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Modelling the dead and what they died from

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Declaration of Authorship

I, Theo Rashid, hereby declare that the work in this thesis is my own original research, and that I have appropriately cited any work within that is not my own.

"*Nobody is going to read your thesis.*"

Kyle Foreman

Abstract

People died in England and we modelled the all cause and cause-specific death rates. This took longer than expected.

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List of Abbreviations

BUGS   **B**ayesian inference **U**sing **G**ibbs **S**ampling

CrI   **Cr**edible **i**nterval

CAR   **C**onditional **auto**regressive

CVD   **C**ardio**v**ascular **D**isease

GBD   **G**lobal **B**urden of **D**isease

ICAR   **I**ntrinsic **C**onditional **auto**regressive

IMD   **I**ndex of **M**ultiple **D**eprivation

LSOA   **L**ower Layer **S**uper **O**utput **A**rea

MCMC   **M**arkov **c**hain **M**onte **C**arlo

MSOA   **M**iddle Layer **S**uper **O**utput **A**rea

NCD   **N**on-**c**ommunicable **D**isease

OA   **O**utput **A**rea

NUTS   **N**o **U**-**t**urn **S**ampler

SAHSU   **S**mall **A**rea **H**ealth **S**tatistics **U**nit

Chapter 1

Overview

Thesis title is adapted from Mathers et al. (2005): *Counting the dead and what they died from.*

Code for models, plots and analysis, and this thesis can be found on GitHub.

Chapter 2

Background

2.1 Small area health statistics (unit)

In 1983, a documentary on the fallout produced from a fire at the Sellafield nuclear site in Cumbria claimed that there was a ten-fold increase in cases of childhood leukaemia in the surrounding community. This anomaly had gone undetected by public health authorities, raising concern that routinely collected data were not able to identify local clusters of disease. The subsequent enquiry confirmed the excess, and recommended that a research unit was set up to monitor small area statistics and respond quickly to *ad hoc* queries on local health hazards. The Small Area Health Statistics Unit (SAHSU) was established in 1987 (Elliott et al., 1992).

Beyond producing substantive research studies on environment and health, a core aim of SAHSU is to develop small area statistical methodology (Wakefield and Elliott, 1999) for:

- *Point source type studies.* Is there an increased risk close to an environmental hazard?
- *Geographic correlation studies.* Is there a correlation between disease risk and environmental variables?
- *Clustering.* Does a disease to produce non-random spatial patterns of incidence? If the aetiology is unknown, this could suggest the disease is infectious.
- *Disease mapping.* Summarising the spatial variation in risk.

In a pilot study for SAHSU, Elliott et al. (1992) investigated the mortality from mesothelioma and asbestosis near the Plymouth docks. Death registrations with postcode information were held by SAHSU. Both diseases are related to industrial exposure and asbestos, so concentric circular bands were drawn around the Plymouth dockyards as a way to approximate the exposure from a point source of environmental pollution. There was a clear increase in risk within $3km$ of the docks. A similar distance-based approach was adopted to look at excess respiratory disease mortality near two factories in Barking and Havering (Aylin et al., 1999), kidney disease mortality near chemical plants in Runcorn (Hodgson et al., 2004) In response to public concern over exposure to toxic chemicals in landfill, SAHSU conducted the most extensive study ever into health effects of landfill sites. Postocdes within a $2km$ buffer of a landfill site were classified as exposed. Compared to those living beyond $2km$, SAHSU found a small unexplained excess of congenital anomalies (Elliott et al., 2001a), no increase in rates of cancer (Jarup et al., 2002b), and no excess risk of Down syndrome (Jarup et al., 2007).

Distance from source is, however, only a basic model for the exposure, which can often exhibit more complex, directional spatial patterns. A number of SAHSU studies have employed physics-informed models to create an exposure surface, and assess the geographic correlations between this surface and the health outcome, notably for a plume of mercury pollution (Hodgson et al., 2007), exposure to mobile phone base station during pregnancy (Elliott et al., 2010), noise from aircrafts near Heathrow (Hansell et al., 2013), road traffic noise in London (Halonen et al., 2015), and PM10 from incinerators during pregnancy (Parkes et al., 2020). SAHSU published an environment and health atlas for England and Wales, showing the geographic patters of 14 health conditions at census ward level over an aggregated 25 year period alongside five environmental exposure surfaces (Hansell, Anna L. et al., 2014).

2.1.1 Disease mapping at SAHSU

Many of the studies at SAHSU focus on rare diseases at small areas. The data for the number of cases, or number of deaths, in a region are likely to small numbers. This sparseness issue is even more pertinant when the population is also statified by

age group. Rates calculated from observed data present apparent variability between spatial units, which is larger than the true differences in the risk. There is a need for statistical smoothing techniques to obtain robust estimates of rates by sharing information between strata. Aylin et al. (1999) mapped diseases for wards in Kensington, Chelsea and Westminster using a simple model that smoothed rates towards the mean of the risks across the region. SAHSU thereafter published a plethora of studies for disease mapping models with explicit spatial dependence, which are designed to give more weight to nearby areas than those further away.

There are three main categories for modelling spatial effects. First, we can treat space a continous surface, such as Gaussian processes or splines. Second, we can use areal models, which make use of spatial neighbourhood structure of the units. Thirdly, we can explicitly build effects based on a nested hierarchy of geographical units, for example between state, county and census tract in the US.

In the context of disease mapping, events are usually aggregated to areas rather than assigned specific geographical coordinates. Wakefield and Elliott (1999) model aggregated counts as realisations of a Poisson process, in which the expected number of cases is calculated by integrating a continuous surface that generates the cases integrated over the area. The surface was some function of spatially-referenced covariates. Kelsall and Wakefield (2002) describe an alterative model, where the log-transformed risk surface is modelled by a Gaussian process, whose correlation function depends on distance.

Best et al. (2005) provide a review of the use of hierarchical models with spatial dependence for disease mapping. In particular, the authors focus on Bayesian estimation, and different classes of spatial prior distributions.

The first prior proposed for spatial effects $\mathbf{S} = S_1, ..., S_n$ is the multivariate normal

$$\mathbf{S} \sim \mathcal{N}(\boldsymbol{\mu}, \boldsymbol{\Sigma}), \tag{2.1}$$

where $\boldsymbol{\mu}$ is the mean effect vector, $\boldsymbol{\Sigma} = \sigma^2 \boldsymbol{\Omega}$ and $\boldsymbol{\Omega}$ is a symmetric, positive semi-definite matrix defining the correlation between spatial units. A common choice

when specifying the structure of the correlation matrix is to assume a function that decays with the distance between the centroids of the areas, so that places nearby in space share similar disease profiles. Note, this is mathematically equivalent to the practical implementation of a Gaussian process, whcih uses a finite set of points. An example in Elliott et al. (2001b) chooses the exponential decay function to map cancer risk in northwest England.

A more popular prior is the conditional autoregressive (CAR) prior, also known as a Gaussian Markov random field. These form a joint distribution as in Equation 2.1, but the covariance is usually defined instead in terms of the preicision matrix

$$\mathbf{P} = \mathbf{\Sigma}^{-1} = \tau(\mathbf{D} - \rho\mathbf{A}), \tag{2.2}$$

where τ controls the overall precision of the effects, $\mathbf{A}$ is the spatial adjacency matrix formed by the small areas, $\mathbf{D}$ is a diagonal matrix with entries equal to the number of neighbours for each spatial unit, and the autocorrelation parameter ρ describes the amount of correlation. This can be seen as a tuning the degree of spatial dependence, where $\rho = 0$ implies independence between areas, and $\rho = 1$ full dependence. The case with $\rho = 1$ is called the intrinsic conditional autoregressive (ICAR) model. Besag et al. (1991) proposed the model (hereafter called BYM)

$$S_i = U_i + V_i, \tag{2.3}$$

where U_i follow an ICAR distribution, and V_i are independent and identically distributed random effects. The BYM distribution was employed to model spatial variation in the relative risk of testicular (Toledano et al., 2001) and prostate (Jarup et al., 2002a) cancers for small areas in regions of England.

Further disease mapping studies at SAHSU using spatially structured effects have also extended the methdology to look at age patterns and trends over time of disease. Asaria et al. (2012) analysed cardiovasuclar disease death rates by fitting a spatial model for all wards in England separately for each age group and time period. Bennett et al. (2015) considered a model to jointly forecast all-cause mortality for districts

in England, age groups and years. The model used BYM spatial effects and random walk effects over age and time to capture non-linear relationships. It is also possible to borrow information across causes of death, as applied in Foreman et al. (2017) on forecasting cause-specific mortality for states in the US. Random walk effects were again used to non-linear temporal effects, a CAR prior was used for spatial effects, and a multivariate normal where the covariance matrix describes the correlation structure between the 15 cause groups. The model did not, however, share information between age groups. Although this is not directly a SAHSU study, the model was developed by a several people in the department.

In building models which consider the hierarchy of geographical units, these relationships are often incorporated into the model as a nested hierarchy of random effects. These models account for which spatial units lie within common administrative boundaries, but, by design, there is no knowledge of spatial distance included. This is often a desirable property of the model for certain geographies, like states in the US, which are administrative. Policy is decided at these geographies, so there is reason to believe these boundaries may have a greater effect on health outcomes than spatial structure. Although not used in previous SAHSU studies, Finucane et al. (2014) demonstrate how country-level blood pressure can be modelled as such, in this case exploiting the hierarchy global, subregion, region and country. Note, although these models group by geographical region, these models are not spatial as they do not contain any information on the position relative to other units.

2.1.2 Small area analyses of mortality

In order to compare the health status between areas, health authorities require a measure of mortality that collapses age-specific information into a single number. Indirectly standardised measures such as the standardised mortality ratio – the ratio between total deaths and expected deaths in an area – are easy to calculate but are not easily understood by laypeople. Directly standardised methods, in contrast, require knowledge of the full age structure of death rates rather than just the total number of deaths. Age-standardised death rates, however, suffer the same interpretability issue as the standardised mortality ratio, and are only comparable between studies

if the same reference population is used. An alternative choice is life expectancy. Silcocks et al. (2001) explain that life expectancy is a "more intuitive and immediate measure of the mortality experience of a population, [and] is likely to have greater impact… than other measures that are incomprehensible to most people." For studies of small geographies where there are often small number issues, the calculation of life expectancy is either extremely unstable or impossible (Jonker et al., 2012).

The estimation of death rates requires two data sources: deaths counts and popualtions. Modern vital registrations systems are complete and accurate, so data on deaths are usually reliable and comprehensive. On the other hand, although usually treated as a known quantity, the population denominator is often problematic. Populations for small geographies are only recorded during a decennial census, and estimates are generated for the years in between using limited survey data on births, deaths and migration. And although the census is considered the "gold standard", it is subject to enumaration errors, particularly for areas with special populations such as students or armed forced Elliott et al. (2001b).

Beyond the population issue, finer scale studies are restricted by data availability. Where data are available, there is still the need to overcome small number issues before feeding death rates through the life table. Eayres and Williams (2004) recommend a minimum population size of 5000 when using traditional life table methods, below which the error estimates in life expectancy become so large that any comparison between subgroups becomes meaningless. One approach, often taken by statistical agencies, is to build larger populations by either aggregating multiple years of data Bahk et al. (2020) or combining spatial units (Ezzati et al., 2008). Here, we focus on studies using Bayesian hierarchical models to generate robust estimates of age-specific death rates by recognising the correlations between spatial units and age groups, which produce lower bias and smaller, more accuate estimates for small population studies of life expectancy Jonker et al. (2012).

Jonker et al. (2012) demonstrated the advantages of the Bayesian approach to stabilitising estimates for 89 small areas in Rotterdam using a joint model for sex, space and age effects, finding a 8.2 year and 9.2 year gap in life expectancy for women and

men. Stephens et al. (2013) employed the same model for 153 administrative areas in New South Wales, Australia.

Bayesian spatial models for mortality have been scaled up to relatively small areas for entire countries, and also consider trends in these regions over time. Bennett et al. (2015) forecasted life expectancy for 375 districts in England and Wales using an ensemble of spatiotemproal models trained over a 31 year period, and Dwyer-Lindgren et al. (2017a) explored mortality trends 3110 US counties from 1980 to 2014.

There have also been studies on specific cities at a finer resolution. In order to obtain better estimates for disability-free life expectancy, Congdon (2014) consider both ill-health and mortality in a joint likelihood with spatial effects for 625 wards in London, finding more than a two-fold variation in the percent of life spent in disability for men. Bilal et al. (2019) looked at 266 subcity units for six large cities in Latin America. As there is no contiguous boundary in this case, a random effects model for each city was used instead of a spatial model. The largest difference between the top and bottom decile of life expectancy at birth was 17.7 years for women in Santiago, Chile.

Two studies in North America have looked below the county level, at census tracts, with wide ranging popualtion sizes as small as 40. Dwyer-Lindgren et al. (2017b) studies trends for life expectancy and many causes of death for 397 tracts in King County, Washington, uncovering an 18.3 year gap in life expectancy for men. Using the same model for Vancouver, Canada, Yu et al. (2021) found widening inequalities over time and a difference of 9.5 years for men.

2.2 Mortality by specific causes of death (counting the dead and what they died from)

In the mid-twentieth century, a team in the US Public Health Service, led by Iwao Moriyama, began looking into the decomposition of mortality for the first half of the century into all diseases and injuries. Notably, Moriyama and Gover (1948) grouped vital registration data into primary causes, and found as the US saw overall downward trend in mortality, leading causes of death changed from communicable diseases, such

as tuberculosis and diptheria, toward non-communicable, "chronic disease of older ages", such as heart diseases and cancers. The success of the reduction – and in the case of typhoid fever, near-elimination – of infectious diseases was attributed to the strategy of the health officer in the early 1900s, who was preoccupied with improving water and sanitation, and public health intervations such immunisation and quartantines.

By comparing vital registration data over several centuries, Abdel Omran observed this shift of mortality from communicable to non-communicable diseases (NCDs) in many countries (Omran, 1977, 1971). Specifically, although the pace and determinants of the transition varied between countries, Omran formalised three common successive stages of the shift in mortality:

1. *The Age of Pestilence and Famine.* Mortality is high and largely governed by malthusian "positive checks" – epidemics, famines, and wars.

2. *The Age of Receding Pandemics.* Mortality decreases as epidemics become less frequent, but infectious diseases remain the leading causes of death.

3. *The Age of Degenerative and Man-made diseases.* Mortality declines further along with fertility, increasing the average age of population and NCDs take over as the leading causes of death.

He termed this the *Epidemiologic Transition theory.* Omran (1971) explained that England and Wales took the classic transition path followed by western societies, whereby socioeconomic factors such as improvements to living standards are crucial in causing easily preventable diseases to subside and shifting towards the third phase of the transition, and medical and other public health technology only help society much later in the final stage. Later, Olshansky and Ault (1986) would propose a fourth stage to the theory, *the Age of Delayed Degenerative Diseases*, in which the structure of causes of death is stable, but the age at which degenerative diseases kill is postponed, thus causing decreasing in older age mortality. There are, however, questions around the universality and unidirectionality of the theory, with many examples in which age-specific death rates for population subgroups have risen over time, most notably the HIV/AIDS pandemic (Gaylin and Kates, 1997). Gersten and Wilmoth (2002)

also criticise the lack of attention Omran's theory pays towards the role infection in chronic and degenerative diseases, in particular certain cancers.

Around the same time as Omran, Samuel Preston collated cause-specific mortality data for a huge number of populations, spanning 48 nations and nearly a century (Preston, 1970; Preston and Nelson, 1974). This would enable international comparisons of groups of causes of death over different time periods, and a deeper understanding of the upward trends in life expectancy. In particular, by plotting cause-specific disease rates against overall mortality, Preston and Nelson (1974) saw that, over time, the contribution of infectious diseases to a particular *level* of mortality had become ever smaller. That is to say, as mortality declines, the contribution from infectious diseases also declines. Preston attributed this to an accerlating rate of medical progress guided by the "germ theory of disease", which public health and science were not able to replicate for NCDs. Preston also traced the excess deaths in older males observed in western societies to cardiovascular diseases, cancer and bronchitis – a direct result of dramatic increases in cigarette smoking (Preston, 1970).

Since its first edition in 1990, the subject of international comparisons of the cause-specific composition of mortality has been the remit of the Global Burden of Disease (GBD) studies (Murray and Lopez, 1996). The studies aim to quantify and compare the burden of diseases, injuries, and risk factors, usually through cross-sectional methods but occasionally by examining trends and subnational populations (for example, Ezzati et al. (2008) and Dwyer-Lindgren et al. (2017a)). An important innovation of the GBD study was the introduction of a hierarchical classification of groups of causes, with the broadest level divided into three groups: communicable, maternal, perinatal, and nutritional diseases (Group 1), NCDs (Group 2), and injuries (Group 3). Salomon and Murray (2002) made use of the wide-ranging dataset and grouping from the GBD to revisit the epidemiologic transition for the second half of the twentieth century, finding the majority of the change in cause structure occurs among children, with a shift from Group 1 to Groups 2 and 3, and in young adults, where the role of injuries is more dominant for men.

2.3 Health inequalities in the UK

While the UK is, by global standards, a wealthy nation with relatively high life expectancy, and the breadth of health inequalities are nowhere near the extremes seen in many other countries, the nation suffers still vast, preventible inequalities in mortality and morbidity. There are several ways to stratify the UK population and comapare inequalities between subgroups. Here, we focus on class, income, geography, and deprivation.

The notion of class is prominent in UK society, but health outcomes between classes are difficult to separate from other risk factors such as hazards in manual labour or smoking rates. The Whitehall study of 1967 followed 17,530 men working in the civil service and recorded their mortality over a 10-year period. Marmot et al. (1984) found, by classifying the civil servants into social class according to their employment grade, there was a three-fold difference in mortality between the highest class, administrators, and men in the lowest class, mainly messengers and unskilled manual workers. They found, in general, a strong inverse association between grade and mortality – a term Marmot has coined a "social gradient". The men were working stable, sedentary jobs in the same office building in London, so the gradient could not be fully explained by smoking or industrial exposure alone. There authors concluded be other factors inherent to social class (defined here by employment), which explain the mortality differences. A second cohort of Whitehall employees from 1985 to 1988, this time including women as well as men, were screened and asked to answer questions on self-reported ill-health. Marmot et al. (1991) found the social gradient in health had persisted in the 20 years separating the studies. In 2008, Marmot was asked by the Secretary of State to conduct a review into the state of health inequalities in England and to use the evidence to design policy for reducing these inequalities. A key plot in the first Marmot Review, released in 2010, depicted the social gradient in mortality for regions in England by socio-economic classification of jobs [].

Income data is not a routinely collected statistic in the UK. Nevertheless, using a small survey of 7000 people on three measures of morbidity, Wilkinson (1992) showed health improved sharply from the lowest to the middle of the income range.

In 2015, the GBD Study released its first subational estimates of mortality, starting with the UK and Japan. Steel et al. (2018) assess these data, which divided the UK into 150 regions, finding mortality from all-causes varied twofold across the country, with the highest years of life lost in Blackpool and the lowest in Wokingham. In a study on forecasting subnational life expectancy in England and Wales, Bennett et al. (2015) estimated a 8.2 year range in life expectancy for men and 7.1 year range for women in 2012 between 375 districts. The lowest life expectancies were seen in urban northern England, and the highest in the south and London's affluent districts. Within London itself, male and female life expectancy showed 5-6 years of variation.

There have been substantial efforts in the UK to measure the deprivation of an area, with the standard deprivation indicator in England since the 2000s is the Index of Multiple Deprivation (IMD) – a composite indicator for each Lower-layer Super Output Area (LSOA) covering income, unemployement, health, crime and environmental data sources ("English indices of deprivation 2019," 2019). The Marmot Report presented life expectancy and disability-free life expectancy against IMD at the Middle-layer Super Output Area, whcih exhibit a strong social gradient (Marmot et al., 2010). The GBD study found the 15 most deprived UTLAs had consistently raised mortality, especially for all causes, lung cancer and chronic obstructive pulmonary disease. Deprived UTLAs in London, such as Tower Hamlets, Hackney, Barking and Dagenham did better than expected for that level of deprivation (Steel et al., 2018). Bennett et al. (2018) jointly estimated death rates by age, year and deprivation decile. They found since 2011, "the rise in female life expectancy has reversed in the two most deprived deciles, and has stalled in the third, fourth, and fifth most deprived deciles but has continued in better-off deciles." The second Marmot Review in 2020 also found female life expectancy declined in the most deprived decile between the periods 2010-12 and 2016-18 (Marmot et al., 2020). Digging further into these trends by region, the report found this trend was seen in all regions except London, the West Midlands and the North West, and that male life expectancy in the bottom decile also decreased in the North East, Yorkshire and the Humber and the East of England.

Since the turn of the millenium, there have been two periods of contrasting health

policy in the UK. The early 2000s saw the implementation of the English health in-equalities strategy under New Labour, with explicit goals of reducing geographical inequalities in life expectancy. The strategy saw a large increase in public spending targeting the social determinants of health, with policies on supporting families, tack-ling deprivation, and preventative healthcare. Barr et al. (2017) analysed the trends in life expectancy for different quantiles of deprivation and provided evidence that the strategy acheived its aim of reducing the gap in life expectancy between the 20% most-deprived areas and the rest of the English population.

Following the change in government in 2010, the strategy came to an end. The Conservative government implemented a series of widespread cuts to public services, collectively known as austerity. The study by Barr et al. (2017) saw that the trends in inequality reduction were reversing since 2012. These trends have been found at both ends of the life course: rising infant mortality associated with childhood poverty (Taylor-Robinson et al., 2019), and falls in female life expectancy at 65 and 85 (Hiam et al., 2018). Although difficult to uncover causal relationships, Alexiou et al. (2021) found strong associations between cuts to local government and the change in life expectancy of the district in the study period 2013-17. As written in the *The New York Times*, "after eight years of budget cutting, Britain is looking less like the rest of Europe and more like the United States, with a shrinking welfare state and spreading poverty" (Goodman, 2018) – a comparison only compounded by the Brexit vote in 2016.

Policies of austerity were brought about as a response to the financial crash of 2008, which were global in scale, and many countries adopted similar fiscal strategies. In an international study comparing mortality trends in England and Wales to 22 compara-tor countries Leon et al. (2019) show, however, that although there was a general slowdown in improvement of life expectancy across many nations, the slowdown in the most recent period of the study, 2011-16, was more pronounced in England and Wales.

After a decade of cuts, the UK entered the 2020s facing the greatest public health challenge for a generation: the Covid-19 pandemic. Unsurprisingly, England and

Wales suffering one of the highest excess deaths tolls relative to other industrialised countries (Kontis et al., 2020). At the current time of writing in 2023, the health service is yet to recover, with waiting lists for operations and waiting times for emergency care unhealthily high (Dorling, 2023). There is no suggestion that the picture of health and health inequalities in the UK should improve in the coming years.

Chapter 3

Some notes on the data and the models

3.1 Counts of the dead

This thesis is primarily concerned with modelling death rates for small areas in England. This requires two data sources: counts of deaths, and populations counts. The dataset is In other words, every death in England from 2002 to 2019.

Data comes with information on postcode of residence

Data is extracted from ONS, held by SAHSU. Security, deaths are identifiable. Data updated every year, depends on extract date. Mostly complete, but some deaths still come through later if waiting on coroner's report to identify cause

In the spirit of the Bayesian workflow, prior to fitting model, exploratory data analysis total mortality varies over different cross sections: sex, age, space, time.

Look at different cross sections, slice by age, space and time By age + sex, log scale, death rates in 2019 Colour geom_tile plot age-specific death rates over time, trans = log Life expectancy male and female over time e0 aggregated 2002-19 by district

Here, taken slices, but the aim is to calculate death rates for each sex-age-space-time unit

3.1.1   Geographies of England

Having already introduced the term "district" in Figure XXs, I'll briefly show the lay of the land in terms of geographies used in this thesis. This thesis is concerned only with England, as Scotland, Wales, and Northern Ireland have their own separate deprivation data which are not comparable. The geographies used here in England form a nested hierarchy of spatial units from regions, districts, Middle-layer Super Output Areas (MSOAs), Lower-layer Super Output Areas (LSOAs). The numbers of each of the units are summarised in Table 3.1.

TABLE 3.1: The different geographical units of England used in thesis and their numbers.

Geography	Number of units
region	9
district	314
MSOA	6791
LSOA	32844

England is divided into 9 regions (London, North West, West Midlands, etc). Within these regions, there are 314 local authority districts. Districts are administative geographies formed from a mixture of London boroughs, metropolitan and non-metropolitan distrcts, and unitary autorities. They are responsible for local policies, and therefore subject to local government restructuring and bounary changes. For stability, we chose the district boundaries from 2020.

LSOAs are a type of census geography made up of around four or five smaller units called Output Areas (OAs). OAs are the smallest building block for census statistics, with between 40 and 250 households and typically 100 to 625 people, and are designed to have some socioeconomic homogeneity. MSOAs are then comprised of around four or five LSOAs, and these MSOAs fit within district boundaries. OAs, LSOAs, and MSOAs are all statisitcal units are designed by the Office for National Statistics (ONS) purely for analysis purposes, so researchers can use spatial units with similar,

but small, population sizes. No policies are created using these units ("2011 Census geographies," 2022).

3.1.2 Counts of the living

This second data sources we require are populations counts. These are taken from mid-year population estimates of the usual resident population by the ONS ("Lower layer Super Output Area population estimates," 2021; "Middle layer Super Output Area population estimates," 2021). The ONS estimates inter-censal populations on a rolling basis, updating the previous year's value using the change in the population in the GP patient registration data as an indicator of the true population change. The LSOA populations are fully consistent with estimates for higher levels in the nested geographical hierarchical including MSOAs, districts, regions and the national total for England ("Population estimates by output areas, electoral, health and other geographies, England and Wales," 2021).

3.1.3 Deprivation data

We used data for the following measures of socioeconomic deprivation from the English Indices of Deprivation:

- Income deprivation (referred to as *poverty* hereafter). The proportion of the geographical population claiming income-related benefits due to being out of work or having low earnings.

- Employment deprivation (referred to as *unemployment* hereafter). The proportion of the relevant population of the geography involuntarily excluded from the labour market due to unemployment, sickness or disability, or caring responsibilities.

- Education, skills and training deprivation (referred to as *low education* hereafter). Lack of attainment and skills, including education attainment levels, school attendance, and language proficiency indicators in the geographical population.

The above measures are the three largest contributors to the Index of Multiple Deprivation (IMD), excluding a domain on health that also uses mortality data. The data are produced at the LSOA level ("English indices of deprivation 2019," 2019).

IMD data are not available for every year. The analysis period for the thesis is 2002 to 2019, so we used data for these measures for 2004, as data for 2002 were not available, and 2019. The 2004 data on deprivation domains were reported for LSOA boundaries from the 2001 census. We mapped these data to the 2011 census LSOA boundaries by assigning the 2001 LSOA score to all postcodes contained within it, then overlaying the 2011 LSOA boundaries, and averaging the score for all constituent postcodes of each LSOA, to obtain the corresponding score for each 2011 LSOA.

The definition of the indicators can change over time. Further, the indicator used for measuring education, skills and training deprivation (low education) is not directly interpretable because it combines multiple concepts cannot be simply expressed as a proportion of the population. Therefore, we used ranking rather than scores so that comparisons can be made not only across spatial units in a single year, but also across the different years.

The data for geographies larger than LSOAs in Table 3.1 were created by ranking the population-weighted average of scores for all constituent LSOAs, as done previously for districts ("English indices of deprivation 2019," 2019).

3.2 Modelling the dead

For each chapter, the quantity of interest is the same: mortality in each age group, spatial unit and year. Empirically, death rates can be calculated from observed data as the number of deaths divided by the population in each strata. Formally, using a, s, and t to index age, spatial unit and time respectively, we write

$$\hat{m}_{ast} = \frac{\text{deaths}_{ast}}{\text{population}_{ast}}, \tag{3.1}$$

where $\hat{m}_{ast}$ is the death rate. When the number of deaths becomes small, however, the empirical death rate presents an apparent variability from year to year, or from

spatial unit to spatial unit, which is larger than the true differences in the risk of death. The problem is exarcerbated for young ages or rare diseases, where the number of deaths might be zero, or for smaller geographical units, where the population might be zero. Thus, we use Bayesian hierarchical models to obtain stable estimates of death rates by sharing information across age groups, spatial units, and years. An added advantage of the Bayesian paradigm is the robust error estimates.

This is a regression task. We simply want to smooth over the data – the models aren't being used for prediction. We tried to design as complex a model as possible, to capture as much of the true variation in the data as possible using epidemiologcial knowledge to choose plausible effects. In other words, the model is "full", enough paramaters to capture all the true variability. Models are overspecified, like Bayesian neural networks (AGW paper) The downside of this approach is that more parameters is harder to fit, and fewer parameters, or parsimonious models, makes Bayesian inference easier.

3.3 Inference

The decision was made early in the PhD to use Markov chain Monte Carlo (MCMC) sampling methods for inference, as this is the "gold standard" with guarantees that the sequence of samples will asmyptotically converge to the true posterior. Furthermore, the state-of-the-art approximate inference package for spatial models, INLA, scales badly with the number of effects, and hence would struggle with the models of dimensionality in this thesis.

Bayesian models are specified in a probabilistic programming language. The starting point for this project was the `NIMBLE` package (de Valpine et al., 2022, 2017). `NIMBLE` uses the BUGS ("Bayesian inference Using Gibbs Sampling") syntax for defining a hierarchical model, which the group has a lot of experience with, as `WinBUGS`, one of the earliest software packages for Bayesian analysis, was developed largely in the department for use on SAHSU studies. `NIMBLE` has an `R` interface but compiles models to `C++` for speed and scalability. It also increases the efficiency of Gibbs sampling efficiently by automatically finding conjugate relationships between parameters in

the model and marginalising over them wherever possible. An added advantage is that the group has a close relationship with the lead developer of `NIMBLE`.

Nevertheless, Bayesian inference is difficult to scale, and some of the models in this thesis had in excess of 10^6 parameters and took `NIMBLE` between 10 and 14 days to collect enough samples of the posterior. One of the main issues with `NIMBLE` was that the vast majority of the parameters in the model could not exploit efficient conjugate samplers, and instead used variants of basic Metropolis-Hastings samplers, which, despite numerous efforts at tuning, were inefficient. Although `NIMBLE` could execute a reasonable number of samples per second, the MCMC chains were struggling to explore the posterior quickly so the *effective* sample size per second was low. This is a common problem in spatial and spatiotemporal models, where the parameters are correlated by design. To overcome these mixing issues, the chains had to be run for longer and thinned (i.e. take every n^{th} sample so the Markov chain samples are closer to independent).

I spent a lot of time trying different probabilsitic programming languages across `R`, `python` and `Julia`, in particular packages that implemented the more efficient No U-Turn Sampler (NUTS) (Rashid, 2022). In the end, I settled on `NumPyro` (Phan et al., 2019) because it was the fastest and inference could be performed on a GPU, rather than CPUs, which is faster for large models (Lao et al., 2020). The major downside was that `NumPyro` had not been used extensively by the spatial community, so I had to implement the CAR distribution from Equation 2.2, which has since been contributed to the source code. Rewriting the model in `NumPyro` and sampling on a GPU cut the required runtime down to around a day. `NumPyro` also has built-in methods for approximate variational inference, such as the Laplace approximation, but these failed to converge to sensible values for these models without heavy customisation of variational function, so I stuck with sampling methods.

Chapter 4

Small: Life expectancy trends in England, LPH

4.1 Introduction

Studies at the MSOA level national Congdon (2019); Congdon (2020)

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4.1.1 Methods

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4.1.2 Results

4.1.3 Discussion

4.1.4 Conclusion

Chapter 5

Smaller: Life expectancy inequality in London

5.1 Introduction

London wards, joint modelling of disability free and total life expectancy in census years, obtain better DFLE Congdon (2014)

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5.1.1 Methods

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5.1.2 Results

5.1.3 Discussion

5.1.4 Conclusion

Chapter 6

Cancers

6.1 Introduction

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6.1.1 Methods

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6.1.2 Results

6.1.3 Discussion

6.1.4 Conclusion

Chapter 7

Cause-specific

7.1 Introduction

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7.1.1 Methods

Nunc posuere quam at lectus tristique eu ultrices augue venenatis. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Aliquam erat volutpat. Vivamus sodales tortor eget quam adipiscing in vulputate ante ullamcorper. Sed eros ante, lacinia et sollicitudin et, aliquam sit amet augue. In hac habitasse platea dictumst.

7.1.2 Results

7.1.3 Discussion

7.1.4 Conclusion

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Appendix A

Frequently Asked Questions

A.1 How do I change the colors of links?

Pass in `urlcolor:` in yaml. Or set these in the include-in-header file.

If you want to completely hide the links, you can use:

{\hypersetup{allcolors=.}}, or even better:

{\hypersetup{hidelinks}}.

If you want to have obvious links in the PDF but not the printed text, use:

{\hypersetup{colorlinks=false}}.