



Modelling the dead and what they died from

Theo Rashid

Supervisors: Majid Ezzati, James E Bennett, Seth Flaxman

A thesis submitted for the degree of Doctor of Philosophy

Department of Epidemiology and Biostatistics, School of Public Health

February 2023

Copyright

The copyright of this thesis rests with the author and is made available under a Creative Commons Attribution Non-Commercial No Derivatives licence. Researchers are free to copy, distribute or transmit the thesis on the condition that they attribute it, that they do not use it for commercial purposes and that they do not alter, transform or build upon it. For any reuse or redistribution, researchers must make clear to others the licence terms of this work.

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.

Acknowledgements

Thanks be to James Bennett.

Majid Ezzati, Seth Flaxman. Eric Johnson Kyle Foreman, Robbie Parks. Barbara Metzler, Emily Muller. Ricky Nathvani, Honor Bixby, Sierra Clark, Victor Lhoste. Sam Acors Solange. Parents, Ros Geoff Hardern.

Table of contents

Copyright	iii
Declaration of Authorship	v
Abstract	ix
Acknowledgements	xi
1 Overview	1
2 Background	3
2.1 Small area health statistics (unit)	3
2.2 Mortality by specific causes of death (counting the dead and what they died from)	9
2.3 Health inequalities in the UK	12
3 The model	17
3.1 The data	17
3.2 Model	18
3.3 Inference	18
4 Small: Life expectancy trends in England, LPH	19
4.1 Introduction	19
5 Smaller: Life expectancy inequality in London	21
5.1 Introduction	21
6 Cancers	23
6.1 Introduction	23

7 Cause-specific	25
7.1 Introduction	25
References	27
Appendices	34
A Frequently Asked Questions	35
A.1 How do I change the colors of links?	35

List of Figures

List of Tables

List of Abbreviations

CrI	C redible i nterval
CAR	C onditional a utoregressive
CVD	C ardio v ascular D isease
GBD	G lobal B urden of D isease
ICAR	I ntrinsic C onditional a utoregressive
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-communicable D isease
NUTS	N o U -turn 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.*

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 & 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. Postcodes 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, Briggs, et al., 2001), no increase in rates of cancer (Jarup, Briggs, et al., 2002), 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 patterns 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 be small numbers. This sparseness issue is even more pertinent when the population is also stratified 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 continuous 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 & 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 & Wakefield (2002) describe an alternative 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 $\mathbf{S} = S_1, \dots, S_n$ is the multivariate normal

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

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, which uses a finite set of points. An example in Elliott, Wakefield, et al. (2001) 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 precision matrix

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

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)

$$S_i = U_i + V_i, \tag{2.2}$$

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, Best, et al., 2002) cancers for small areas in regions of England.

Further disease mapping studies at SAHSU using spatially structured effects have also extended the methodology to look at age patterns and trends over time of disease. Asaria et al. (2012) analysed cardiovascular 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 populations. 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 enumeration errors, particularly for areas with special populations such as students or armed forces (Elliott, Wakefield, et al. (2001).

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 & 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 (cite ONS and PHE, 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 accurate estimates for small population studies of life expectancy (Jonker et al. (2012)).

Jonker et al. (2012) demonstrated the advantages of the Bayesian approach to stabilising 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 spatiotemporal models trained over a 31 year period, and Dwyer-Lindgren, Bertozzi-Villa, et al. (2017) 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 population sizes as small as 40. Dwyer-Lindgren, Stubbs, et al. (2017) 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 & 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 diphtheria, 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 interventions such as immunisation and quarantines.

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 & 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 & Kates, 1997). Gersten & 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 & 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 & 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 accelerating 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 & 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, Ez-zati et al. (2008) and Dwyer-Lindgren, Bertozzi-Villa, et al. (2017)). 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 & 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, preventable inequalities in mortality and morbidity. There are several ways to stratify the UK population and compare 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. Their authors concluded that 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 [1].

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 subnational 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, unemployment, 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, which 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 inequalities 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, tackling 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 achieved 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 2018.

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 comparator 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

The model

Bayesian workflow

3.1 The data

Same dataset for each By age + sex, log scale Age specific and Life expectancy male and female over time Colour geom_tile plot PCA for age (Alexander) Death rate 2002-19 by district

3.1.1 Other data sources

Population data from ONS. Estimates, modelled for inter-censal years using births, deaths, migration The mid-2020 Small Area population estimates covered by this bulletin are fully consistent with population estimates for higher levels of geography including local authorities, regions and the national total for England and Wales.

<https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/bu>

The description of the methodology in the following sections uses the example of creating rolled-forward mid-2020 Lower layer Super Output Area (LSOA) estimates. For example, we produced the mid-2020 LSOA estimates using the mid-2019 LSOA estimates as the population base. Middle layer Super Output Area (MSOA) estimates are created in a similar manner using derived MSA quinary age-by-sex change ratios and are constrained to local authority mid-year estimates. Change ratios were calculated by quinary age group and sex for the patient register data. The change ratios are calculated by dividing for each dataset the mid-2020 count by

quinary age and sex by the mid-2019 count by quinary age and sex. For example, a mid-2020 count of 50 divided by a mid-2019 count of 40 gives a change ratio of 1.25. The ratios are then constrained to the mid-2020 MSOA estimates (less mid-2020 special population), which have been constrained to the local authority mid-2020 estimates less mid-2020 special population. The number of patients registered on GP lists in each OA at the mid-year point is used as a proxy for the true size of the population at the same point in time.

IMD data Focus on income, education, – not health Aggregate to different geographies map of IMD for London (LSOA), and IMD for England (MSOA) in 2019

3.2 Model

Why we model? Robust estimates Explanation of death rates, small numbers, zero population, variability Regression, statistical smoothing Same model

As complex a model as possible, capture as more variation “Full” model More parameters is harder to fit, fewer parameters makes inference easier Models are overspecified, like Bayesian neural networks (AGW paper)

3.3 Inference

Choice made to do sampling – gold standard Approximate inference state-of-the-art for spatial models, INLA, scales badly with the number of effects

Start with NIMBLE, group has experience with BUGS Gibbs sampling, finds conjugate relationships where they exist R interface but C++ backend, scales well to a large problem like this

Move to numpyro. Created CAR distribution, contributed to open source Sampling faster, more efficient NUTS Sampling on GPU, much faster Tried VI methods in numpyro, such as laplace approx, but failed to converge to sensible values

Chapter 4

Small: Life expectancy trends in England, LPH

4.1 Introduction

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

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Aliquam ultricies lacinia euismod. Nam tempus risus in dolor rhoncus in interdum enim tincidunt. Donec vel nunc neque. In condimentum ullamcorper quam non consequat. Fusce sagittis tempor feugiat. Fusce magna erat, molestie eu convallis ut, tempus sed arcu. Quisque molestie, ante a tincidunt ullamcorper, sapien enim dignissim lacus, in semper nibh erat lobortis purus. Integer dapibus ligula ac risus convallis pellentesque.

4.1.1 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.

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)

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Aliquam ultricies lacinia euismod. Nam tempus risus in dolor rhoncus in interdum enim tincidunt. Donec vel nunc neque. In condimentum ullamcorper quam non consequat. Fusce sagittis tempor feugiat. Fusce magna erat, molestie eu convallis ut, tempus sed arcu. Quisque molestie, ante a tincidunt ullamcorper, sapien enim dignissim lacus, in semper nibh erat lobortis purus. Integer dapibus ligula ac risus convallis pellentesque.

5.1.1 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.

5.1.2 Results**5.1.3 Discussion****5.1.4 Conclusion**

Chapter 6

Cancers

6.1 Introduction

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Aliquam ultricies lacinia euismod. Nam tempus risus in dolor rhoncus in interdum enim tincidunt. Donec vel nunc neque. In condimentum ullamcorper quam non consequat. Fusce sagittis tempor feugiat. Fusce magna erat, molestie eu convallis ut, tempus sed arcu. Quisque molestie, ante a tincidunt ullamcorper, sapien enim dignissim lacus, in semper nibh erat lobortis purus. Integer dapibus ligula ac risus convallis pellentesque.

6.1.1 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.

6.1.2 Results

6.1.3 Discussion

6.1.4 Conclusion

Chapter 7

Cause-specific

7.1 Introduction

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Aliquam ultricies lacinia euismod. Nam tempus risus in dolor rhoncus in interdum enim tincidunt. Donec vel nunc neque. In condimentum ullamcorper quam non consequat. Fusce sagittis tempor feugiat. Fusce magna erat, molestie eu convallis ut, tempus sed arcu. Quisque molestie, ante a tincidunt ullamcorper, sapien enim dignissim lacus, in semper nibh erat lobortis purus. Integer dapibus ligula ac risus convallis pellentesque.

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

References

- Alexiou, A., Fahy, K., Mason, K., Bennett, D., Brown, H., Bambra, C., Taylor-Robinson, D., & Barr, B. (2021). Local government funding and life expectancy in England: A longitudinal ecological study. *The Lancet Public Health*, 6(9), e641–e647. [https://doi.org/10.1016/S2468-2667\(21\)00110-9](https://doi.org/10.1016/S2468-2667(21)00110-9)
- Asaria, P., Fortunato, L., Fecht, D., Tzoulaki, I., Abellan, J. J., Hambly, P., de Hoogh, K., Ezzati, M., & Elliott, P. (2012). Trends and inequalities in cardiovascular disease mortality across 7932 English electoral wards, 1982–2006: Bayesian spatial analysis. *International Journal of Epidemiology*, 41(6), 1737–1749. <https://doi.org/10.1093/ije/dys151>
- Aylin, P., Maheswaran, R., Wakefield, J., Cockings, S., Jarup, L., Arnold, R., Wheeler, G., & Elliott, P. (1999). A national facility for small area disease mapping and rapid initial assessment of apparent disease clusters around a point source: The UK Small Area Health Statistics Unit. *Journal of Public Health*, 21(3), 289–298. <https://doi.org/10.1093/pubmed/21.3.289>
- Bahk, J., Kang, H.-Y., & Khang, Y.-H. (2020). Life expectancy and inequalities therein by income from 2016 to 2018 across the 253 electoral constituencies of the National Assembly of the Republic of Korea. *Journal of Preventive Medicine and Public Health*, 53(2), 143–148. <https://doi.org/10.3961/jpmph.20.050>
- Barr, B., Higgerson, J., & Whitehead, M. (2017). Investigating the impact of the English health inequalities strategy: Time trend analysis. *BMJ*, 358, j3310. <https://doi.org/10.1136/bmj.j3310>
- Bennett, J. E., Li, G., Foreman, K., Best, N., Kontis, V., Pearson, C., Hambly, P., & Ezzati, M. (2015). The future of life expectancy and life expectancy inequalities in England and Wales: Bayesian spatiotemporal forecasting. *The Lancet*, 386(9989), 163–170. [https://doi.org/10.1016/S0140-6736\(15\)60296-3](https://doi.org/10.1016/S0140-6736(15)60296-3)

- Bennett, J. E., Pearson-Stuttard, J., Kontis, V., Capewell, S., Wolfe, I., & Ezzati, M. (2018). Contributions of diseases and injuries to widening life expectancy inequalities in England from 2001 to 2016: A population-based analysis of vital registration data. *The Lancet Public Health*, 3(12), e586–e597. [https://doi.org/10.1016/S2468-2667\(18\)30214-7](https://doi.org/10.1016/S2468-2667(18)30214-7)
- Besag, J., York, J., & Mollié, A. (1991). Bayesian image restoration, with two applications in spatial statistics. *Annals of the Institute of Statistical Mathematics*, 43(1), 1–20. <https://doi.org/10.1007/BF00116466>
- Best, N., Richardson, S., & Thomson, A. (2005). A comparison of Bayesian spatial models for disease mapping. *Statistical Methods in Medical Research*, 14(1), 35–59. <https://doi.org/10.1191/0962280205sm388oa>
- Bilal, U., Alazraqui, M., Caiaffa, W. T., Lopez-Olmedo, N., Martinez-Folgar, K., Miranda, J. J., Rodriguez, D. A., Vives, A., & Diez-Roux, A. V. (2019). Inequalities in life expectancy in six large Latin American cities from the SALURBAL study: An ecological analysis. *The Lancet Planetary Health*, 3(12), e503–e510. [https://doi.org/10.1016/S2542-5196\(19\)30235-9](https://doi.org/10.1016/S2542-5196(19)30235-9)
- Congdon, P. (2019). Geographical Patterns in Drug-Related Mortality and Suicide: Investigating Commonalities in English Small Areas. *International Journal of Environmental Research and Public Health*, 16(10), 1831. <https://doi.org/10.3390/ijerph16101831>
- Congdon, P. (2020). A diabetes risk index for small areas in England. *Health & Place*, 63, 102340. <https://doi.org/10.1016/j.healthplace.2020.102340>
- Congdon, P. (2009). Life Expectancies for Small Areas: A Bayesian Random Effects Methodology. *International Statistical Review*, 77(2), 222–240. <https://doi.org/10.1111/j.1751-5823.2009.00080.x>
- Congdon, P. (2014). Modelling changes in small area disability free life expectancy: Trends in London wards between 2001 and 2011. *Statistics in Medicine*, 33(29), 5138–5150. <https://doi.org/10.1002/sim.6298>
- Dorling, D. (2023). How austerity caused the NHS crisis. In *openDemocracy*. <https://www.opendemocracy.net/en/nhs-a-and-e-delays-austerity-emergency-care-hospitals-hunt-hancock-lansley/>.
- Dwyer-Lindgren, L., Bertozzi-Villa, A., Stubbs, R. W., Morozoff, C., Mackenbach, J.

- P., van Lenthe, F. J., Mokdad, A. H., & Murray, C. J. L. (2017). Inequalities in Life Expectancy Among US Counties, 1980 to 2014: Temporal Trends and Key Drivers. *JAMA Internal Medicine*, 177(7), 1003–1011. <https://doi.org/10.1001/jamainternmed.2017.0918>
- Dwyer-Lindgren, L., Stubbs, R. W., Bertozzi-Villa, A., Morozoff, C., Callender, C., Finegold, S. B., Shirude, S., Flaxman, A. D., Laurent, A., Kern, E., Duchin, J. S., Fleming, D., Mokdad, A. H., & Murray, C. J. L. (2017). Variation in life expectancy and mortality by cause among neighbourhoods in King County, WA, USA, 1990–2014: A census tract-level analysis for the Global Burden of Disease Study 2015. *The Lancet Public Health*, 2(9), e400–e410. [https://doi.org/10.1016/S2468-2667\(17\)30165-2](https://doi.org/10.1016/S2468-2667(17)30165-2)
- Eayres, D., & Williams, E. S. (2004). Evaluation of methodologies for small area life expectancy estimation. *Journal of Epidemiology & Community Health*, 58(3), 243–249. <https://doi.org/10.1136/jech.2003.009654>
- Elliott, P., Briggs, D., Morris, S., Hoogh, C. de, Hurt, C., Jensen, T. K., Maitland, I., Richardson, S., Wakefield, J., & Jarup, L. (2001). Risk of adverse birth outcomes in populations living near landfill sites. *BMJ*, 323(7309), 363–368. <https://doi.org/10.1136/bmj.323.7309.363>
- Elliott, P., Toledano, M. B., Bennett, J. E., Beale, L., Hoogh, C. de, Best, N., & Briggs, D. (2010). Mobile phone base stations and early childhood cancers: Case-control study. *BMJ*, 340, c3077. <https://doi.org/10.1136/bmj.c3077>
- Elliott, P., Wakefield, J., Best, N., & Briggs, D. (2001). *Spatial epidemiology: Methods and applications*. Oxford University Press.
- Elliott, P., Westlake, A. J., Hills, M., Kleinschmidt, I., Rodrigues, L., McGale, P., Marshall, K., & Rose, G. (1992). The Small Area Health Statistics Unit: A national facility for investigating health around point sources of environmental pollution in the United Kingdom. *Journal of Epidemiology & Community Health*, 46(4), 345–349. <https://doi.org/10.1136/jech.46.4.345>
- English indices of deprivation 2019*. (2019). <https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019>.
- Ezzati, M., Friedman, A. B., Kulkarni, S. C., & Murray, C. J. L. (2008). The Reversal of Fortunes: Trends in County Mortality and Cross-County Mortality Disparities

- in the United States. *PLOS Medicine*, 5(4), e66. <https://doi.org/10.1371/journal.pmed.0050066>
- Finucane, M. M., Paciorek, C. J., Danaei, G., & Ezzati, M. (2014). Bayesian Estimation of Population-Level Trends in Measures of Health Status. *Statistical Science*, 29(1), 18–25. <https://doi.org/10.1214/13-STS427>
- Foreman, K. J., Li, G., Best, N., & Ezzati, M. (2017). Small area forecasts of cause-specific mortality: Application of a Bayesian hierarchical model to US vital registration data. *Journal of the Royal Statistical Society. Series C (Applied Statistics)*, 66(1), 121–139.
- Gaylin, D. S., & Kates, J. (1997). Refocusing the lens: Epidemiologic transition theory, mortality differentials, and the AIDS pandemic. *Social Science & Medicine*, 44(5), 609–621. [https://doi.org/10.1016/S0277-9536\(96\)00212-2](https://doi.org/10.1016/S0277-9536(96)00212-2)
- Gersten, O., & Wilmoth, J. R. (2002). The Cancer Transition in Japan since 1951. *Demographic Research*, 7(5), 271–306. <https://doi.org/10.4054/DemRes.2002.7.5>
- Goodman, P. S. (2018). In Britain, Austerity Is Changing Everything. *The New York Times*.
- Halonen, J. I., Hansell, A. L., Gulliver, J., Morley, D., Blangiardo, M., Fecht, D., Toledano, M. B., Beevers, S. D., Anderson, H. R., Kelly, F. J., & Tonne, C. (2015). Road traffic noise is associated with increased cardiovascular morbidity and mortality and all-cause mortality in London. *European Heart Journal*, 36(39), 2653–2661. <https://doi.org/10.1093/eurheartj/ehv216>
- Hansell, A. L., Blangiardo, M., Fortunato, L., Floud, S., Hoogh, K. de, Fecht, D., Ghosh, R. E., Laszlo, H. E., Pearson, C., Beale, L., Beevers, S., Gulliver, J., Best, N., Richardson, S., & Elliott, P. (2013). Aircraft noise and cardiovascular disease near Heathrow airport in London: Small area study. *BMJ*, 347, f5432. <https://doi.org/10.1136/bmj.f5432>
- Hansell, Anna L., Beale, Linda, Ghosh, Rebecca E., Fortunato, Lea, Fecht, Daniela, Jarup, Lars, & Elliott, Paul. (2014). *The Environment and Health Atlas for England and Wales*. Oxford University Press.
- Hiam, L., Harrison, D., McKee, M., & Dorling, D. (2018). Why is life expectancy in England and Wales “stalling”? *J Epidemiol Community Health*, 72(5), 404–408. <https://doi.org/10.1136/jech-2017-210401>

- Hodgson, S., Nieuwenhuijsen, M. J., Colvile, R., & Jarup, L. (2007). Assessment of exposure to mercury from industrial emissions: Comparing “distance as a proxy” and dispersion modelling approaches. *Occupational and Environmental Medicine*, 64(6), 380–388. <https://doi.org/10.1136/oem.2006.026781>
- Hodgson, S., Nieuwenhuijsen, M. J., Hansell, A., Shepperd, S., Flute, T., Staples, B., Elliott, P., & Jarup, L. (2004). Excess risk of kidney disease in a population living near industrial plants. *Occupational and Environmental Medicine*, 61(8), 717–719. <https://doi.org/10.1136/oem.2003.010629>
- Jarup, L., Best, N., Toledano, M. B., Wakefield, J., & Elliott, P. (2002). Geographical epidemiology of prostate cancer in Great Britain. *International Journal of Cancer*, 97(5), 695–699. <https://doi.org/10.1002/ijc.10113>
- Jarup, L., Briggs, D., de Hoogh, C., Morris, S., Hurt, C., Lewin, A., Maitland, I., Richardson, S., Wakefield, J., & Elliott, P. (2002). Cancer risks in populations living near landfill sites in Great Britain. *British Journal of Cancer*, 86(11), 1732–1736. <https://doi.org/10.1038/sj.bjc.6600311>
- Jarup, L., Morris, S., Richardson, S., Briggs, D., Cobley, N., de Hoogh, C., Gorog, K., & Elliott, P. (2007). Down syndrome in births near landfill sites. *Prenatal Diagnosis*, 27(13), 1191–1196. <https://doi.org/10.1002/pd.1873>
- Jonker, M. F., van Lenthe, F. J., Congdon, P. D., Donkers, B., Burdorf, A., & Mackenbach, J. P. (2012). Comparison of Bayesian Random-Effects and Traditional Life Expectancy Estimations in Small-Area Applications. *American Journal of Epidemiology*, 176(10), 929–937. <https://doi.org/10.1093/aje/kws152>
- Kelsall, J., & Wakefield, J. (2002). Modeling Spatial Variation in Disease Risk. *Journal of the American Statistical Association*, 97(459), 692–701. <https://doi.org/10.1198/016214502388618438>
- Kontis, V., Bennett, J. E., Rashid, T., Parks, R. M., Pearson-Stuttard, J., Guillot, M., Asaria, P., Zhou, B., Battaglini, M., Corsetti, G., McKee, M., Di Cesare, M., Mathers, C. D., & Ezzati, M. (2020). Magnitude, demographics and dynamics of the effect of the first wave of the COVID-19 pandemic on all-cause mortality in 21 industrialized countries. *Nature Medicine*, 26(12), 1919–1928. <https://doi.org/10.1038/s41591-020-1112-0>
- Leon, D. A., Jdanov, D. A., & Shkolnikov, V. M. (2019). Trends in life expectancy

- and age-specific mortality in England and Wales, 1970–2016, in comparison with a set of 22 high-income countries: An analysis of vital statistics data. *The Lancet Public Health*, 4(11), e575–e582. [https://doi.org/10.1016/S2468-2667\(19\)30177-X](https://doi.org/10.1016/S2468-2667(19)30177-X)
- Marmot, M. G., Allen, J., Boyce, T., Goldblatt, P., & Morrison, J. (2020). *Marmot Review: 10 years on*. Institute of Health Equity.
- Marmot, M. G., Davey Smith, G., Stansfeld, S., Patel, C., North, F., Head, J., White, I., Brunner, E., & Feeney, A. (1991). Health inequalities among British civil servants: The Whitehall II study. *The Lancet*, 337(8754), 1387–1393. [https://doi.org/10.1016/0140-6736\(91\)93068-K](https://doi.org/10.1016/0140-6736(91)93068-K)
- Marmot, M. G., Goldblatt, P., Allen, J., Boyce, T., McNeish, D., Grady, M., Strelitz, J., Geddes, I., Friel, S., Porritt, F., Reinertsen, E., Bell, R., & Allen, M. (2010). *The Marmot Review: Fair society, healthy lives*. Institute of Health Equity.
- Marmot, M. G., Shipley, M. J., & Rose, G. (1984). Inequalities in death - specific explanations of a general pattern? *The Lancet*, 323(8384), 1003–1006. [https://doi.org/10.1016/S0140-6736\(84\)92337-7](https://doi.org/10.1016/S0140-6736(84)92337-7)
- Mathers, C. D., Fat, D. M., Inoue, M., Rao, C., & Lopez, A. D. (2005). [Counting the dead and what they died from: An assessment of the global status of cause of death data](#). *Bulletin of the World Health Organization*, 83(3), 171–177.
- Moriyama, I. M., & Gover, M. (1948). Statistical Studies of Heart Diseases: I. Heart Diseases and Allied Causes of Death in Relation to Age Changes in the Population. *Public Health Reports (1896-1970)*, 63(17), 537–545. <https://doi.org/10.2307/4586527>
- Murray, C. J. L., & Lopez, A. D. (1996). *The Global Burden of Disease: A comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected in 2020*. World Health Organization.
- Olshansky, S. J., & Ault, A. B. (1986). The Fourth Stage of the Epidemiologic Transition: The Age of Delayed Degenerative Diseases. *The Milbank Quarterly*, 64(3), 355–391. <https://doi.org/10.2307/3350025>
- Omran, A. R. (1977). A century of epidemiologic transition in the United States. *Preventive Medicine*, 6(1), 30–51. [https://doi.org/10.1016/0091-7435\(77\)90003-2](https://doi.org/10.1016/0091-7435(77)90003-2)
- Omran, A. R. (1971). The Epidemiologic Transition: A Theory of the Epidemiology of Population Change. *The Milbank Memorial Fund Quarterly*, 49(4), 509–538.

- <https://doi.org/10.2307/3349375>
- Parkes, B., Hansell, A. L., Ghosh, R. E., Douglas, P., Fecht, D., Wellesley, D., Kurinczuk, J. J., Rankin, J., de Hoogh, K., Fuller, G. W., Elliott, P., & Toledano, M. B. (2020). Risk of congenital anomalies near municipal waste incinerators in England and Scotland: Retrospective population-based cohort study. *Environment International*, 134, 104845. <https://doi.org/10.1016/j.envint.2019.05.039>
- Preston, S. H. (1970). An International Comparison of Excessive Adult Mortality. *Population Studies*, 24(1), 5–20. <https://doi.org/10.2307/2173259>
- Preston, S. H., & Nelson, V. E. (1974). Structure and change in causes of death: An international summary. *Population Studies*, 28(1), 19–51. <https://doi.org/10.1080/00324728.1974.10404577>
- Salomon, J. A., & Murray, C. J. L. (2002). The Epidemiologic Transition Revisited: Compositional Models for Causes of Death by Age and Sex. *Population and Development Review*, 28(2), 205–228.
- Silcocks, P. B. S., Jenner, D. A., & Reza, R. (2001). Life expectancy as a summary of mortality in a population: Statistical considerations and suitability for use by health authorities. *Journal of Epidemiology & Community Health*, 55(1), 38–43. <https://doi.org/10.1136/jech.55.1.38>
- Steel, N., Ford, J. A., Newton, J. N., Davis, A. C. J., Vos, T., Naghavi, M., Glenn, S., Hughes, A., Dalton, A. M., Stockton, D., Humphreys, C., Dallat, M., Schmidt, J., Flowers, J., Fox, S., Abubakar, I., Aldridge, R. W., Baker, A., Brayne, C., ... Murray, C. J. L. (2018). Changes in health in the countries of the UK and 150 English Local Authority areas 1990–2016: A systematic analysis for the Global Burden of Disease Study 2016. *The Lancet*, 392(10158), 1647–1661. [https://doi.org/10.1016/S0140-6736\(18\)32207-4](https://doi.org/10.1016/S0140-6736(18)32207-4)
- Stephens, A. S., Purdie, S., Yang, B., & Moore, H. (2013). Life expectancy estimation in small administrative areas with non-uniform population sizes: Application to Australian New South Wales local government areas. *BMJ Open*, 3(12), e003710. <https://doi.org/10.1136/bmjopen-2013-003710>
- Taylor-Robinson, D., Lai, E. T. C., Wickham, S., Rose, T., Norman, P., Bambra, C., Whitehead, M., & Barr, B. (2019). Assessing the impact of rising child poverty on the unprecedented rise in infant mortality in England, 2000–2017: Time trend

- analysis. *BMJ Open*, 9(10), e029424. <https://doi.org/10.1136/bmjopen-2019-029424>
- Toledano, M. B., Jarup, L., Best, N., Wakefield, J., & Elliott, P. (2001). Spatial variation and temporal trends of testicular cancer in Great Britain. *British Journal of Cancer*, 84(11), 1482–1487. <https://doi.org/10.1054/bjoc.2001.1739>
- Wakefield, J., & Elliott, P. (1999). Issues in the statistical analysis of small area health data. *Statistics in Medicine*, 18(17-18), 2377–2399. [https://doi.org/10.1002/\(SICI\)1097-0258\(19990915/30\)18:17/18%3C2377::AID-SIM263%3E3.0.CO;2-G](https://doi.org/10.1002/(SICI)1097-0258(19990915/30)18:17/18%3C2377::AID-SIM263%3E3.0.CO;2-G)
- Wilkinson, R. G. (1992). Income distribution and life expectancy. *British Medical Journal*, 304(6820), 165–168. <https://doi.org/10.1136/bmj.304.6820.165>
- Yu, J., Dwyer-Lindgren, L., Bennett, J., Ezzati, M., Gustafson, P., Tran, M., & Brauer, M. (2021). A spatiotemporal analysis of inequalities in life expectancy and 20 causes of mortality in sub-neighbourhoods of Metro Vancouver, British Columbia, Canada, 1990–2016. *Health & Place*, 72, 102692. <https://doi.org/10.1016/j.healthplace.2021.102692>

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}}.
```