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Title: Ethnic density and other neighbourhood associations for mortality in severe mental illnesses: Retrospective cohort study with multi-level analysis from an urbanised and ethnically diverse location in the UK

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ABSTRACT

Background: To assess, among people with severe mental illnesses (SMI), whether mortality risk in ethnic minority groups, relative to White British people, is modified by ethnic density. In addition, to investigate whether neighbourhood deprivation, urbanicity and social fragmentation are associated with elevated mortality in SMI.

Methods: Cohort study with linked data on deaths and areas of residence, comprising 18201 individuals with an SMI diagnosis from January 1st 2007 to December 31st 2014, identified from the case-registry of a large secondary mental healthcare Trust covering an urbanised, ethnically diverse location in London, UK.

Outcomes: There were 1767 deaths from all causes, 1417 from natural causes and 192 from unnatural causes. In the least ethnically dense areas, the adjusted Rate Ratio (aRR) for all-cause mortality in ethnic minority groups with SMI compared with White British people with SMI were similar, however in the highest ethnic density areas ethnic minority groups with SMI had a lower risk of death (aRR: 0.52 (95% CI: 0.38,0.71; $p<0.0001$), with similar trends for natural-cause mortality. In the SMI cohort, residency in deprived, urban and socially fragmented neighbourhoods was not associated with higher mortality rates. Compared with the general population, age- sex-standardised mortality ratios were elevated in the SMI cohort across all neighbourhood-level characteristics assessed.

Interpretation: For ethnic minority groups with SMI, residency in areas of higher own-group ethnic density is associated with lower mortality compared to White British groups with SMI.

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RESEARCH IN CONTEXT

Evidence before this study

People with severe mental illnesses experience major reductions in life expectancy and a markedly elevated risk of death compared with the general population, across all international contexts surveyed. To date, most previous studies have focussed on risk factors at the individual level (such as tobacco use, diet and physical activity) for mortality; however, there are growing calls to consider the role of broader social / contextual determinants. .

We reviewed MEDLINE database for studies examining area-level factors associated with mortality in people with mental illness, from inception to 6th February 2019, with no restriction placed on language. We used the MeSH terms, "Mortality" and "Mental illness", and keywords including "residential characteristics", "neighbourhood characteristics", "multilevel analysis", "ethnic density", "social fragmentation", "urban" and "deprivation". We used a previous systematic review to inform the search terms used in our searches (see appendix). We also manually searched the reference list of another recently published systematic review. For inclusion, eligible studies had to have relevant area-level indicators and associations with mortality presented, include populations comprised of people with severe mental illnesses and also have an effect size for the association of the area-level indicator with mortality outcomes. We excluded ecological studies. A total of 1,281 studies were identified, which were screened by abstract and / or full text for possible inclusion. A total of eight studies were identified as relevant. Six focused on all-cause mortality of which one study also included deaths from natural and unnatural causes, two studies focused on suicide. The studies also assessed area-level exposures across international settings, which included Ethiopia (2 studies), China (1), Taiwan (1), UK and devolved countries (2) and Canada (2).

Across all studies, irrespective of area-level associations, people with severe mental illnesses experienced elevated mortality compared to reference groups without severe mental illnesses. Associations with area-level indicators and mortality outcomes followed differing patterns, dependent on context. There were mixed findings across studies examining the effect of urbanicity on mortality outcomes in severe mental illness; This included one study suggesting an increased risk of death in urban compared to rural areas (from Ethiopia), one study indicating an increased risk in rural compared to urban areas (from China) and two studies suggesting no association (from Canada and Ethiopia). Four out of five retrieved studies supported an association between residency in more deprived areas being associated with elevated mortality in people with severe mental illness. However, in one study from a nationally representative sample from the UK, the investigators reported that people with severe mental illnesses resident in more deprived areas had a lower risk of suicide than people resident in less deprived areas. No studies were identified which assessed the association of ethnic density or social fragmentation with mortality in severe mental illnesses.

Added value of this study

This is the first study to systematically assess a range of neighbourhood-level exposures and, specifically, ethnic density, with mortality in severe mental illnesses. The study was situated in a geographically defined, ethnically and socioeconomically diverse location in the UK. We found strong support for the observation that, for certain ethnic minority groups with severe mental illnesses, mortality risks (especially for deaths from all-causes and natural causes) are lower in areas of higher own group density relative to White British people with severe mental illnesses. Other area-level indicators (social fragmentation, urbanicity and area-level deprivation) as assessed in this study were not associated with excess mortality in severe mental illness. Our findings build on a previous analysis which had shown that risks of all-cause, natural and unnatural-cause mortality where lower in most UK ethnic minority groups with severe mental illness compared with a White British reference group with severe mental illness. The present study sheds light on this finding since it suggests that the ethnic density of the area where ethnic minority groups with severe mental illnesses reside, may play an important role in modifying mortality risks. Residency in areas of higher own group density may buffer against social isolation or may be associated with

exposure to stronger health-protective social norms, which may ultimately protect against premature mortality in severe mental illnesses. Our findings challenge approaches which focus purely on individual-level risk factors.

Implications of all the available evidence

Premature mortality in people with mental illness may reflect a complex array of both individual and contextual / neighbourhood-level influences. In the present study, we found that certain ethnic minority groups with severe mental illnesses residing in areas of higher own-group density experienced lower mortality risks. Future studies must account for both individual-level and group-level sources of variation in mortality in these populations. A clearer understanding of the sources of variation could be used to guide the development of interventions to address premature mortality in people with severe mental illness and should be explored in future.

Introduction

Across international settings, people with severe mental illnesses (SMI) such as schizophrenia and bipolar disorder, experience a markedly elevated risk of death[1]. Mortality in these populations is mostly from preventable physical causes, and the gap in life expectancy is thought to be increasing over time[1]. Current approaches to address this have tended to focus on individual-level risks for physical health[2], despite a growing acknowledgement that such approaches miss opportunities at the population-level for intervention[3].

Almost twenty years ago the World Health Organization (WHO) coordinated a series of studies on the long-term outcomes of schizophrenia, using identical epidemiological case-finding methods for schizophrenia across international centres[4-7]. The investigators noted that although the absolute risk of mortality in SMI was elevated compared with national populations across all surveyed contexts[4-7]; standardised mortality ratios (SMRs) were most elevated in industrialised compared with non-industrialised centres[4-7]. The notion that outcomes in SMI, including mortality, may be more 'benign' in 'less developed' countries has been severely critiqued[8]. However, it remains a possibility that strong social factors in the environment, beyond traditional risk factors measured at the individual level may modify the excess risk of mortality in people living with SMI. The WHO study investigators postulated that socioenvironmental factors, such as family involvement, community 'solidarity', cohesive neighbourhoods, and other factors mitigating against social isolation, potentially played an important role in outcomes such as mortality[5-7, 9]. In particular, a more recent finding has been that for certain ethnic minority groups with SMI, mortality outcomes may be lower than in reference groups with SMI[10]. For ethnic minority groups in the general population, residency in areas of higher own ethnic density may confer health benefits through enhanced social support and buffering against social exclusion for marginalised groups[11]. No studies to date have assessed either this, or the possibility that other neighbourhood or group-level factors may play a role in mitigating against elevated mortality, in people with SMI.

To address this gap in the literature, we undertook a cohort study, from a UK ethnically diverse and urban location, with the aim of assessing the association of neighbourhood-level characteristics alongside individual-level factors, with all-cause, natural-cause and unnatural-cause mortality in people with SMI. As previous research has highlighted that for ethnic minority groups, residency in areas of higher own group density may buffer against social isolation and exclusion[11, 12], we assessed an interaction between area-level ethnic density and individual-level ethnicity. Other neighbourhood-level characteristics assessed included deprivation, urbanicity and social fragmentation (based on a theoretical construct of anomie, social disorganisation and social isolation)[13, 14]. We hypothesised that individuals of an ethnic minority background with SMI would experience lower mortality risks when living in areas of higher ethnic density and that mortality would be elevated in all people with SMI living in neighbourhoods which were more deprived, urbanised and socially fragmented.

Methods

Setting and participants

South London & Maudsley (SLaM) NHS Trust is one of Europe's largest secondary mental healthcare providers[15]. The Trust provides comprehensive secondary mental healthcare to a catchment area of approximately 1.36 million people in an ethnically and socioeconomically diverse location in South London, which includes the London Boroughs of Lambeth, Lewisham, Croydon and Southwark. According to the 2011 Office for National Statistics rural-urban classification system,

these boroughs are considered "urban with major conurbation" areas, defined as built-up areas with resident populations of more than 10,000 people. The London Borough of Croydon also contains rural areas towards the south of the borough.

Since 2006 SLaM Trust has operated fully electronic health records. The Clinical Record Interactive Search (CRIS) system, established in 2008, is an ethically approved electronic health records interface system that allows researchers to access de-identified electronic health records from SLaM Trust, for research[15, 16]. All clinicians and mental health teams are required to assign psychiatric diagnoses according to the *International Classification of Mental Disorders-10* (ICD-10), to patients who make contact with the mental health Trust. Individuals with ICD-10 diagnoses of SMI, specifically schizophrenia-spectrum disorders (F2*) and bipolar disorders (F30 and F31) were identified through searches of CRIS structured fields, supplemented by a Natural Language Processing (NLP) application developed with Generalised Architecture for Text Engineering (GATE), which extracts diagnostic statements from the free text of case notes and clinical correspondence[15]. A recent audit (2018) of the performance of the NLP algorithm which was used to determine clinical diagnoses from the free text fields (which supplemented the structured field diagnoses entered by clinicians) found that for severe mental illness as a whole recall (sensitivity) was 0.43 and precision (positive predictive value(PPV)) was 0.95. For schizophrenia this was 0.63 (sensitivity) and 0.96 (PPV). This figure reflects performance of the application at annotation level; we would expect sensitivity to be higher at the patient-level since there would be repeat annotations, this has not been assessed yet to date.

All individuals aged 15 years or over at the time of diagnosis after contact with any of SLaM services (inpatient, outpatient and Accident & Emergency contacts) were included in the cohort. Individuals with comorbid dementia diagnoses prior to the SMI diagnosis were excluded. The observation period for the study was from January 1st 2007 to December 31st 2014, with individuals entering the cohort at the date of their SMI diagnosis.

Measures

Individual-level indicators

Individual-level information used in analyses included gender, marital status (married/ cohabiting, divorced, separated, widowed and single) and the presence of current or previous substance use disorders (alcohol and drug use). Birth date was used to derive age, handled in analyses as a time-changing variable (see below). Self-ascribed ethnicity was classified according to the UK Office for National Statistics criteria for the main ethnic groups and included: White British, Black Caribbean, Black African, South Asian and Irish groups, which were also aggregated into a binary White British/ ethnic minority variable. ICD-10 F30 and F31 codes were classified as affective diagnoses and ICD-10 code F2* were classified as non-affective disorders. Previous/ current substance use disorder diagnoses were determined by the presence of an ICD-10 code for F10-F19 (mental and behavioural disorders due to psychoactive substance use), noted at some point in the clinical record.

Area-level indicators

Neighbourhood/ area-level indicators were assessed at Lower Super Output Area-level (LSOA). LSOAs are national administrative areas which have a mean population of 1614 individuals [17]. Area-level measures were calculated for the LSOAs based on individuals' addresses at the time of their first recorded SMI diagnosis. The Index for Multiple Deprivation (IMD) from 2010 was used to assess multiple deprivation, across income, employment, health and disability, education, housing, crime

and living environment domains[18], mapped to LSOA boundaries from 2011 (ie. the midpoint of the observation window).

All other area-level indicators at LSOA were determined using publicly available data from the UK Office for National Statistics (https://www.nomisweb.co.uk/). Urbanicity at LSOA-level was derived from 2011 Census data by calculating the number of people/ per hectare of land[19]. An indicator for 'social fragmentation' based on the theoretically informed approaches taken by previous investigators[13, 14, 20] was derived, utilising 2011 census data at LSOA-level. Census variables for numbers of: privately rented households, single person households and unmarried individuals/ individuals not in cohabiting relationships, at LSOA level, and 'mobility in the previous year' (numbers not resident at the same address one year previously) at Middle Super Output Area (MSOA) level were used and then standardised, generating Z-scores. Z-scores for each of these variables were then added together, resulting in a 'social fragmentation' variable, which was divided at the quartile, leading to four categories, with the upper fourth further divided at the 90th percentile, due to the skew of the variable[14]. The resultant social fragmentation variable comprised five categories ranging from the least to the most socially fragmented areas.

Own group ethnic density for each of the LSOAs was determined as the percentage of the total population accounted for by each of the minority ethnic groups resident in the area at the time of the 2011 Census and derived for Black Caribbean, Black African, South Asian and Irish groups. An overall ethnic density variable was also derived, which was the proportion of the total population in each area who were ethnic minority residents. The ethnic density variable was retained as a continuous variable across all regression models (see statistical methods section below). In order to estimate standardised mortality ratios (SMRs) in the sample, we also derived a categorical ethnic density variable, whereby the continuous variable was cut into ten equal groups, with SMRs estimated for the lowest and highest groups.

Linkage to death certificates

Details of deaths for patients who had received SLaM Trust care were provided by the UK Office of National Statistics and linked to health records using unique patient identifiers. The linkage meant that death certificate information with date and cause of death according to the *International Classification of Diseases-10* (ICD-10) was available for all cohort members who died during the study observation period[21]. Deaths were classified as deaths from all causes (A00-R99; U00-Y89), deaths from natural causes (A00-Q99) and deaths from unnatural causes, which included deaths from suicide and external causes (U509, V01-Y89). Deaths not otherwise classified (R00-R99) were included in analyses of all-cause mortality but not analysed separately..

Statistical methods

We derived Standardised Mortality Ratios (SMRs), through indirect age- and sex- standardisation to the resident population and deaths in England and Wales, in 2011. Age was determined at the mid-point of the observation period (Jan 1st 2011) or at the diagnosis date of the mental disorder, if this occurred after Jan 1st 2011. Age was categorised into ten-year bands corresponding to the reference population's age groups. As the cohort was followed for varying periods, depending on diagnosis dates within the 8-year observation window, we derived weights taking the mean observation periods contributed by cohort members within each age and sex band. Weights were then multiplied by the number of deaths recorded in each corresponding –age and -sex band for the standard population (which had been observed for one year only) to generate the expected numbers of death as the

denominators of SMRs, for the cohort. SMRs were then calculated for all-cause, natural-cause and unnatural-cause mortality for each of the area-level indicators (deprivation, urbanicity, social fragmentation and ethnic density), at the highest and lowest levels.

Individuals were followed from date of SMI diagnosis until death, emigration or the end of the observation window on December 31st, 2014. For all-cause mortality, multi-level Poisson regression utilising the *mepoisson* command in Stata, were used specifying individuals nested within LSOA areas. A cross-level interaction was fitted between self-ascribed ethnicity (at the individual-level) and own ethnic density (at the area-level) for all models. Initially this was for a binary ethnicity variable (White British (reference), all ethnic minority groups (exposure)), but was then repeated for each of the ethnic minority groups X own ethnic density. For the latter analyses we present the stratum specific estimates for the ethnic minority group in question. Lexis expansion was used to model age as a time-changing variable, which was grouped into three bands (age 15-44, 45-64 and ≥65 years). To model deaths from natural and unnatural causes, a competing-risks regression was fitted, utilising the *stcrreg* command in Stata[22]. These approaches estimate sub-distribution Hazard Ratios, with 95% Confidence Intervals, for deaths from a specified cause, while taking into account the competing risk of death from other causes occurring during the observation period[22]. Using this approach, models assessing the association of risk factors with natural cause-mortality were assessed, specifying unnatural cause mortality as the competing risk and *vice versa*. Robust standard errors to adjust for clustering at LSOA-level were utilised across these models and Wald tests were used to assess for associations and interactions. We also used this approach to run a post hoc sensitivity analyses, testing our models against the possibility that migrant groups with poorer health may be more likely to migrate back to their country of origin prior to death, leading to a numerator/ denominator mismatch and a false impression of 'healthy migrant' effects[23]. This is relevant as a large proportion of the ethnic minority groups in the cohort may have been first generation migrant groups. We specified date of emigration out of the cohort as a competing risk against all-cause mortality in this sensitivity analysis[10]. For each continuous variable (area-level deprivation, urbanicity, social fragmentation, ethnic density and age) a linear association for the variable with outcome was assessed compared with a categorical or quadratic association, using Likelihood Ratio Tests (in multi-level models for all-cause mortality) or Wald tests (in competing risk regression models for natural and unnatural mortality). A quadratic relationship between age and outcomes and a linear relationship between area-level variables and outcomes were noted across all models and therefore utilised in this form in final analyses. Analyses were conducted in Stata/ SE 13.1[24]. The protocol for the study is registered on Open Science Framework (OSF) (https://osf.io/x3tf6/).

Results

A total of 18,201 individuals contributed 122,731 person years to the cohort for analyses, with a median follow-up time of 6.36 years. There were 1767 deaths from all causes, including 1417 deaths due to natural causes, 192 deaths due to unnatural causes and 159 deaths from unknown causes, corresponding to an overall all-cause crude mortality rate of 14.4 deaths per 1000 person years (95% CI: 13.7 to 15.1) (Table 1).

There was considerable variation across the sample for area-level variables. For example, for urbanicity, this ranged from 36.7 persons per hectare (10^{th} percentile) to 173.1 persons per hectare (90^{th} percentile). For ethnic density this ranged from 20.3% ethnic minorities (10^{th} percentile) to 67.1% ethnic minorities (90^{th} percentile). Both variables were normally distributed.

When compared with the total population of England and Wales, the age- and sex- standardised mortality ratios (SMRs) were elevated for the sample, irrespective of the neighbourhood-level characteristics of areas of residence (supplementary table 1). SMRs by each area-level characteristic were broadly similar with overlapping 95% confidence intervals. Deaths from all causes and natural causes were elevated approximately 2-3 fold in the sample, whereas deaths from unnatural causes were elevated around 4-7-fold in the sample, when age- and sex- standardised to the population of England and Wales.

In the cohort with SMI, we found that none of the area-level indicators for deprivation, urbanicity or social fragmentation appeared to have an association with any of the mortality risks, across adjusted models (tables 2-4), although there were noteworthy associations for individual-level variables with causes of death. Women with SMI had a lower risk of deaths from all causes and from unnatural causes compared to men, the presence of an affective diagnosis (compared to non-affective) was associated with a lower risk of death from all causes and from natural causes and people with SMI who were divorced or in disrupted relationships had a higher risk of death from all causes and from natural causes, compared to people with SMI who were married or cohabiting. A history of current/ previous substance use disorders was associated with an increased risk of death from all causes and from unnatural causes in the SMI cohort (tables 2-4).

We assessed the cross-level interaction of individual-level ethnicity (all of the ethnic minority groups in the study aggregated) with area-level total ethnic density across mortality outcomes. Significant ethnicity-ethnic density cross-level interactions were noted for all-cause mortality (see Figure 1). In the least ethnically dense areas (lowest decile category range: 0.30% to 19% ethnic minorities, aIRR estimated at 0% ethnic minorities), individuals with SMI, belonging to an ethnic minority group, had a similar adjusted Rate Ratio (aRR) of death compared with White British individuals with SMI (aRR: 0.96 (95% CI: 0.71, 1.29)); whereas in the highest ethnic density areas (highest decile category range: 67.1% to 96.4%, aIRR estimated at 95% ethnic minorities) this relative risk reduced to half that of White British individuals with SMI (aRR 0.52 (95% CI: 0.38 to 0.71)), with strong evidence in support of a statistical interaction between individual-level ethnicity and area-level ethnic density (*p-value for statistical interaction: 0.036)* (table 2, figure 1). A similar trend was noted for deaths from natural causes although with weaker evidence in support of a cross-level statistical interaction (*p-value for statistical interaction: 0.071*) (table 3, figure 1). No cross-level interactions were noted for deaths from unnatural causes (table 4, figure 1).

We also assessed cross-level ethnicity X own group ethnic density associations for each of the ethnic minority groups within the sample. In general, similar trends were supported across Black African,

Black Caribbean and South Asian groups with SMI, but most pronounced in the South Asian group. In adjusted models, adjusted Rate Ratios (aRRs) for deaths from all-causes in South Asian people with SMI were similar to White British people with SMI in the lowest South Asian ethnic density areas (lowest decile category ranged from 0% to 4.1%, calculated at 0% South Asian ethnic density) (aRR: 1.08 (95% CI: 0.76, 1.54). This reduced to aRR 0.07 (95% CI: 0.01, 0.49) in the highest South Asian ethnic density areas (highest decile category ranged from 19.8% to 86.8%, calculated at 90% South Asian ethnic density). A similar trend was noted for deaths from natural causes for this group with SMI (relative to White British people with SMI, aRR was 1.03 (95% CI 0.73, 1.45; p=0.88) in the areas of the lowest South Asian ethnic density, which had reduced to aRR 0.04 (95% CI: 0.01, 0.23; p<0.0001) in the areas of highest South Asian ethnic density. Similar, albeit weaker associations were noted for the Black African group with SMI, with similar trends for all cause and natural cause mortality in Black Caribbean groups with SMI (supplementary figures 2-5 and supplementary tables 2-3).

Sensitivity analyses

Sensitivity analyses were run specifying the risk of emigration out of the cohort as a competing risk in regression models, for all-cause mortality. On the whole, most associations across the cohort were retained. Ethnic density associations highlighting a reduced risk of all-cause mortality in areas of higher ethnic density in ethnic minority cohort members with SMI (relative to White British people with SMI) were still observed across models, although the statistical tests for the ethnicity X ethnic density cross-level interaction across the adjusted model was weaker (see supplementary table S10).

Discussion

We found that in areas of low ethnic density, risks for all-cause and natural cause mortality were similar in ethnic minority groups with SMI compared with White British people with SMI. In contrast, in neighbourhoods of high ethnic density, risks for death from all-causes and from natural causes were significantly reduced in ethnic minority groups with SMI relative to White British people with SMI. Similar trends were observed across most of the ethnic minority groups in the study, with the strongest associations noted for all-cause and natural-cause mortality in South Asian groups with SMI compared with White British groups with SMI. Residency in areas that were more deprived, urban or socially fragmented did not appear to be associated with elevated all-cause, natural cause or unnatural cause mortality in people with SMI. People with SMI in this study experienced a 2-3 fold increased risk of all-cause and natural-cause mortality and 4-7 fold increased risk of unnatural cause mortality, when age and sex-standardised to a (non-SMI) reference population. These differences persisted when compared across the different characteristics of the neighbourhoods surveyed.

Our literature reviews did not identify any studies which have previously directly assessed the association of residency in socially fragmented neighbourhoods with mortality in SMI, although previous ecological studies have suggested an association between increasing social fragmentation and suicide mortality, in the general population[13, 20]. The lack of an association between social fragmentation and mortality in our study, in contrast to previous work, may be because previously noted associations were only observed at the whole-population level, whereas our study had a primary focus on an SMI population. Previous work may have also been affected by ecological bias, whereby inferences about individuals are erroneously determined from ecological/ area-level characteristics. The differences between our study and this previous work may also reflect that we were able to include both individual-level and area-level covariates, avoiding such biases.

For area-level deprivation, research findings have been inconsistent. Although associations have been noted in some studies between residency in more deprived areas and increased mortality in SMI[3, 25, 26], in one study from a UK nationally representative sample, the investigators reported that people with SMI resident in more deprived areas had a lower risk of suicide than people resident in less deprived areas[27]. Our findings may indicate that for ethnic minority groups with SMI, area-level factors such as ethnic density, which may buffer against social isolation and be associated with enhanced social support[11, 12] and social capital[28], may counteract any neighbourhood material advantages on health.

Markedly elevated standardised mortality ratios observed in this cohort, when compared with the non-SMI population, are consistent with previous work in international samples, and underlie an urgent need to address premature mortality in people with SMI[1, 2]. Across international contexts, associations between residency in urban areas and mortality in people with SMI have been mixed[29, 30]. Investigators in the original WHO international studies of schizophrenia observed that all-cause mortality in people with SMI was lower in less industrialised settings compared with industrialised settings[4], whereas investigators in a more recent systematic review did not find an association between urbanicity and mortality in SMI[31]. The notion that outcomes including mortality, for people living with SMI in 'developing' versus 'developed' countries are better, has been critiqued[8]. We did not find an association between urbanicity and mortality in SMI in our study, although we observed that residency in areas of higher own group ethnic density for some ethnic minority groups was associated with less adverse mortality outcomes in SMI. An understanding of possible aetiological mechanisms underlying observed associations may be informed by previous research, in which the association of own ethnic density with physical health morbidity and mortality outcomes in non-SMI

populations, has been explored[32]. For example, in the UK, Black African, Black Caribbean and South Asian individuals resident in areas of higher own group density report lower levels of alcohol use[33]. Mechanisms underlying these findings may include the mutual support of others of a similar ethnic background, as well as the health protective effects of social norms mitigating against adverse health-related behaviours[32]. Conversely, residency in areas of low ethnic density for ethnic minority groups may be associated with lower social support, greater social isolation and greater discrimination[11, 12]. Therefore, the findings in the present study may not just be specific to SMI but may reflect the wider impact of own group ethnic density on health-related behaviours and mortality in general. The role of neighbourhood/ group-level factors in accounting for mortality risks in SMI could be an important area of future enquiry[2].

Ethnic density trends were most notable for South Asian and Black African groups. There is a large literature indicating poorer mental and physical health in Irish people in the UK[34] which for common mental disorders and suicidal ideation, may be offset by residency in areas of higher own group density[12, 35], however this was not observed in the present study. It is therefore possible that smaller sample sizes in the present study may have limited the power to detect differences for Irish people with SMI. In addition, unlike the other ethnic minority groups within the study, in supplementary analyses, we found that whereas strong positive correlations were observed with own group density and the total ethnic minority density variable for Black African, Black Caribbean and South Asian groups, this was not observed for Irish own group density (supplementary figure S11), possibly reflecting differing historical patterns of settlement across each of these groups in the catchment area of the study. Within this catchment area, Irish groups with SMI were resident in areas of lower total ethnic minority density and were more dispersed. This may be another reason why we did not find an ethnic density association for the Irish group and could be explored in larger nationally representative samples.

We used reliable methodologies to derive each of the area-level variables, which have been widely used previously, have a strong theoretical basis, and have been validated[11, 13, 14, 18]. A strength of the present study was in the possibility of using both neighbourhood and individual-level variables. It may be a limitation that we assessed area-level factors at one time point only (time of diagnosis) and could not assess all individual-level variables at cohort entry.This may have led to random measurement error. If this was the case, then associations between exposures with outcomes may have been under-estimated. As we used address at the time of diagnosis, linked to area-level indicators from the study midpoint (2010-2011), this may also have further contributed to imprecise estimates.

People with SMI are more likely to experience downward ‘social drift’ as their illness progresses. Such drift effects may also operate in the prodromal phase, prior to onset. A possible limitation of our methods is that the location of residency was obtained at the point of diagnosis. It is unclear how such ‘drift’ effects may have biased our findings. As ethnically dense areas are also in general more deprived and urban, it is unlikely that individuals with SMI from minority ethnic groups would be able to ‘drift’ into ethnically less dense areas (as such areas would be expected to be more affluent and less urban). On the other hand, White British people with severe mental illness may ‘drift’ into higher ethnic density areas. As we would also expect that ethnic minority groups with SMI in low ethnic density areas could ‘drift’ into higher ethnic density areas, it is difficult to quantify how far such ‘drift effects’ would operate selectively for ethnic groups with SMI, and how this would then impact on the mortality findings.

Other limitations of the study included our inability to assess other important individual-level variables such as health-related behaviours, physical health comorbidities, individual-level socioeconomic status and social support. Work is currently underway to link the cohort to other data sources, which may eventually allow us to directly assess these indicators as potential confounders or mediators for mortality. A further limitation is that it was also not possible to derive SMRs standardised by ethnicity, as this information is currently not routinely recorded in UK death certificates[36]. Although the catchment area of the study is typical of many large urbanised locations in Britain and internationally, with potentially good generalizability to other metropolitan locations elsewhere, it is a limitation that we were not able to include locations outside of the Greater London area, which could be considered in future work. We focussed the analyses on key ethnic minority groups who were well represented within the catchment area of the study and have previously been included in national surveys of ethnic minority health, however it is a potential limitation that other ethnic minority groups were not included, such as those who may self-identify as 'white other'. Future work could explore health inequalities impacting on these groups also. The southern part of the catchment area for this study included less urbanised areas and there is a possibility that overall there was inadequate variation in the degree of urbanisation to enable associations to be detected. However, previous work from this location has indicated "considerable heterogeneity" across this catchment area for ethnic density, population density and other measures of social fragmentation such as voter turnout[37], which was also observed in the range of urbanicity and ethnic density variables in the present study. In addition, our scoping of the literature indicated inconsistent associations between residency in urban versus rural areas and mortality in SMI[29, 38, 39], so our findings are not inconsistent with the broader literature; future work could explore these associations using national data. Finally, most of the ethnic density comparisons were made internally to the SMI cohort, therefore it is possible that these findings reflect ethnic density associations for ethnic minority people in general and should be explored in future, using non-SMI population controls.

For ethnic minority groups with SMI, we may speculate that residency in areas of higher own group density may buffer against social exclusion, social isolation and/ or promote health-protective behaviours, which may play a role in mitigating against premature mortality in SMI, however the study was unable to directly assess this. Future research should explore the role of contextual factors in accounting for mortality outcomes in SMI, which could be used to guide intervention development[2].

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Declaration of interest

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Data sharing statement

Data are owned by a 3rd party SLaM BRC CRIS tool which provides access to anonymised data derived from SLaM electronic medical records. These data can only be accessed by permitted individuals from within a secure firewall (i.e. remote access is not possible and the data cannot be sent elsewhere) in the same manner as the authors.

Ethical approvals

Permission to conduct secondary analysis of the Clinical Record Interactive Search system was granted by the Oxfordshire Research Ethics Committee C (reference 18/SC/0372). Separate approvals to examine linked mortality data with approved researcher status were obtained from the UK Health & Social Care Information Centre.

Contributor statement

JD conceived of the study idea, conducted all analyses, and led the drafting of the final manuscript for publication. The design of the analysis was determined by JD with input from MP and PS. VB assisted with literature searches. MED advised on statistical aspects of the analysis. All authors contributed to the interpretation of findings. All authors contributed to the drafting of the manuscript and approved the final version for publication. JD is the guarantor of the data and analyses. All authors agree to be accountable for all aspects of the work.

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Table 1: Demographic composition, deaths and crude mortality rates in the sample

	All-cause mortality					Natural cause mortality				Unnatural cause mortality			
	Total sample	All-cause deaths	Crude rate	(95% CI)		Natural cause deaths	Crude rate	(95% CI)		Unnatural cause deaths	Crude rate	(95% CI)	
	N	N (%)				N (%)				N (%)			
Total	**18201**	**1767 (9.7)**	**14.4**	**13.7**	**15.1**	**1417 (7.8)**	**11.5**	**11.0**	**12.2**	**192 (1.1)**	**1.6**	**1.4**	**1.8**
Area level indicators													
IMD (rank score)													
4 (most deprived)	3667	377 (10.3)	14.4	13.0	16.0	305 (8.3)	11.7	10.4	13.1	33 (0.9)	1.3	0.9	1.8
4276	3646	342 (9.4)	13.3	12.0	14.8	273 (7.5)	10.6	9.4	12.0	35 (1.0)	1.4	1.0	1.9
6144	3629	313 (8.6)	12.5	11.2	14.0	247 (6.8)	9.9	8.7	11.2	37 (1.0)	1.5	1.1	2.0
8747	3673	371 (10.1)	14.9	13.5	16.5	297 (8.1)	12.0	10.7	13.4	39 (1.1)	1.6	1.1	2.1
12859 (least deprived)	3586	364 (10.2)	17.3	15.6	19.2	295 (8.2)	14.0	12.5	15.7	48 (1.3)	2.3	1.7	3.0
Urbanicity (persons/ hectare)													
0.1 (least populous)	3613	377 (10.4)	17.5	15.8	19.4	301 (8.3)	14.0	12.5	15.7	42 (1.2)	2.0	1.4	2.6
55.3	3762	370 (9.8)	15.0	13.5	16.6	282 (7.5)	11.4	10.2	12.8	49 (1.3)	2.0	1.5	2.6
88.6	3667	347 (9.5)	13.5	12.1	14.9	275 (7.5)	10.7	9.5	12.0	41 (1.1)	1.6	1.2	2.2
111.4	3652	374 (10.2)	14.7	13.3	16.2	315 (8.6)	12.4	11.1	13.8	29 (0.8)	1.1	0.8	1.6
145.0 (most populous)	3507	299 (8.5)	11.8	10.6	13.3	244 (7.0)	9.7	8.5	11.0	31 (0.9)	1.2	0.9	1.7
Social fragmentation													
-7.2 (least fragmented)	4669	451 (9.7)	15.8	14.4	17.3	364 (7.8)	12.7	11.5	14.1	51 (1.1)	1.8	1.4	2.3
-2.4	4593	477 (10.4)	15.0	13.7	16.4	390 (8.5)	12.3	11.1	13.6	45 (1.0)	1.4	1.1	1.9
-0.2	4534	469 (10.3)	14.7	13.4	16.1	366 (8.1)	11.5	10.4	12.7	52 (1.2)	1.6	1.2	2.1
2.0	2686	227 (8.5)	12.2	10.7	13.9	185 (6.9)	9.9	8.6	11.5	25 (0.9)	1.3	0.9	2.0
>4.7 (most fragmented)	1719	143 (8.3)	12.1	10.3	14.3	112 (6.5)	9.5	7.9	11.4	19 (1.1)	1.6	1.0	2.5
Ethnic density (% ethnic minorities)													
0.3 (lowest ethnic density)	1665	138 (8.3)	16.6	14.0	19.7	107 (6.4)	12.9	10.7	15.6	23 (1.3)	2.8	1.8	4.2
19.0	1783	189 (10.6)	16.3	14.1	18.8	154 (8.6)	13.3	11.3	15.5	21 (1.2)	1.8	1.2	2.8
28.7	1788	187 (10.5)	15.2	13.2	17.6	152 (8.5)	12.4	10.6	14.5	20 (1.1)	1.6	1.1	2.5
35.0	1765	173 (9.8)	13.8	11.8	16.0	135 (7.7)	10.7	9.1	12.7	19 (1.1)	1.5	1.0	2.4

39.6	1861	171 (9.2)	13.2	11.4	15.4	135 (7.3)	10.5	8.8	12.4	24 (1.3)	1.9	1.2	2.8
43.8	1851	208 (11.2)	16.0	14.0	18.3	166 (9.0)	12.8	11.0	14.9	22 (1.2)	1.7	1.1	2.6
48.4	1840	190 (10.3)	14.6	12.7	16.8	149 (8.1)	11.5	9.8	13.5	15 (0.8)	1.2	0.7	1.9
53.3	1884	181 (9.6)	13.5	11.7	15.6	146 (7.8)	10.9	9.3	12.8	18 (1.0)	1.3	0.8	2.1
60.0	1872	162 (8.7)	12.5	10.8	14.6	137 (7.3)	10.6	9.0	12.5	11 (0.6)	0.9	0.5	1.5
67.1 (highest ethnic density)	1892	168 (8.9)	13.2	11.3	15.4	136 (7.2)	10.7	9.0	12.6	19 (1.0)	1.5	1.0	2.3
Individual-level indicators													
Age at diagnosis (years)*													
<38.1 years	8723	230 (2.6)	3.92	3.4	4.5	121 (1.4)	2.1	1.7	2.5	92 (1.1)	1.6	1.3	1.9
38.2 years or older	9478	1537 (16.2)	24.0	22.8	25.2	1296 (13.7)	20.2	19.2	21.4	100 (1.1)	1.6	1.3	1.9
Sex													
Male	9610	908 (9.5)	13.4	12.6	14.3	707 (7.4)	10.4	9.7	11.2	132 (1.4)	1.9	1.6	2.3
Female	8591	859 (10.0)	15.6	14.6	16.7	710 (8.3)	12.9	12.0	13.9	60 (0.7)	1.1	0.8	1.4
Diagnosis													
Non-affective	13160	1358 (10.3)	14.7	14.0	15.5	1090 (8.3)	11.8	11.1	12.5	141 (1.1)	1.5	1.3	1.8
Affective	5041	409 (8.1)	13.4	12.2	14.8	327 (6.5)	10.7	9.6	11.9	51 (1.0)	1.7	1.3	2.2
Marital status													
Married/ cohabiting	2781	267 (9.6)	15.8	14.0	17.8	220 (7.9)	13.0	11.4	14.9	22 (0.8)	1.3	0.9	2.0
Divorced/separated/ widowed/single	15420	1500 (9.7)	14.2	13.5	14.9	1197 (7.8)	11.3	10.7	12.0	170 (1.1)	1.6	1.4	1.9
Substance use disorder (SUD)													
None	15046	1519 (10.1)	15.1	14.3	15.8	1251 (8.3)	12.4	11.7	13.1	128 (0.9)	1.3	1.1	1.5
SUD	3155	248 (7.9)	11.3	10.0	12.9	166 (5.3)	7.6	6.5	8.8	64 (2.0)	2.9	2.3	3.7
Ethnicity													
White British	9047	1130 (12.5)	19.9	18.8	21.1	913 (10.1)	16.1	15.1	17.2	125 (1.4)	2.2	1.8	2.6
Ethnic minorities	9154	637 (7.0)	9.7	8.9	10.4	504 (5.5)	7.6	7.0	8.3	67 (0.7)	1.0	0.8	1.3

Key: *Crude rates are per 1000 person years; *Age was handled as a time-varying covariate in all regression models, and is displayed here cut at the median; IMD Index of Multiple Deprivation. 158 deaths were from causes not otherwise classified (R00-R99) and contribute to all-cause mortality totals in the sample.*

Table 2: Association of area-level and individual-level indicators with all-cause mortality in people with severe mental illnesses; crude and adjusted Incidence Risk Ratios (IRR/ aIRR)

	Total sample	All-cause deaths	Model 1 IRR	Model 1 (95% CI)	Model 1 p value	Model 2 aIRR	Model 2 (95% CI)	Model 2 p value
Area level indicators								
IMD (per increase in fifths; from less to more deprived)	-	-	0.98	0.95 ,1.02	0.34[t]	1.03	0.99 ,1.07	0.19[t]
Urbanicity (per increase in fifths; from less to more urban)	-	-	0.95	0.92 ,0.99	0.01[t]	0.97	0.93 ,1.01	0.14[t]
Social fragmentation (per unit increase; from less to more fragmented)	-	-	0.95	0.92 ,1.00	0.03[t]	0.98	0.94 ,1.03	0.45[t]
Individual-level indicators								
Sex								
Male	9610	908	REF	-	-	REF	-	-
Female	8591	859	1.07	0.98 ,1.18	0.13	0.86	0.78 ,0.94	0.0015
Diagnosis								
Non-affective	13160	1358	REF	-	-	REF	-	-
Affective	5041	409	0.82	0.73 ,0.91	<0.0001	0.83	0.74 ,0.93	0.0015
Marital status								
Married/ cohabiting	2781	267	REF	-	-	REF	-	-
Divorced/separated/widowed/single	15420	1500	1.01	0.89 ,1.15	0.89	1.28	1.12 ,1.46	<0.0001
Substance use disorder								
None	15046	1519	REF	-	-	REF	-	-
SUD	3155	248	0.79	0.69 ,0.90	<0.001	1.17	1.02 ,1.35	0.024
Interaction of ethnicity with areal ethnic density								
Lowest ethnic density area (0% ethnic minorities)								
White British	-	-	REF			REF		
Ethnic minorities	-	-	0.88	0.65, 1.17	0.38	0.96	0.71, 1.29	0.77
Highest ethnic density area (95% ethnic minorities)								
White British	-	-	REF			REF		
Ethnic minorities	-	-	0.31	0.23, 0.43	<0.0001	0.52	0.38, 0.71	<0.0001
p-value for ethnicity X ethnic density interaction					*<0.0001*			*0.036*

Key: *-1767 deaths from all causes (total 18201 individuals with SMI); IMD: Index for Multiple Deprivation; Model 1 crude estimates; Model 2 adjusted for: age, interaction between area-level ethnic density X ethnicity, and all other displayed variables; t: trend; p-values from Wald Tests.*

Table 3: Sub-Hazard Ratios (sHR) for natural-cause mortality in people with severe mental illnesses

	Total sample	Natural cause deaths	Model 1			Model 2		
			sHR	95% CI	p value	sHR	95% CI	p value
Area-level indicators								
IMD (per increase in fifths; from less to more deprived)	-	-	0.95	0.91 ,1.00	0.05 [t]	1.02	0.97 ,1.06	0.49 [t]
Urbanicity (per increase in fifths; from less to more urban)	-	-	0.94	0.90 ,0.98	0.005 [t]	0.99	0.94 ,1.03	0.55 [t]
Social fragmentation (per unit increase; from less to more fragmented)	-	-	0.93	0.88 ,0.97	0.002 [t]	0.98	0.93 ,1.03	0.41 [t]
Individual-level indicators								
Sex								
Male	9610	707	REF	-		REF	-	
Female	8591	710	1.25	1.11 ,1.39	<0.0001	0.92	0.82 ,1.02	0.11
Diagnosis								
Non-affective	13160	1090	REF	-		REF	-	
Affective	5041	327	0.90	0.80 ,1.02	0.11	0.82	0.73 ,0.93	0.002
Marital status								
Married/ cohabiting	2781	220	REF	-		REF	-	
Divorced/ separated/ widowed/ single	15420	1197	0.87	0.74 ,1.01	0.07	1.16	1.00 ,1.35	0.05
Substance use disorder (SUD)								
No SUD	15046	1251	REF	-		REF	-	
Life-time SUD	3155	166	0.61	0.52 ,0.71	<0.0001	0.91	0.77 ,1.06	0.22
Interaction of ethnicity with areal ethnic density								
Lowest ethnic density area (0% ethnic minorities)								
White British	-	-	REF			REF		
Ethnic minorities	-	-	0.69	0.51, 0.94	0.019	0.78	0.57, 1.05	0.11
Highest ethnic density area (95% ethnic minorities)								
White British	-	-	REF			REF		
Ethnic minorities	-	-	0.31	0.22, 0.44	<0.0001	0.44	0.32, 0.62	<0.0001
p-value for ethnicity X ethnic density interaction					*0.013*			*0.071*

***Key** – 1417 deaths from natural causes, (total sample 18201 individuals with SMI). IMD: Index for Multiple Deprivation;*
Models display Sub-hazard (sHR) estimates utilising competing risks regression models, with robust standard errors to adjust for clustering at LSOA-level; Model 1- crude estimates; Model 2 adjusted for: age, an interaction between area-level own ethnic density X ethnicity, and all other displayed variables. t: trend; p-values from Wald Tests.

Table 4: Sub-Hazard Ratio (sHR) estimates for unnatural-cause mortality in people with severe mental illnesses

	Total sample	Unnatural cause deaths	Model 1			Model 2		
			sHR	95% CI	p value	sHR	95% CI	p value
Area level indicators								
IMD (per increase in fifths; from less to more deprived)	-	-	0.88	0.80 ,0.98	0.02[t]	0.94	0.83 ,1.06	0.32[t]
Urbanicity (per increase in fifths; from less to more urban)	-	-	0.87	0.79 ,0.97	0.01[t]	0.94	0.83 ,1.07	0.33[t]
Social fragmentation (per unit increase; from less to more fragmented)	-	-	0.98	0.87 ,1.10	0.70[t]	1.02	0.90 ,1.15	0.80[t]
Individual-level indicators								
Sex								
Male	9610	132	REF	-		REF	-	
Female	8591	60	0.54	0.40 ,0.73	<0.0001	0.61	0.44 ,0.84	0.0026
Diagnosis								
Non-affective	13160	141	REF	-		REF	-	
Affective	5041	51	1.05	0.76 ,1.45	0.75	1.01	0.73 ,1.41	0.95
Marital status								
Married/ cohabiting	2781	22	REF	-		REF	-	
Divorced/ separated/ widowed/ single	15420	170	1.29	0.83 ,2.00	0.26	1.08	0.69 ,1.68	0.75
Substance use disorder (SUD)								
No SUD	15046	128	REF	-		REF	-	
Life-time SUD	3155	64	2.36	1.74 ,3.20	<0.0001	2.07	1.52 ,2.81	<0.0001
Interaction of ethnicity with areal ethnic density								
Lowest ethnic density area (0% ethnic minorities)								
White British	-	-	REF			REF		
Ethnic minorities	-	-	0.57	0.24, 1.39	0.22	0.52	0.21, 1.26	0.15
Highest ethnic density area (95% ethnic minorities)								
White British	-	-	REF			REF		
Ethnic minorities	-	-	0.47	0.17, 1.30	0.15	0.51	0.19, 1.40	0.19
p-value for ethnicity X ethnic density interaction					*0.84*			*0.99*

Key *-192 deaths from unnatural causes, (total sample 18201 individuals with SMI). IMD: Index for Multiple Deprivation;*
Models display Sub-hazard (sHR) estimates utilising competing risks regression models, with robust standard errors to adjust for clustering at LSOA-level; Model 1- crude estimates; Model 2 adjusted for: age, an interaction between area-level own ethnic density X ethnicity, and all other displayed variables; t: p-value for trend; P values from Wald tests.

Figure 1: Ethnic density associations at Lower Super Output Area (LSOA) level, with (1a) All-cause mortality; (1b) Natural cause mortality; (1c) Unnatural cause mortality; full sample

Figure a: Adjusted Incidence Risk Ratios (aIRR) for all-cause mortality by ethnic density

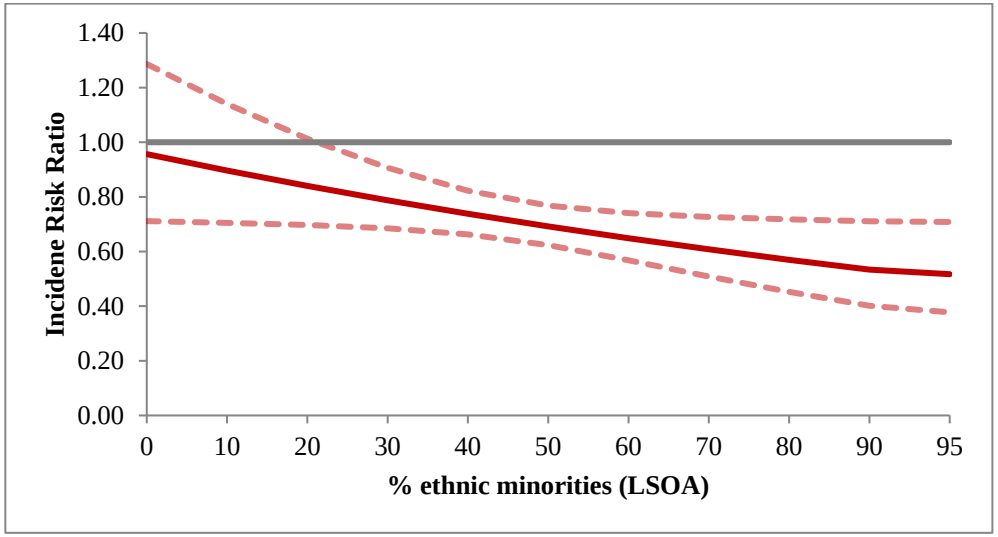


Figure b: Adjusted sub-Hazard Ratios (asHR) for natural cause mortality by ethnic density

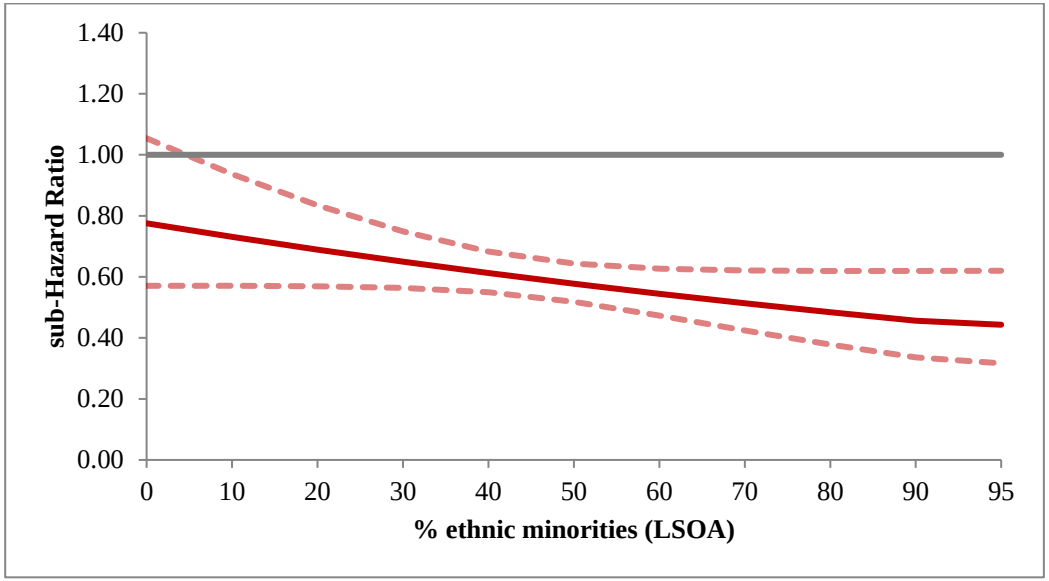
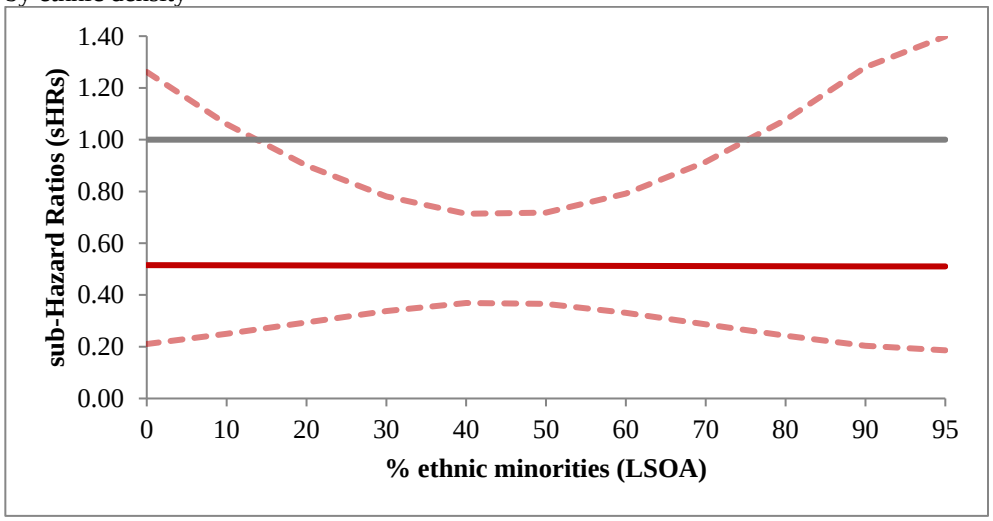


Figure c: Adjusted sub-Hazard Ratios (asHRs) for unnatural cause mortality by ethnic density



Legend

Adjusted IRR (All-cause mortality) or adjusted sHR (natural cause/ unnatural cause mortality) in ethnic minority groups relative to White British people with SMI, cohort followed for eight years

95% Confidence Intervals

Reference-White British group with SMI

Estimates are adjusted for area-level deprivation, urbanicity, social fragmentation, sex, diagnosis, marital status, substance use disorders and age. P values for ethnicity X ethnic density interactions were: All-cause mortality: p=0.036; Natural cause mortality: p=0.071 and Unnatural cause mortality p=0.99

Total sample N=18201