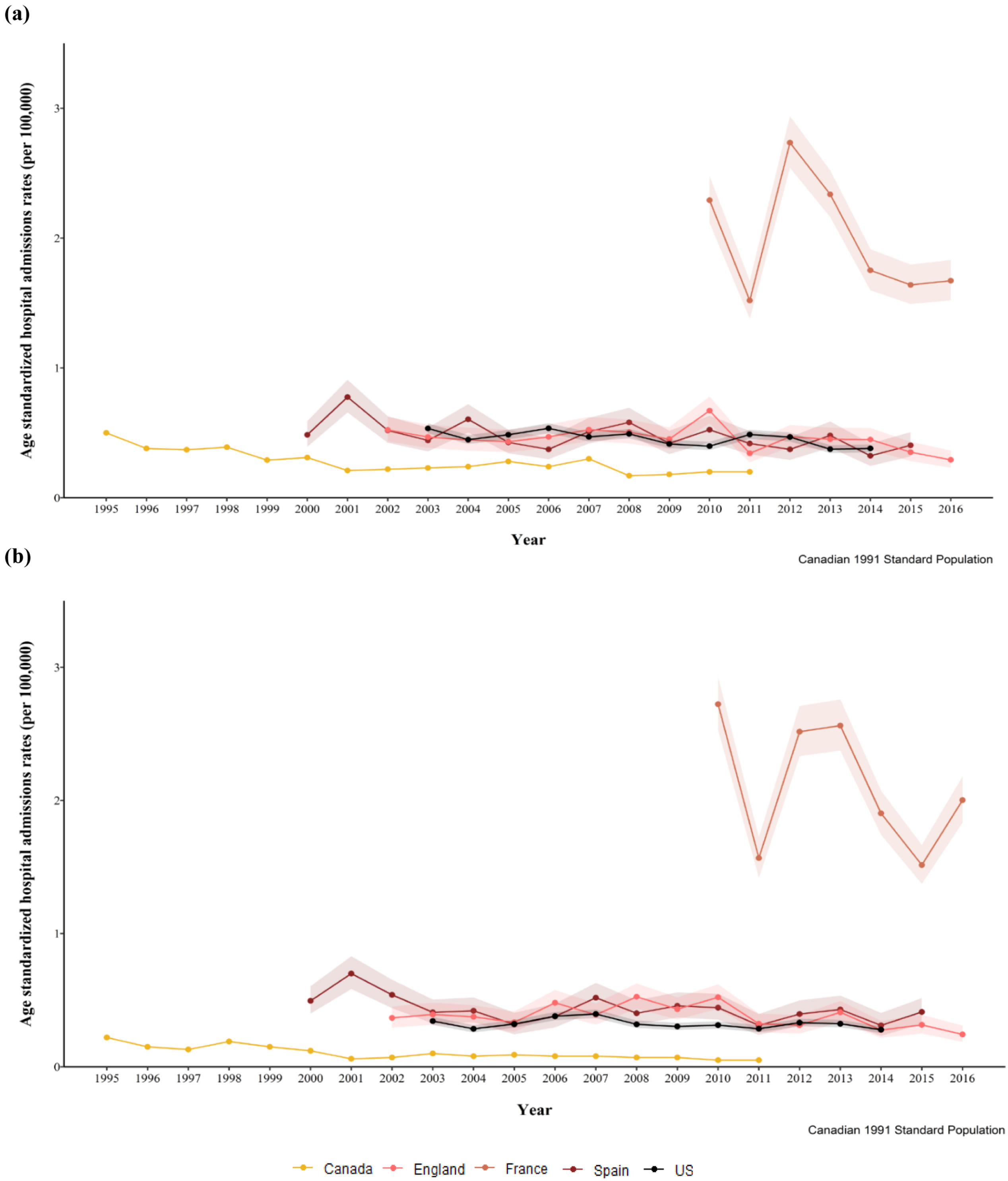

(a)
Age standardized hospital admissions rates (per 100,000)
0
1
2
3
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
Year
Canadian 1991 Standard Population
(b)
Age standardized hospital admissions rates (per 100,000)
0
1
2
3
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
Year
Canadian 1991 Standard Population
Canada
England
France
Spain
US

Figure 3

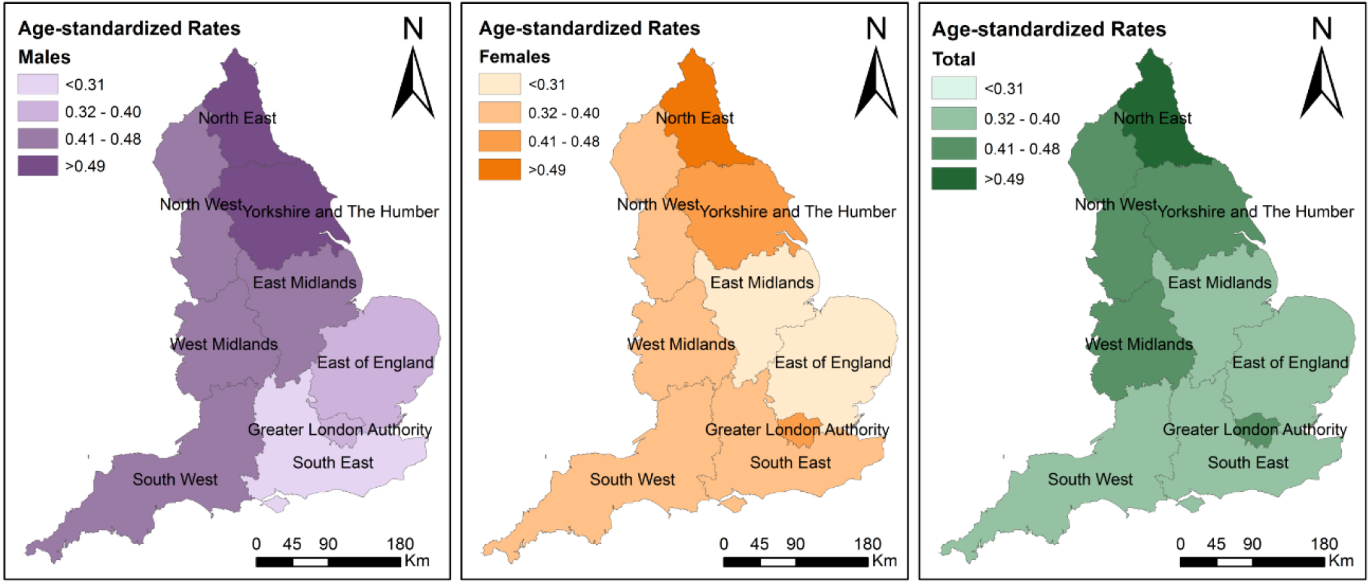

Age-standardized Rates
Males
<0.31
0.32 - 0.40
0.41 - 0.48
>0.49
N
North East
North West
Yorkshire and The Humber
East Midlands
West Midlands
East of England
Greater London Authority
South East
South West
0 45 90 180
Km
Age-standardized Rates
Females
<0.31
0.32 - 0.40
0.41 - 0.48
>0.49
N
North East
North West
Yorkshire and The Humber
East Midlands
West Midlands
East of England
Greater London Authority
South East
South West
0 45 90 180
Km
Age-standardized Rates
Total
<0.31
0.32 - 0.40
0.41 - 0.48
>0.49
N
North East
North West
Yorkshire and The Humber
East Midlands
West Midlands
East of England
Greater London Authority
South East
South West
0 45 90 180
Km

Figure 4

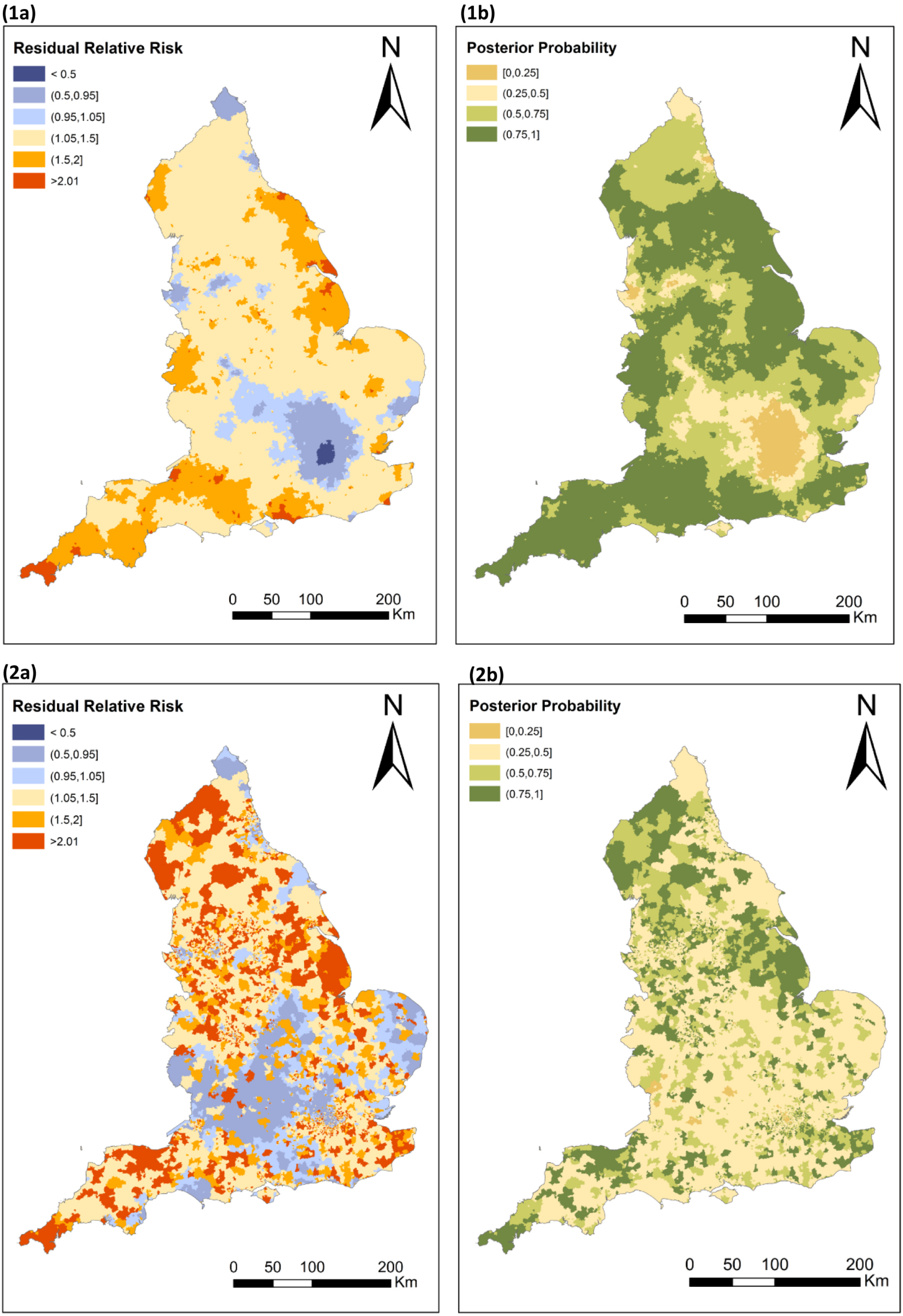

(1a)
Residual Relative Risk
< 0.5
(0.5,0.95]
(0.95,1.05]
(1.05,1.5]
(1.5,2]
>2.01
N
0 50 100 200
Km
(1b)
Posterior Probability
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
N
0 50 100 200
Km
(2a)
Residual Relative Risk
< 0.5
(0.5,0.95]
(0.95,1.05]
(1.05,1.5]
(1.5,2]
>2.01
N
0 50 100 200
Km
(2b)
Posterior Probability
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
N
0 50 100 200
Km

Figure 5