Bayesian small-area modelling of COVID-19 cases and deaths in England and association with key risk factors: a combined space–time Susceptible-Exposed-Infected-Removed (SEIR) model

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Title Page

Bayesian small-area modelling of COVID-19 cases and deaths in England and association with key risk factors: a combined space–time Susceptible-Exposed-Infected-Removed (SEIR) model

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Abstract

Background: COVID-19 caseloads in England appear have passed through a first peak, with evidence of an emerging second wave. To ensure continued response to the epidemic is most effective, it is imperative to better understand both retrospectively and prospectively the geographical evolution of COVID-19 caseloads and deaths, identify localised areas in space-time at significantly higher risk, quantify the impact of changes in localised population mobility (or movement) on caseloads, identify localised risk factors for increased mortality and project the likely course of the epidemic at small-area resolution in coming weeks.

Methods: We applied a Bayesian space–time SEIR model to assess the spatiotemporal variability of COVID-19 caseloads (transmission) and deaths at small-area scale in England (Middle Layer Super Output Area [MSOA], 6791 units) and by week (using observed data from week 5 to 34), including key determinants, the modelled transmission dynamics and spatial-temporal random effects. We also estimate the number of cases and deaths at small-area resolution with uncertainty projected forward in time by MSA (up to week 51 of 2020), the impact mobility reductions (and subsequent easing) have had on COVID-19 caseloads and quantify the impact of key socio-demographic risk factors on COVID-19 related mortality risk by MSA.

Results: Reductions in population mobility due the course of the first lockdown had a significant impact on the reduction of COVID-19 caseloads across England, however local authorities have had a varied rate of reduction in population movement which our model suggest has substantially impacted the geographic heterogeneity in caseloads at small-area scale. The steady gain in population mobility, observed from late April, appears to have contributed to a slowdown in caseload reductions towards late June and subsequent steady increase signalling the start of the second wave. MSA with higher proportions of elderly (70+ years of age) and elderly living in

deprivation, both with very distinct geographic distributions, have a significantly elevated COVID-19 mortality rates.

Conclusions: While non-pharmaceutical interventions (that is, reductions in population mobility and social distancing) had a profound impact on the trajectory of the first wave of the COVID-19 outbreak in England, increased population mobility appears to have contributed to the current increase signalling the start of the second wave. A number of contiguous small-areas appear to be at a significant elevated risk of high COVID-19 transmission, many of which are also at increased risk for higher mortality rates. A geographically staggered re-introduction of intensified social distancing measures is advised and limited cross MSOA movement if the magnitude and geographic extent of the second wave is to be reduced.

Keywords: COVID-19, SARS-CoV-2, small-area Bayesian estimation, Susceptible-Exposed-Infected-Removed (SEIR), mobility, non-pharmaceutical intervention, Middle Layer Super Output Area, England

Introduction

The first cases of COVID-19 in the United Kingdom were confirmed on 31 January 2020¹. Despite implementation of non-pharmaceutical interventions, including closure of non-essential services and subsequent stay at home orders and school closures on 20 and 23 March 2020 respectively, this was not sufficient to contain the first wave of the UK outbreak, although these measures did serve to slow early transmission². The full extent of the effect of the mobility restrictions on COVID-19 transmission has not been fully elucidated nor explicitly quantified^{3,4}. In addition, the attributability of hypothesised socio-demographic risk factors for COVID-19 related mortality such as deprivation, crowding and ethnicity have also not been fully quantified nor unpacked at small-area resolution.

66

67 As COVID-19 caseloads in England appear to rising towards a second peak (wave), to ensure
68 continued response to the epidemic is most effective, it is imperative that we better understand,
69 both retrospectively and prospectively, the geographical evolution of COVID-19 and localised areas
70 in space-time at higher risk of severe disease burden and mortality. Assessing the impact of mobility
71 and population-density (crowding) on differences in caseloads at small area scale will not only allow
72 assessment of the impact that social distance measures have had on the magnitude and timing of
73 the waves, but also allow counterfactual assessment of what this magnitude may have been in the
74 absence of these non-pharmaceutical interventions. More importantly as we enter the second wave
75 with increased likelihood of local outbreaks, this work will help identify small-areas at elevated risk
76 of transmission and mortality and subsequently inform when it might be safe to start lifting social
77 distancing measures at small-area scale in a geographic staggered approach. Furthermore, a better
78 understanding of the spatiotemporal dynamics of this COVID-19 outbreak, and accurate
79 characterisation of the likely spread and magnitude, will be critical for the design of timely and cost-
80 effective control strategies to minimise the spread of future such pandemics, and to help establish
81 better early warning systems ⁵⁻⁷.

82

83 We apply a stochastic Susceptible-Exposed-Infected-Removed (SEIR) space–time model for publicly
84 available COVID-19 confirmed case and death data in England at small area scale and by week to
85 map the likely trajectory, peak and duration of the outbreak at MSOA level by week, quantifying the
86 impact of mobility. We utilise weekly MSOA level population mobility data against observed
87 confirmed COVID-19 case data to assess the impact mobility reduction at small-area scale has had on
88 case transmission, and counterfactually what the magnitude may have been under the scenario of
89 no mobility loss. Furthermore, the inclusion of the death compartment of the model using observed
90 weekly COVID-19 related deaths at MSOA level and linkage to key socio-demographic risk factors
91 allows this framework to identify not only small-areas with significantly elevated mortality risk but

also what localised contextual factors may be significantly contributing to this. We apply an extension of the basic model⁸ by combining the SEIR implementation with a spatial conditional autoregressive (CAR) model, and also extend this implementation by considering neighbourhood infection effects for the infection process⁹. The space-time dynamics of COVID-19 related mortality in England and associated risk factors/determinants at MSOA level are also assessed to identify vulnerable MSOA.

Results

Observed spatial patterns for COVID-19 caseloads at MSOA: A spatial assessment of COVID-19 caseloads (scaled by population totals) for the observed data input period (week 9 to 34 of 2020), suggests a non-random distribution to high incidence MSOA across England with distinct pockets of high case rates centred in and around metropolitan areas (Figure 1a) for example Leicester, Birmingham, Liverpool, Manchester etc. The analysis of localised spatial clustering identified significant hot spots (at MSOA level) in Bedford/Bedfordshire, Leicester, Peterborough, large contiguous band in Cheshire and Merseyside, another contiguous band spanning Leeds-Wakefield-Barnsley-Sheffield and in the north Newcastle-Sunderland (Figure 1b). Additional pockets of significant excess COVID-19 case rates in less metropolitan type areas were identified in pockets throughout England, for example Ashford, Kings Lynn and West Norfolk and Burrow-in-Furness.

Spatial temporal patterns in population mobility at MSOA: Despite an overall significant reduction in population mobility from early March (week 9) to mid-April (week 14) of 2020 (Figure 1c), mobility rates began to increase from week 16 and median mobility levels across MSOA had been almost attained pre-lock March/April down levels by week 34 of 2020. The rate of cumulative mobility loss by mid-April varied across MSOA (Figure 1d), with lower levels of mobility loss generally in part of West and East Midlands, Northwest, York and the Humber land as well as North East England. A large band of significant hotspots for lower cumulative mobility loss at week 14 were identified in a large contiguous aggregation of MSOA spanning from Birmingham through to Leicester, Nottingham,

117 Sheffield, Leeds, Manchester and Liverpool (Figure 1e). Furthermore, significant clustering of lower
118 cumulative mobility loss was also observed in Newcastle and surrounds, Norwich and coastline areas
119 immediately to the east of Norwich, Tendering/Colchester, Canterbury/Dover and west of
120 Southampton for example.

Figure 1: a) cumulative case rates at week 34 at English MSA level (N=6791); b) statistically significant localised hot and cold spots for higher and lower cumulative COVID-19 cases at MSA resolution at week 34 of 2020 using the Getis-Ord G_i^* localised clustering statistic; c) Box plot of mobility by MSA and week ; d) cumulative mobility loss (darker red indicates lower mobility loss) by MSA in England (n=6791) from week 9 to 14 of 2020; e) statistically significant localised hot and cold spots for higher and lower cumulative mobility loss at MSA resolution from week 9 to 14 of 2020 using the Getis-Ord G_i^* statistic

Spatial-temporal patterns for COVID-19 mortality: The highest cumulative death rates for COVID-19 at MSOA resolution from week 9 to 26 of 2020 were observed in parts of North London, most of Birmingham and immediate surrounding MSOA, a large area spanning Cheshire-Merseyside, and lastly in and surrounding Newcastle (Figure 2a). Significant hotspots for COVID-19 related mortality were highly clustered and were identified in contiguous MSOA located in North London (Ealing-Brent-Hillingdon-Harrow-Barnet-Enfield-Three Rivers-Hertsmere-), West Midlands (Birmingham-Sandwell-Walsall-Dudley-Wolverhampton), North West (Liverpool-Manchester-Cheshire), Sheffield, and Newcastle (County Durham-Sunderland-Gateshead) (Figure 2b). The two principle risk factors associated with COVID-19 mortality risk and leveraged in this study, namely proportion of MSOA population aged 70 years or older and elderly population living in deprivation have two very distinct spatial distributions across England (Figure 2c and e respectively). The MSOA with higher proportions of population aged 70 years or older appear significantly clustered along the East of England coastline and the coastline in Southwest and South East regions of England (Figure 2d). Additional significant hot spots for elderly population clustering were identified outside key metropolitan centres, for example: west of Birmingham, north of Liverpool, south of Manchester, north of Nottingham and north of Bradford-Leeds (Figure 2d).

Spatial patterns for deprivation: The most deprived (worst 10 percentile) neighbourhoods (680 MSOA) are not evenly distributed across England (Figure 2e, f), with 50% of these areas located within just 20 local authority districts, notably - Birmingham with 62 such neighbourhoods; Liverpool, 35; Leeds and Manchester, 29 each, and Bradford, 20. Significant spatial clustering of the most deprived neighbourhoods is concentrated in large areas of contiguous MSOA located in London, West Midlands, Northwest, Yorkshire and Northeast England, with pockets of significant deprivation surrounded by less/least deprived neighbourhoods (Figure 2f). Furthermore, concentrations of deprivation among these 680 MSOA are also disproportionately concentrated in in large urban conurbations (142 Industrial and Multi-ethnic, 125 Larger Towns and Cities; 80 Ethnically Diverse Metropolitan Living; 33 urban living), as well as in areas that are (or historically were)

154 classified as heavy industry manufacturing and/or mining sectors (74 Manufacturing legacy, 42
155 service economy; 39 mining legacy). A statistical assessment of spatial clustering for elderly
156 population living in deprivation confirms the significant concentration of hot spots in the
157 metropolitans, namely: London, Birmingham, Liverpool, Manchester, Nottingham, Sheffield-Leeds
158 and Newcastle (Figure 2f).

159

Figure 2: a) Cumulative case rates at week 34 at English MSOA level (N=6791); b) statistically significant localised hot and cold spots for higher and lower cumulative COVID-19 cases at MSOA resolution at week 34 of 2020 using the Getis-Ord G_i^* statistic; c) proportion of population aged 70+ at MSOA resolution; d) statistically significant localised hot and cold spots for higher and lower proportion of population aged 70+ at MSOA resolution using the Getis-Ord G_i^* statistic; e) Index of multiple deprivation at MSOA resolution; f) statistically significant localised hot and cold spots for higher and lower proportion of IMD at MSOA resolution using the Getis-Ord G_i^* statistic.

Space-time SEIR dynamics: The full multivariate Bayesian space-time model estimated an asymptomatic fraction of 0.2 (95% UI: 0.06-0.39) i.e. for every 5 confirmed cases there is likely to be 1 additional asymptomatic case (Table 2). A decrease in mobility at MSOA scale has had a significant reduction on caseloads i.e. each unit increase in cumulative mobility (rescaled to be between 0 and 1) appears to be associated with a +3.6-unit increase in cases on the log scale (95%UI: 3.57-3.61) (Table 1). The change in cumulative mobility also appears to significantly interact with the natural logarithm of population density within a MSOA i.e. the impact of higher mobility is amplified by increasing population density ($\beta=+0.05$). Increasingly proportion of a MSOA population aged 70 years or older was strongly and significantly associated with increased COVID-19 related deaths ($\beta=+4.86$, 95% CI: 4.59-5.15) while a decreasing proportion of the elderly population in a given MSOA living in deprivation appears to have a strong and significant negative association ($\beta=-0.25$, 95% CI: -0.34, -0.10) (Table 1).

Table 1: Posterior statistics from the Bayesian multivariable space-time SEIR model using WinBUGS

Compartment	Node	Coef. (β)	2.50%	97.50%
Cases	Asymptomatic fraction	+0.20	+0.06	+0.39
	Cumulative mobility loss	+3.59	+3.57	+3.61
	Cumulative mobility loss X $\ln$ (Population per km^2)	+0.05	+0.05	+0.05
	$\tau(v_{1i})$ –spatially structured random effect	2.35	2.05	2.70
	$\tau(U_{1i})$ –unstructured random effect	14.53	12.06	17.47
Deaths	Proportion aged 70 years and older	+4.86	+4.59	+5.15
	Elderly population living in material deprivation index ⁱ	-0.25	-0.34	-0.10
	$\tau(v_{2i})$ - spatially structured random effect	0.81	0.73	0.88
	$\tau(U_{2i})$ – unstructured random effect	1.44	1.34	1.55

i: increasing score indicate lower level of material deprivation.

Posterior space-time projections from ST-SEIR model: The posterior projections from the full space-time SEIR model closely fit with the observed temporal course of case and deaths for COVID-19 over the observed data input period (spanning the first wave), namely week 9 to 26 for deaths and week 9 to 34 for cases (Figure 3). From week 27 the model fairly closely tracks the increase in caseloads which appears to signal the start of the second wave. Post week 34 i.e. the model out of prediction

phase, we note an exponential rise in observed cases beginning around week 35. The model prediction based on averted cases from lockdown in the first phase combined with the impact of steadily increasing population mobility appears to fairly accurately track the exponential rise from week 35 and suggests a likely second wave peak of almost 45,000 cases per week by week 43/44 (i.e. latter half of October) of this year (Figure 3). Secondly, the model prediction based on the impact of observed mobility change alone, without accounting for the averted (or counterfactual) caseloads in the first wave, appears to significantly underestimate the trajectory of the outbreak in the current phase post week 34 (Figure 3). Interestingly while the death compartment of the model closely fits the observed death rates in the first wave, the counterfactual projection post week 26 in the death compartment which assumes similar death rates to that observed in the first wave appears to significantly overestimate the death rate observed thus far in the second wave (Figure 3).

Figure 3: Observed and model fitted number of confirmed cases and deaths in England from week 9 to 34 of 2020, with projections to week 51 of 2020. Vertical coloured line represents the truncation

201 point for observed input data for cases (week 34) and deaths (week 26) respectively. Blue solid line =
202 observed number of weekly COVID-19 cases; blue dashed line = model fitted cases; dotted blue line
203 = asymptomatic cases; red solid line = observed number of weekly COVID-19 deaths, red dashed
204 line= model fitted deaths; red dotted line = COVID-19 deaths based on mortality rate from first
205 wave.

206 *Model predicted hotspots for weeks 35-40:* The forward projection of the model for weeks 35 to 40
207 at MSOA level suggests high and significant case rates forecast for large contiguous area spanning
208 North West and Yorkshire regions (Liverpool-Manchester complex, contiguous band spanning
209 Bradford-Calderdale-Kirklees-Leeds-Wakefield-Barnsley-Doncaster-Rotherham-Sheffield, contiguous
210 band of MSOA in and around Kingston upon Hull), large band of connected MSOA in the north east
211 spanning from Newcastle through to Stockton-On-Tees, high risk pockets through the midlands
212 (Stoke-on-Trent, Wolverhampton-Walsall-Dudley-Sandwell, Leicester, Peterborough) and two
213 additional pockets in southern England (Swindon, Ashford-Canterbury-Thamet) (Figure 4a/c). The
214 forecast pockets for significantly high COVID-19 related mortality are more focused/smaller in
215 geographic extent compared to the caseloads with some overlap between areas with project high
216 caseloads and high death rates: Blackpool, Manchester, band spanning Bradford-Leeds-Kirklees-
217 Wakefield, South Tyneside-Sunderland, large band spanning Wolverhampton-Birmingham-Coventry,
218 Leicester and Swindon (Figure 4b/d). Additional pockets of high mortality rate risk but with low-
219 moderate projected caseload rates were identified, with multiple pockets in the south of England
220 (Wiltshire, North Devon, Cornwall, South Somerset-Dorset and Swale).

Figure 4: Model projected COVID case (a) and death (b) rates per 100,000 at MSOA level for week 34 to 40 of 2020; statistically significant localised hot and cold spots for COVID-19 case (c) and death (d) rates at MSOA level for week 34 to 40, 2020

Discussion

To both support and respond effectively to surveillance activities such as NHS Test and Trace or universal weekly testing¹⁰, it is essential to unpack the spatial-temporal dynamics of the COVID-19 outbreak and related mortality at high spatial resolution (e.g. MSOA) over time and assess the contribution of key risk factors to differences in risk across space and time. Our high resolution spatial-temporal (MSOA by week) model suggest that social distancing measures, as estimated by the impact on population mobility patterns, have had a significant impact on the reduction of COVID-19 caseloads across England, in line with previous studies, for example in China and Italy¹¹⁻¹³. However, local authorities have seen varied rates of reduction of population movement, significantly impacting the cumulative caseloads at small-area scale. A sensitivity analysis whereby mobility restrictions are eased at various intensities at MSOA scale suggests that a steady gain in mobility, as observed from late April, may have contributed to a slowdown in caseload reductions towards late June and subsequent steady rise thereafter until late August (Figure 3). Subsequent to that the model prediction and observed caseloads data suggest an exponential rise from week 35 (early September). As such, it would appear that a critical tipping point has been reached, and the model suggests particular groupings of MSOA at significant increased risk of future caseloads and deaths. Further targeted implementation of local lockdown is essential at this stage. A geographically staggered approach combined with enhanced community surveillance¹⁰ will become increasingly important if we are to reduce the magnitude of the second wave in England and plan for subsequent waves/cycles in the absence of an effective vaccine. Crucially, our results highlight differences in epidemic dynamics across small areas in England, emphasising the importance of monitoring at fine sub-national scale. Our findings suggest that a

significant proportion of caseload and death variance is spatially structured, and that caseloads in neighbouring local authorities of a given MSOA in the preceding time point are significantly associated with caseloads in current time point. This - coupled with the large significant regional clustering of high caseloads observed – has important implications for informing limitations on movement between areas in the subsequent phases of lockdown easing. Small-area lockdowns could help reduce COVID-19 transmission while minimizing the size of the population (and economy) that needs to be disrupted to continue to release reduced transmission. Furthermore, deaths due to COVID-19 appear to be significantly clustered in space, with some overlap between areas in and around metropolitan centres with higher levels of elderly population living in deprivation (prominent examples: Wolverhampton-Birmingham complex, Blackpool, Manchester, Bradford-Leeds-Wakefield complex and south of Newcastle). However additional pockets of excess mortality risk were also identified in areas in less deprived coastal areas, however from our analyses many of these localities have much higher proportions of elderly population which may in part explain these clusters.

Human mobility has been demonstrated to play an important role in the early stages of the COVID-19 epidemic ¹¹ and in particular reductions observed in digital data sources of mobility appear to correlate well with incidence ¹² as well as contact patterns ¹⁴. As many countries continue to bring their COVID-19 outbreaks under control, evidence on the effectiveness of current lockdowns continues to emerge ¹⁵⁻¹⁸. Social distancing measures have had a significant impact on the reduction of COVID-19 caseloads across England, however local authorities have had a varied rate of reduction of population movement, which has substantially impacted the cumulative caseloads at small-area scale. While non-pharmaceutical interventions such as social distancing have had a profound impact on the trajectory of the COVID-19 outbreak in England, country wide relaxing of these measures from June 2020 and gradual observed increases in population mobility which started even prior to this, risks a rebound in a number of local authorities which still have caseloads above the threshold required to realise MSOA cessation.

This study is subject to limitations. First, confirmed COVID-19 cases were linked to the MSOA where the test was carried out, rather than patient residence. This is of greater concern for metropolitan areas, where a substantial proportion of patients may have been admitted or transferred to neighbouring trusts before being tested. Secondly, the data are also vulnerable to bias introduced by variable testing rates between Trusts, which may have contributed to greater between MSOA variability. Thirdly, we are assessing the association between aggregated cases/deaths at MSOA level with aggregated risk factor variables at the same level. Thus we cannot discount the possible impact of ecological fallacy in the observed association. A final limitation relates to the mobility data and lack of detail regarding movement between local authorities. While we have demonstrated the importance of mobility loss within a given MSOA on its subsequent caseloads, the impact of movement between local authorities (and density thereof) would provide additional important information regarding cross locality mixing and further targeted restriction of movement between particular higher risk areas.

Conclusions

This study highlights the importance and usefulness of space-time framework to unpack the dynamics of the COVID-19 outbreak at high resolution (MSOA) and in time, identify particular small-areas at elevated risk of transmission as well as COVID-19 related mortality. Furthermore, at small area scale we demonstrated the utility of longitudinal mobility data for real-time surveillance of the impact of social distancing interventions, and thereby can also allow national authorities to assess the impact on outbreak dynamics at small-area. It is advisable to pre-emptively assess what impact changes in mobility post lockdown easing will have on outbreak rebound potential at localised geographic scale, as well as to include monitoring changes in daily/weekly mobility patterns. Lastly areas with high proportions of elderly population and in particularly elderly population living in deprivation are at significantly greater risk of COVID-19 related mortality, and therefore enhanced surveillance/case follow-up should be ensured in these areas.

298 **Methods**

299 **Overview**

300 This analysis adheres to the Guidelines for Accurate and Transparent Health Estimates Reporting
 301 standards (GATHER) ¹⁹ (Supplementary Material Section 1). The data used are all in the public
 302 domain. Data processing and analyses were performed using Stata 16, and WINBUGS. The statistical
 303 code for implementing the Bayesian model in WINBUGS is provided in Supplementary Material
 304 (Supplementary Material Section 2).

305 **Data**

306 A summary of the input data and sources is presented in Table 2. The weekly number of confirmed
 307 COVID-19 cases (Pillar 1 - Government's mass testing programme) and deaths for each MSOA Middle
 308 Layer Super Output Area (MSOA) (6791 areas) in England were obtained from the UK COVID-19
 309 dashboard (<https://coronavirus.data.gov.uk/>) for the period of February 24, 2020 (week 5) to
 310 August 23, 2020 (week 34). The MSOA shape file, used to create the adjacency matrix for the model
 311 below and for mapping of the model posteriors, was obtained from the United Kingdom government
 312 geoportal platform: [https://geoportal.statistics.gov.uk/datasets/middle-layer-super-output-areas-](https://geoportal.statistics.gov.uk/datasets/middle-layer-super-output-areas-december-2011-boundaries-ew-bfc-1)
 313 [december-2011-boundaries-ew-bfc-1](https://geoportal.statistics.gov.uk/datasets/middle-layer-super-output-areas-december-2011-boundaries-ew-bfc-1). Weekly COVID-19 deaths at MSOA resolution were also
 314 extracted from the NHS PHE Dashboard (<https://coronavirus.data.gov.uk/>).

315 Table 2: List of model components, relevant variables and data sources

Model component	Variable	Source (open access unless indicated*)	Spatial resolution	Temporal resolution	Compartment
Outcomes	Confirmed cases	UK COVID-19 Dashboard: https://coronavirus.data.gov.uk/ Number of people with a lab-confirmed positive COVID-19 PCR test. Data include only pillar 1 cases until 2 July, from when pillar 2 cases are also included. Cases are allocated to the person's area of residence.	MSOA	Weekly	Cases
	Deaths within 28 days of positive test result for COVID-19	UK COVID-19 Dashboard: https://coronavirus.data.gov.uk/ Total number of people who had a positive test result for COVID-19 and died within 28 days of the first positive test, reported on or up to the date	MSOA	Weekly	Deaths

		of death or reporting date (depending on availability). Deaths are allocated to the deceased's usual area of residence.			
Covariate (daily varying)	Mobility (population movement index)	Oxford COVID-19 impact monitor (Cuebiq) (https://oxford-covid-19.com/)	MSOA	Daily	Cases
Covariates (annual estimates, weekly fixed)	Age, ethnic structure	ONS (https://www.ons.gov.uk/)	MSOA	2020	Deaths
	Population density	ONS (https://www.ons.gov.uk/)	MSOA	2020	Cases
	Household occupancy (overcrowding)	ONS (https://www.ons.gov.uk/)	MSOA	2019	Cases/Deaths
	Index of Multiple Deprivation (IMD)	Multiple deprivation experienced by Lower Layer Super Output Area (LSOA) in England (https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019)	MSOA	2019	Deaths
	Elderly population proportion living in deprivation	Public Health England – Local Health: https://www.localhealth.org.uk/	MPSA	2019	Deaths
	Emergency hospital admissions for chronic disease	ONS (https://www.ons.gov.uk/)	MSOA	2017/18	Deaths

316 Data on population size, population density and the proportion of the population aged 70 years and
317 older as well as proportion of population that is of Black or mixed ethnicity by MSA were obtained
318 from the Office for National Statistics (ONS) (<https://www.ons.gov.uk/>). Furthermore, we also
319 extracted the Index of Multiple Deprivation (IMD) score and proportion of the elderly population
320 living in deprivation for each MSA in England for 2019 (Public Health England: Local Health.
321 [Accessed: 24/08/2020] <https://www.localhealth.org.uk/#c=home>).

322 Daily population movement data by MSA was extracted from the COVID-19 Impact monitor
323 (<https://www.oxford-covid-19.com/>). Furthermore, rail passenger numbers and crowding statistics
324 (2018) were extracted for use a commuter density index by MSA prior to the local down for use a
325 proxy for likely daily contacts with other individuals and mixing density ([http://maps.dft.gov.uk/rail-](http://maps.dft.gov.uk/rail-passengers-and-crowding/interactive-dashboard/index.html)
326 [passengers-and-crowding/interactive-dashboard/index.html](http://maps.dft.gov.uk/rail-passengers-and-crowding/interactive-dashboard/index.html)).

327 As a proxy for underlying chronic circulatory and respiratory disease burden, we also utilised
328 mortality rates from chronic obstructive pulmonary disease (COPD) from 2016-2018 by MSA.
329 (Public Health England: Local Health. [Accessed: 24/08/2020]
330 <https://www.localhealth.org.uk/#c=home>).

Data analysis

For initial exploratory spatial analysis, we used the Getis–Ord G_i^* statistic (G_i^*)²⁰, also known as hot-spot analysis, to identify significant higher and lower risk MSOA in terms of case and deaths rates for the observed input data period, namely week 9 to 34. The significance level was set as 0.05. A previously developed Bayesian space–time SEIR formulation⁹ was then applied to assess the spatiotemporal variability of COVID-19 transmission at small area scale (MSOA) and by week in England, by accounting for the modelled transmission dynamics of the pathogen, inherent spatial-temporal correlation in the data, and important contextual risk factors for both COVID-19 cases and deaths. We also included a sum of cases in shared neighbours in the preceding time point as an additional parameter in our model to further assess the dependence of caseloads in adjoined areas²¹. Based on the available data provided we the starting study week was denoted as week 9 of 2020 (starting 24 February 2020), with available case data at the time of extraction for this analysis available up to week 34 (starting 17 August 2020) and death data available up to week 26 (starting 22 June 2020). We also limited the end date for the input data at week 34 to assess the predictive performance of the model into the future if we are to prove its predictive utility and thus use as a pre-emptive resource allocation/prioritization tool.

Let y_{ij} be weekly confirmed COVID-19 cases in MSOA region i and week j , ($i=1,\dots,151$; $j=9,\dots,51$). A discrete form SEIR model for the size of susceptible population at week $(j+1)$ and MSOA region i is given by $S_{i,j+1}=S_{i,j}-I_{i,j}-R_{i,j}$, where S , I and R represent the susceptible, infectious and removed (deaths and recovered) populations, respectively. The number of the infected COVID-19 cases in region i and week j were assumed to follow a Poisson distribution, with expected number of cases is a function of the serial interval or generation time as a time measure of disease communicability and defined as the number of infected cases in one median incubation period back $(j-1 \text{ week}^{22})$ i.e. and the susceptible population size in week j . The number of asymptomatic cases by week and MSOA is

assumed to be a function of the observed case load in a given MSOA/week multiplied by a parameter for the additional fraction that are asymptomatic.

Hence, $I_{ij} \sim \text{Pois}(\mu_{ij})$, and μ_{ij} is given by ⁹:

$$\mu_{ij} = \beta_{ij} \times S_{ij} \times I_{i,j-1}$$

$$S_{ij} = S_{i,j-1} - I_{i,j-1} - \text{Asym}_{i,j-1} - \text{deaths}_{i,j-1}$$

$$\log(\mu_{ij}) = \log(\beta_{1ij}) + \log(S_{ij}) + \log(I_{i,j-1})$$

$$\log(\beta_{1ij}) = b_0 + b_1 \times (\text{mobility})_{i,j} + b_2 \times \text{mobility}_{i,j} \times \ln(\text{population density}_i) + u_{1i} + v_{1i}$$

$$\text{Asym}_{ij} \sim \text{Pois}(U_{ij} \times \text{asym})$$

$$\text{asym} \sim \text{Uniform}(0.05, 0.4)$$

And $\text{deaths}_{ij} \sim \text{Pois}(d\mu_{ij})$, and $d\mu_{ij}$ is dependent on caseloads 2 weeks prior ²³ and given by

$$\log(d\mu_{ij}) = \log(\beta_{2ij}) + \log(I_{i,j-2})$$

$$\log(\beta_{2ij}) = b_2 + b_3 \times (\text{p70plus})_i + b_4 \times (\text{e-IMD})_i + u_{2i} + v_{2i}$$

Here $b = (b_0, b_1, b_2)$ is the vector of regression coefficients for the intercept (representing the log-transformed baseline transmission rate across all locations), mobility represents the observed weekly mobility by MSOA; mobility x population represents an interaction term to capture the varying impact of mobility change as a function of changing population density at MSOA level; p70plus represents the proportion of the population in a given MSOA that were 70 years or older in 2020 in a given MSOA; e-IMD represents the proportion of the elderly people living in deprivation in a given MSOA in 2019; u_i corresponds to structured (spatial) heterogeneity and represents spatial variation in transmission rate between regions that captures the effects of unobserved variables with an underlying spatial pattern; v_i correspond to geographically unstructured (i.e. random effect) heterogeneity in the transmission rate; and μ_{ij} is the weekly transmission rate at MSOA i and week j after incorporating the spatiotemporal effects of local social-demographic factors, the

transmission dynamics of COVID-19 outbreak (i.e. SEIR model) and random effects (u_i and v_i). All covariate coefficients had diffuse normal priors, given by $\mathbf{b} \sim N(0.0, 1.0E6)$. The variances of the random effects had uniform priors, $\sigma_u \sim U(0,5)$ and $\sigma_v \sim U(0,5)$.

A convolution CAR model²⁴ was applied to decompose the log of area-level relative risks into the sum of two random effects, namely a structured spatial dependency effect and unstructured areal level heterogeneity effect through the random effects u_i and V_i respectively. The convolution approach has demonstrated good robust estimates across multiple studies and a range of disease clustering/modelling scenarios, for example²⁵. This spatial structured effect models the effect of proximity using a first-order neighbourhood structure (i.e. MSOA adjacency matrix), whereby the random effect is assumed to have a normal distribution, with the conditional weighted mean given by the average of the neighbours.

We conducted various sensitivity analyses to estimate the impact of social distancing (as proxied by the daily population mobility covariate) on COVID-19 caseloads in England. The model coefficients for the mobility covariates from the full multivariable space-time model was applied to the baseline mobility prior to lockdown and propagated throughout the period assuming no change in mobility from baseline (that is, daily mobility patterns remained unchanged). Secondly, the observed rate of change of mobility at week 34 was propagated forward to week 51. Lastly, we assumed various fractions of mobility gain post week 34 and applied these to the difference between the counterfactual of no reduction in population movement and observed first wave outbreak dynamics under full lockdown to characterise the likely trajectory in England in the coming weeks.

A comparison of model fit was performed using the deviance information criterion (DIC). Posterior distributions for parameters of interest were obtained through Markov chain Monte Carlo (MCMC) sampling. Convergence was assessed by visual inspection of the trace/autocorrelation plots for the

sample chains, using Gelman-Rubin statistical plots ²⁶ and by confirming the MCMC error for all posteriors were less than 5% of the standard deviation for a given posterior. We ran 100,000 MCMC iterations and discarded the first 10,000 MCMC iterations as part of the model burn-in. We extracted the mean point estimate for a given posterior as well as the 95% uncertainty intervals (2.5 to 97.5 percentile). This analysis was performed using WinBUGS version 1.4.3.

We validated the performance of the model using out of sample prediction by comparing the predicted number of cases from the model post week 34 (observed case data truncation point) with the observed cases to prove its utility as an early warning (pre-emptive) tool for resource allocation and prioritization by MSOA resolution (Supplementary Material Section 3).

Contributors

BS and RP conceived and designed the study. AL assisted with adaptation of the statistical framework. BS acquired and analysed the data. All authors interpreted the data. BS drafted the manuscript. All authors critically revised the manuscript and approved the final version for submission.

Declaration of interests

All authors declare no competing interests.

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Figures

Figure 1

a) cumulative case rates at week 34 at English MSOA level (N=6791); b) statistically significant localised hot and cold spots for higher and lower cumulative COVID-19 cases at MSOA resolution at week 34 of 2020 using the Getis-Ord Gi* localised clustering statistic; c) Box plot of mobility by MSOA and week ; d) cumulative mobility loss (darker red indicates lower mobility loss) by MSOA in England (n=6791) from week 9 to 14 of 2020; e) statistically significant localised hot and cold spots for higher and lower cumulative mobility loss at MSOA resolution from week 9 to 14 of 2020 using the Getis-Ord Gi* statistic

Figure 2

a) Cumulative case rates at week 34 at English MSOA level (N=6791); b) statistically significant localised hot and cold spots for higher and lower cumulative COVID-19 cases at MSOA resolution at week 34 of 2020 using the Getis-Ord G_i^* statistic; c) proportion of population aged 70+ at MSOA resolution; d) statistically significant localised hot and cold spots for higher and lower proportion of population aged 70+ at MSOA resolution using the Getis-Ord G_i^* statistic; e) Index of multiple deprivation at MSOA resolution; f) statistically significant localised hot and cold spots for higher and lower proportion of IMD at MSOA resolution using the Getis-Ord G_i^* statistic.

Figure 3

Observed and model fitted number of confirmed cases and deaths in England from week 9 to 34 of 2020, with projections to week 51 of 2020. Vertical coloured line represents the truncation point for observed input data for cases (week 34) and deaths (week 26) respectively. Blue solid line = observed number of weekly COVID-19 cases; blue dashed line = model fitted cases; dotted blue line = asymptomatic cases; red solid line = observed number of weekly COVID-19 deaths, red dashed line= model fitted deaths; red dotted line = COVID-19 deaths based on mortality rate from first wave.

Figure 4

Model projected COVID case (a) and death (b) rates per 100,000 at MSOA level for week 34 to 40 of 2020; statistically significant localised hot and cold spots for COVID-19 case (c) and death (d) rates at MSOA level for week 34 to 40, 2020

Supplementary Files

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