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Trends in Socioeconomic Inequalities in incidence of Severe Mental Illness – A Population-Based Linkage Study Using Primary and Secondary Care Routinely Collected Data between 2000 and 2017

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Abstract

Objective: In 2008, the UK entered a period of economic recession followed by sustained austerity measures. We investigate changes in inequalities by area deprivation and urbanicity in incidence of severe mental illness (SMI, including schizophrenia-related disorders and bipolar disorder) between 2000 and 2017.

Methods: We analysed 4.4 million individuals from primary and secondary care routinely collected datasets (2000-2017) in Wales and estimated the incidence of SMI by deprivation and urbanicity measured by the Welsh Index of Multiple Deprivation (WIMD) and urban/rural indicator respectively. Using linear modelling and joinpoint regression approaches, we examined time trends of the incidence and incidence rate ratios (IRR) of SMI by the WIMD and urban/rural indicator adjusted for available confounders.

Results: We observed a turning point of time trends of incidence of SMI at 2008/2009 where slope changes of time trends were significantly increasing. IRRs by deprivation/urbanicity remained stable or significantly decreased over the study period except for those with bipolar disorder sourced from secondary care settings, with increasing trend of IRRs (increase in IRR by deprivation after 2010: 1.6% per year, 95% CI: 1.0%-2.2%; increase in IRR by urbanicity 1.0% per year, 95% CI: 0.6%-1.3%).

Conclusions: There was an association between recession/austerity and an increase in the incidence of SMI over time. There were variations in the effects of deprivation/urbanicity on incidence of SMI associated with short- and long-term socioeconomic change. These findings may support targeted interventions and social protection systems to reduce incidence of SMI.

Keyword

austerity, deprivation, inequality, recession, severe mental illness, urbanicity

Abbreviations

APC –Annual Percentage Change

CI – Confidence Interval

CPRD – Clinical Practice Research Datalink

GPD – General Practice Database

ICD – International Classification of Diseases

IGRP – Information Governance Review Panel

IRR – Incidence Rate Ratio

LSOA – Lower-Layer Super-Output Area

ONS – Office for National Statistics

PEDW – Patient Episode Database for Wales

pyar – person-years at risk

SAIL – Secure Anonymised Information Linkage

SMI – Severe Mental Illness

WIMD – Welsh Index of Multiple Deprivation

1. Introduction

The complex aetiology of severe mental illness (SMI), including schizophrenia-related disorders and bipolar disorder has been well documented (Radua et al., 2018). Although the direction of causality remains a source of debate (Collip et al., 2008; Dunham, 1965; Goldberg and Morrison, 1963; Hudson, 2012, 2005; Sariaslan et al., 2016; Selten et al., 2013; Van Os et al., 2008), SMI is more prevalent in urban and socially deprived areas (Allardyce and Boydell, 2006; Faris and Dunham, 1939; Heinz et al., 2013; Kaymaz et al., 2006; Lee et al., 2020; March et al., 2008). This socioeconomic inequality, however, may vary due to person-level factors (age and sex), different pace of urbanisation, population growth between areas and socioeconomic changes (Haukka et al., 2001; Marcelis et al., 1998; Pedersen, 2006).

The global financial crisis of 2007/8 triggered an economic recession in the UK characterised by a sharp rise in unmanageable household debt, house repossessions, falls in financial markets, rises in unemployment and under-employment, and falling wages (Carrera and Beaumont, 2011; Coope et al., 2014; Gamble, 2009; ONS, 2018). Following the recession, the UK government implemented a stringent policy of austerity where public spending was pervasively cut to reduce expenditure and restore economic growth (Crawford and Phillips, 2012; Karanikolos et al., 2013; Kitson et al., 2011; Reeves et al., 2013). These measures potentially reduced funding to healthcare and social welfare services in real terms and introduced reforms in social security and welfare benefits (Akhter et al., 2018). The Welfare Reform Act 2012 (The UK government, 2012) was enacted to cap and restrict social security and housing benefits (e.g., 'bedroom tax'). Besides, a controversial reassessment on the eligibility of approximately 1.5 million existing claimants was performed via the Work Capability Assessment (The UK government, 2013) and those who were reassessed fit for work were moved from the benefit (Barr et al., 2016; Harrington, 2010; Litchfield, 2014).

Substantial research has suggested that social and geographical inequalities were widened in already vulnerable individuals during the period of the 2007/8 recession and austerity measures, particularly those from disadvantaged social groups, were impacted disproportionately (Akhter et al., 2018; Beatty and Fothergill, 2014; Browne and Levell, 2010; Crawford and Phillips, 2012; De Agostini et al., 2014; Taylor-Robinson et al., 2014). There have been quantitative studies evaluating the effects of the recession and austerity on social inequalities in mental health (Akhter et al., 2018; Barr et al., 2015, 2016; Katikireddi et al., 2012). However, few targeted those with SMIs specifically, nor were they free from methodological limitations, including non-representative/small samples, reliance on self-reported surveys often with un-validated measures on mental health, and limited data coverage after the onset of recession through to austerity (from 2008, up to 2015). Using the

UK clinical practice research datalink (CPRD) gathered between 2003 and 2013 from primary care settings, Kendrick and colleagues (Kendrick et al., 2015) reported a significant increase in prevalence of depression only for the most socioeconomically deprived quintile of practices after the second quarter of 2008. However, this widening gap following recession was not replicated in another study comparing prevalence of SMIs from 2000 to 2012 by area deprivation using the same CPRD dataset (Reilly et al., 2015). In this study, we explored the time trends of socioeconomic inequalities in incidence of SMIs, including the period of recession and austerity, using both population-based primary and secondary care routinely collected data in Wales, UK. We estimated both incidence and change in incidence of SMIs by level of area deprivation and urbanicity between 01/01/2000 and 31/12/2017.

2. Materials and methods

2.1 Study design

This is a retrospective population-based observational electronic cohort study.

2.2 Study population and setting

The eligible study population was all individuals (~4.4 million) aged 15 years or above and who continuously lived in Wales, UK for one or more years between 01/01/2000 and 31/12/2017 (Suppl. Figure 1A). Inclusion and exclusion criteria for calculation of annual incidences are described below (section 2.5.3).

2.3 Data Source

We interrogated the Secure Anonymised Information Linkage (SAIL) databank (www.saildatabank.com), a databank that contains anonymised privacy protecting person-based linkable data from healthcare and public settings (Ford et al., 2009; Lyons et al., 2009). In this study, we used data extracted from the General Practice Database (GPD) that includes contacts to general practices, the Patient Episode Database for Wales (PEDW) that contains inpatient hospital admissions, Welsh Demographic Service and the Office for National Statistics (ONS) deaths register datasets. Description of each dataset is outlined in the Suppl. Methods.

2.4 Ethical approval

Ethical approval was granted by the Information Governance Review Panel (IGRP) with the approval number 0466. The IGRP is an independent body including representatives with a variety of expertise from different organisations to oversee study approvals in line with

permissions already granted to the analysis of data in the SAIL databank (Ford et al., 2009; Lyons et al., 2009).

2.5 Measures

2.5.1 Outcomes (SMI diagnoses)

We classified SMI diagnoses into schizophrenia-related disorders (schizophrenia, schizotypal, delusional and schizoaffective disorders) and bipolar disorder as described in our previous study (Lee et al., 2020). We used Read Code version 2 (5-byte) for the GPD (primary care cohort) and the International Classification of Diseases (ICD) version 10 for the PEDW (secondary care cohort) to identify both disorders. The use and validation of diagnostic codes for SMI have been described elsewhere (Economou et al., 2012; Ford et al., 2009; John et al., 2018; Lee et al., 2020; Lloyd et al., 2015), with codes being cross-mappped between Read and ICD-10 classifications by the NHS used in our recent study (Lee et al., 2020).

2.5.2 Exposure (Area deprivation and urbanicity)

We adopted the previously used measures for area deprivation and urbanicity (Lee et al., 2020). For area deprivation, the Welsh Index of Multiple Deprivation (WIMD) 2011 was used (Welsh Government, 2017) throughout the study period (01/01/2000-31/12/2017). The WIMD measures deprivation for each Lower-layer super-output area (LSOA), geographic unit used in reporting small area statistics comprised of approximately 1,500 individuals, by a weighted score that combines eight domains of deprivation. These domains were income, housing, employment, geographical access to services, education, health, community safety and physical environment. We used WIMD quintiles where the WIMD scores were ranked and grouped from the least (Q1) to most (Q5) deprived areas. For urbanicity, we used the urban/rural indicator for England and Wales to categorise LSOAs as either urban or rural (Barham and Begum, 2006). Rural areas contained town and fringe, villages, hamlets and isolated dwellings while urban areas contained all urban settlement types with a population of 10,000 or more. To capture moving of individuals, both WIMD quintile and urban/rural indicator were extracted at the beginning of each year (1st January) until the date of the respective first SMI diagnosis in the respective cohorts. However, these exposures were time-fixed with respect to LSOAs (e.g., an urban LSOA remained urban throughout the study period).

2.5.3 Incidence of SMIs

We calculated first recorded incidence of SMIs between 01/01/2000 and 31/12/2017. Incidence was defined as the number of first diagnoses (with no previous recorded schizophrenia-related or bipolar disorders) over the whole 18-year period divided by the

number of person years at risk (pyar) within each WIMD quintile or urban/rural group. Incidence rates by calendar year were calculated by grouping incident cases and pyar for each year. Individuals and time at risk were included whenever they resided in Wales and were 15 years or above. Person-time were excluded whenever they moved out Wales and they were excluded (permanently) after the date of death (if present within the study period). Individuals and time at risk were not included in the incidence calculations if information of LSOA was not available on 1st January each year or at the date of incident diagnosis of SMIs.

Incidence was calculated separately for the primary and secondary care cohorts because these two cohorts did not share the same denominators for their differences in data coverage. However, individuals with both schizophrenia-related disorders and bipolar disorder were considered in the calculation of incidence of each of the conditions (i.e., the incident population of the two conditions were not mutually exclusive). For the primary care cohort, we adopted an algorithm (Davies et al., 2018) to identify periods of valid GP data coverage within the study period to avoid biased estimation of incidence due to non-complete data coverage. For the denominator of incidence within the GP population, the pyar of an individual was the summation of all valid periods bounded by the GP registration start and end dates within the study period. For the secondary care cohort, the whole population in Wales and the corresponding pyar within the study period contributed to the incidence calculation. Incidences (and pyars) were stratified by year throughout the study period.

2.6 Analysis and statistical methods

We extracted linked data in SAIL via structured query language (SQL DB2). We summarised sociodemographic characteristics of the study population as descriptive statistics with 95% confidence intervals (CIs). We adopted two-tailed mid-*p* exact CIs (assuming Poisson distribution) for incidence rates (Rothman and Boice, 1979), Wilson score with continuity correction for estimating CIs for proportions (Newcombe, 1998). Incidence were expressed as number of individuals per 100,000 pyar. Unless otherwise stated, all statistical analyses were performed using Stata version 16.1 (StataCorp, 2019) and the level of statistical significance was set at $p = 0.05$.

2.6.1 Gradient of incidence by deprivation and urbanicity

We estimated gradients of incidence by deprivation and urbanicity across time using Poisson regression. Four regressions were run separately for deprivation and urbanicity, as well as for data sourced from primary and secondary care cohort. Details of model specifications are described in the Suppl. Methods. The parameter of interest was the incidence rate ratio (IRR) by WIMD quintile and urban/rural indicator by year, which quantifies the direction and

magnitude of socioeconomic inequality at a particular year. An IRR greater than one indicated higher incidence in more deprived/urban areas. Widening of inequalities over the study period would be evident if an increase in IRRs over time was observed.

Stratified analyses were conducted for sex and age groups (15-24, 25-34, 35-44, 45-54; 55-64, 65-74, and ≥ 75 years). Due to sample size issues, stratification by age could not be performed. We alternatively restricted individuals aged between 25 and 64 years only as a sensitivity analysis (see below).

2.6.2 Trends of gradient of incidence by deprivation and urbanicity

We performed joinpoint regressions (Kim et al., 2000; National Cancer Institute, 2015; Wagner et al., 2002) using the Joinpoint software (Version 4.7.0.0) on the incidences rates and by deprivation and urbanicity by year to identify years where change in trends is evident (see Suppl. Methods for details). For IRRs, increasing (decreasing) trends indicated widening (narrowing) of social inequalities over the respective period. We reported annual percentage change (APC), i.e., exponentiating the slope (β coefficient) in incidence rates/IRRs within a line segment, years where the break points occurred, change in slope (change in β) at break points with corresponding 95% CIs.

2.6.3 Sensitivity Analysis

We carried out three sensitivity analyses to examine robustness of our results. The first one was to test the sensitivity of age inclusion criteria. The second and the third addressed the potential effects of temporal change in health service provision on our trends. The last two sensitivity analyses utilised the annual counts of available diagnoses to measure overall service provision. Detailed analytical strategies for the sensitivity analyses are outlined in Suppl. Methods.

3. Results

3.1 Study population

We identified 3,771,811 eligible individuals (68.9%) who were 15 years or older and continuously registered in Wales between 01/01/2000 and 31/12/2017 (Suppl. Figure 1A). There were 3,054,737 individuals (81.0% of 3,771,811) in the primary care cohort. Demographic characteristics, including population distributions over deprivation/urbanicity between primary and secondary care cohorts were similar (Suppl. Table 1A). Among the 35,394 individuals identified with schizophrenia-related disorders or bipolar disorder (Suppl. Figure 1A), 20,558 individuals (58.1%) identified with schizophrenia-related disorders only,

12,154 (34.3%) with bipolar disorder only and 2,682 (7.6%) with both disorders (Suppl. Figure 1B). Respectively 29.8% (10,563 out of 35,394) and 44.9% (15,894) of the individuals with SMIs were sourced from primary and secondary care cohorts only, and the remaining 25.3% (8,397) were from both cohorts (Suppl. Figure 1C). For the primary care cohort, 12,907 and 7,400 individuals were identified having schizophrenia-related disorders and bipolar disorder respectively whereas 15,469 for schizophrenia-related disorders and 11,028 for bipolar disorder individuals were identified from the secondary care cohort (Suppl. Figure 1A). During the 18-year study period, incidence of schizophrenia-related disorders were 39.2 and 33.8 per 100,000 pyar from primary and secondary care cohort respectively whereas for bipolar disorder the corresponding incidences were 22.5 and 24.0 per 100,000 pyar respectively (Suppl. Table 2).

3.2 Time trends of incidence of SMIs

Incidence of schizophrenia-related disorders and bipolar disorder by year from primary and secondary care cohort and the respective joinpoint regression estimates are summarised in Figure 1. In general, incidences of schizophrenia-related disorders (26.4-61.1 per 100,000 pyar) were higher than Bipolar disorder (15.6-36.3 per 100,000 pyar). Before 2004, we found incidences were increasing only in primary care cohort (Figure 1A and C). Incidences of schizophrenia-related disorders were significantly decreasing between 2004 and 2009 but then significantly increased over 2009 and 2014, with a significant positive change of slope at 2009 for both cohorts (change in β = 0.215, 95% CI: 0.154-0.265, $p < 0.001$ for primary and change in β = 0.120, 95% CI: 0.061-0.178, p = 0.005 for secondary). While for the primary care cohort incidence of schizophrenia-related disorders decreased again from 2014, the increase started from 2009 continued to the end of study period for the secondary care cohort. For bipolar disorder, incidence trend sourced from the primary care cohort significantly changed from decreasing between 2003 and 2008 to increasing between 2008 and 2014 (change in β = 0.096, 95% CI: 0.046-0.146, p = 0.007). A similar break point with a significant increase in slope at 2008 was found for the secondary care cohort (change in β = 0.062, 95% CI: 0.015-0.110, p = 0.037). From 2014 onwards, incidence of bipolar disorder sourced from the primary but not the secondary care cohort resumed decreasing.

3.3 Time trends of gradients of incidence of SMIs by deprivation and urbanicity

Incidence of schizophrenia-related disorders and bipolar disorder stratified by WIMD quintile/urbanicity per calendar year from primary and secondary care cohort are depicted in panel A, B, E and F of Figure 2-3 respectively (see also Suppl. Table 3-4). In general, we observed associations of higher incidence of SMIs in more deprived and urban areas. For bipolar disorder, these gaps were still evident but smaller.

Annual IRRs by deprivation/urbanicity also reflected the presence of inequalities (panel C, D. G and H of Figure 2-3). IRRs were significantly > 1 for all years for schizophrenia-related disorders (IRRs from 1.2 to 1.4) in the deprivation model (Suppl. Table 5). For bipolar disorder, the corresponding IRRs ranged from 1.0 to 1.3 over the study period. In the urbanicity models (Suppl. Table 6), statistical significance of IRRs > 1 was much less prevalent compared to deprivation models (IRRs from 0.9 to 1.5 and 0.8-1.4 for schizophrenia-related disorders and bipolar disorder respectively) due to their wider CIs.

Results from the joinpoint regression modelling (Table 1, Figure 2-3) for the IRRs shows that all but two time trends of IRRs by deprivation and urbanicity within the study period consisted of only one linear segment. One exception was the IRRs by deprivation for schizophrenia-related disorders sourced from the primary care cohort, consisting of three linear segments with joinpoints at 2004 and 2014 (Figure 2C). The other exception was the IRR by deprivation for bipolar disorder sourced from the secondary care cohort; containing two linear segments with a joinpoint at 2010 (Figure 3H). In the secondary care cohort, we found significant increasing trends of IRRs by deprivation after 2010 (APC = 1.6%, 95% CI: 1.0% to 2.2%, $p < 0.001$) and by urbanicity throughout the whole study period (APC = 1.0%, 95% CI: 0.6% to 1.3%, $p < 0.001$) for bipolar disorder. IRR by deprivation for schizophrenia-related disorders sourced from the primary care cohort increased from 2000 to 2004 and then decreased until 2014. Starting from 2014, the increasing trend resumed (APC = 2.6%, 95% CI: 0.7% to 4.5%, $p < 0.022$). All other IRRs decreased or remained stable with slopes not significantly different from zero.

3.4 Sex-specific time trends of gradients of incidence of SMIs by deprivation and urbanicity

Annual IRRs by deprivation and urbanicity stratified by sex (Suppl. Figure 2-3 and Suppl. Table 7-11) showed slightly larger IRRs by deprivation in males for schizophrenia-related disorders (average IRR for males vs. females: 1.3 vs. 1.2). Time trends of IRRs were not identical between sexes but consistent with the overall trends (Figure 2-3). For the primary care cohort, the increasing IRRs by deprivation after 2014 (Suppl. Figure 2A) and the overall decreasing IRRs by urbanicity (Suppl. Figure 2B) for schizophrenia-related disorders were contributed by females. The monotonic decrease in IRRs by urbanicity for bipolar disorder consisted of a decreasing trend from males before 2007 and another from females after 2013 (Suppl. Figure 2D). For the secondary care cohort, trends in IRRs by deprivation for schizophrenia-related disorders was significantly increasing for males but not females (Suppl. Figure 3B) while the increasing trends of IRRs for bipolar disorder was mainly observed in females (Suppl. Figure 3D).

3.5 Sensitivity analysis

Table 2 schematically summarises the post-2008 trends in incidences, proportions, gradients of incidences and proportions by deprivation and urbanicity from the main analysis and the three sensitivity analyses. The first sensitivity analysis by including individuals aged between 25 and 64 years only revealed similar results to the main analysis (Suppl. Figure 4 and Suppl. Table 12-14). The significant increasing trend of gradient of incidence by deprivation for bipolar disorder sourced from secondary care cohort were still robust after 2008. The second sensitivity analysis (including an additional term of overall available diagnosis to the models) yielded nearly identical results with the main analysis (Suppl. Figure 5 and Suppl. Table 15-17). Our third sensitivity analysis using proportion outcomes generally tallied with the main analysis (Suppl. Figure 6-8 and Suppl. Table 18-20). Proportion trends (Suppl. Figure 6) were similar to the incidence trends from the main analysis (Figure 1) with the exception in schizophrenia-related disorders. Besides, annual relative risks (RRs) by urbanicity appeared slightly higher than the IRRs from the main analysis, particularly for schizophrenia-related disorders. Comparisons of trends of annual RRs and IRRs by deprivation/urbanicity showed robust the increasing trends of gradients by deprivation for bipolar disorders sourced secondary care cohort (Figure 3E and 3G and Suppl. Figure 8E and 8G).

4. Discussion

4.1 Main findings

We found changes in time trends of incidence of SMIs, including schizophrenia-related disorders and bipolar disorder, and associated variations in socioeconomic inequalities in terms of area deprivation and urbanicity from 2000 to 2017. Our study period covered the 2007/8 economic recession and the subsequent implementation of austerity measures by the UK government. Regardless of the cohorts and conditions we examined, we found the period 2008/2009 was a time associated with significant increases in the slopes of time trends of incidences of SMIs. These changes in slopes occurred roughly at the time of the recession. For trends of socioeconomic inequalities of incidence of SMIs (quantified by IRRs), although we did not observe significant widening of inequalities at the time of recession/austerity, inequality was significantly increasing for those with bipolar disorder for data sourced from the secondary care cohort (apparently irrespective of the recession/austerity), which has not been previously reported in literature to our knowledge. Results from our sensitivity analyses were generally consistent with the main analysis with few exceptions. Our analyses were able to mutually adjust between area deprivation and urbanicity, to capture the sex-specific effects on socioeconomic inequalities in incidence of SMIs. To our knowledge, these analyses are not commonly reported in the available literature.

Our overall incidence rates of SMIs are comparable to other studies (Hardoon et al., 2013; Jongsma et al., 2019, 2018; Kirkbride et al., 2012; Lee et al., 2020; Saha et al., 2005; Simeone et al., 2015). Differences in demographic characteristics between primary and secondary care cohort were minimal and outcomes between cohorts were highly comparable. Our time trend of incidence of SMIs and proportion of SMIs diagnoses to all available diagnoses were generally decreasing or did not change before 2008/2009 and then began increasing. This pattern was previously demonstrated in mental health outcomes such as depression (Katikireddi et al., 2012; Kendrick et al., 2015), population mental health (Barr et al., 2015), and suicide (Coope et al., 2014), indicating the robust impact of recession on mental health.

Possible reasons for the increases in incidences in SMIs include chronic stressors such as financial adversity associated with the economic recession on mental health, including debt, reduction of income, house repossession, and (anticipated) unemployment/job insecurity at personal/household level (Coope et al., 2014). Such adversities during economic downturn may also place strains on relationships further deteriorating individuals' mental health. It has also been proposed that changes in public spending or reallocation of resources particularly on healthcare and social welfare services during times of economic uncertainty may curtail the usual social and financial support for prevention, personal resources to help seek and access to treatments for mental health problems to the individuals at-risk and the community (Akhter et al., 2018; Barr et al., 2015, 2016; Katikireddi et al., 2012). Additionally greater and widening inequalities within societies are associated with increased levels of mental disorders (Wilkinson and Pickett, 2009). It is possible that causal relationships in the development and expression of SMIs are mediated by complex gene-environment (socio-economic) interactions.

We believe the increase in incidences from 2000 and 2004 in the primary care cohort only are associated with the Quality and Outcomes Framework (QOF) introduced in 2004, aiming to improve quality of primary care provision by providing financial incentive for family doctors in managing and documenting certain health indicators/outcomes (Fichera et al., 2016). Brief increases of diagnoses on physical and mental health were reported elsewhere reflecting improved case finding associated with QOF (Fichera et al., 2016; John et al., 2016; McLintock et al., 2014; O'Donoghue, 2009).

We also replicated robust associations between incidence of SMIs and deprivation/urbanicity as demonstrated by numerous research studies (Hardoon et al., 2013; Kaymaz et al., 2006; Lee et al., 2020; O'Donoghue et al., 2016; Radua et al., 2018; Vassos et al., 2012). Our IRRs of schizophrenia-related disorders between the most and least deprived and between urban and rural areas are consistent with others (Hardoon et al., 2013; Kelly et al., 2010; Lee et al.,

2020; O'Donoghue et al., 2016). In keeping with others, we reported smaller socioeconomic inequalities for bipolar disorder compared with schizophrenia-related disorders (Gruebner et al., 2017; Hardoon et al., 2013; Heinz et al., 2013; Kaymaz et al., 2006; Laursen et al., 2007; Lee et al., 2020; March et al., 2008).

We discovered that changes in socioeconomic inequalities in incidence of SMIs over time might not be consistent between primary and secondary (individuals with higher severity or less social support) care cohorts. For schizophrenia-related disorders, socioeconomic inequalities significantly decreased over the majority of the study period from the primary but remained stable in the secondary care cohort. Interestingly, we observed signs of increasing inequality by deprivation for the primary care cohort from 2014. For bipolar disorder, we found significant widening of inequality from the secondary but not in primary care cohort. The increasing gap in incidence of bipolar disorder by deprivation found from hospitalisation data over the 18-year period is novel, alarming and requires further investigation. We also argue for further research to disentangle the relationships between severity of illness, contacts with types of health services and the socioeconomic inequalities of SMIs. Apart from cohort settings, we observed discordance of time trends of inequality between deprivation and urbanicity. This could be explained by the joint adjustments between deprivation and urbanicity in our models to reduce confounding between level of deprivation and urbanicity as previously reported (Lee et al., 2020).

Overall, we did not identify significant increase in socioeconomic gap of incidence of SMIs associated with recession and austerity. Quantitative evidence supporting widening socioeconomic inequalities in population mental health following recession/austerity was inconclusive using self-reported population survey data (Akhter et al., 2018; Barr et al., 2016, 2015; Coope et al., 2014; Katikireddi et al., 2012). Results were also mixed from population-based routinely collected data. From a UK analysis on primary care data using the CPRD, prevalence of depression was found statistically increased after the second quarter of 2008 for GPs located at the most deprived quintile only (Kendrick et al., 2015). In a recent study using the same data source, Reilly and others (Reilly et al., 2015) compared prevalences of SMIs including schizophrenia and bipolar disorders across four nations in the UK and deprivation from 2000 to 2012. For the UK data, they found that the gap by deprivation in SMIs did not increase corresponding to the recession (Reilly et al., 2015).

Our findings of relatively stable/decreasing trends in urban-rural inequality of schizophrenia-related disorders over the 18-year study period is not consistent with earlier European studies showing long-term increase in the effects of urban birth to schizophrenia/psychoses throughout the 20th century (Haukka et al., 2001; Marcelis et al., 1998; Pedersen, 2006). In

contrast, a more recent study from the ONS using the same urban/rural classification as in this study showed that population growth in rural- and urban-Wales were very similar between 2001 and 2009 (Pateman, 2011). We believe that this similar expansion of urban and rural areas in Wales implies a stable urbanisation phase in recent years and could further explain our relatively stable trends compared with earlier studies where rapid urbanisation was still underway (Haukka et al., 2001; Marcelis et al., 1998; Pedersen, 2006).

This study also identify differences in socioeconomic inequalities between sexes. Our comparison of gradients of incidence between males and females did not indicate wider inequalities for either sex in most studied conditions, except that wider inequalities existed in males for schizophrenia-related disorders. This tallies with the findings that the effect of urban birth on the elevated risk of schizophrenia and other psychoses is stronger in males (Haukka et al., 2001; Kelly et al., 2010; Marcelis et al., 1998; Pedersen, 2006).

4.2 Strength and limitations

This study revealed changes in inequalities in incidence of schizophrenia-related disorders and bipolar disorder by deprivation/urbanicity over time for data sourced from primary and secondary care settings. Besides the main analysis with sex-specific trends of socioeconomic inequalities, we replicated our findings by using different age inclusion criteria, controlling for overall use of health services and using alternative outcome (proportion of diagnoses). Such comprehensive analyses are not commonly performed using population-based datasets. Similar to our previous study (Lee et al., 2020), our complete data coverage of the Wales population in the hospital admission dataset and >70% coverage in the GP dataset is advantageous in terms of data coverage and representation. To circumvent the issue of incomplete data coverage in the primary care cohort, we reported outcomes sourced from both primary and secondary care cohorts to obtain results representative to the general population. We identified individuals with SMIs using diagnostic codes adopted and validated in previous studies to ensure validity and reliability (Economou et al., 2012; John et al., 2018; Lee et al., 2020; Lloyd et al., 2015). We also believe our study period between 2000 and 2017 was long enough to capture possible effects of recession/austerity on socioeconomic inequalities compared with other studies (Akhter et al., 2018; Barr et al., 2016, 2015; Katikireddi et al., 2012).

One major limitation of our study is the lack of single agreed measures on area deprivation nor urbanicity (Lee et al., 2020). We used WIMD and urban/rural indicator because of their popularity of use (Barham and Begum, 2006; Welsh Government, 2017) and data availability. Nonetheless, our results on the gradients of incidence of SMIs were comparable to others using alternative measures of deprivation and urbanicity. Using WIMD and urban/rural

indicator as area variable for individual characteristics may lead to ecological bias (March et al., 2008). We acknowledge that socioeconomic characteristics in an area may change over time and indeed the WIMD is recalculated from time to time. However, comparing the WIMD from different versions does not inform absolute change of deprivation over time (Welsh Government, 2017). We need further efforts to establish absolute level of deprivation and urbanicity.

We might underestimate change in socioeconomic inequalities associated with recession/austerity. The widening inequality associated with recession/austerity could be masked by floor effects e.g., individuals already resided in the most deprived areas before recession and further deterioration of socioeconomic circumstance/environment could not be captured (Akhter et al., 2018). Our 18-year study period might not capture longer-term mechanisms that change mental health outcomes in response to change in neighbourhood characteristics, Mechanisms underlying the presence of the inequalities of SMIs could be lifelong or inter-generational processes (Faris and Dunham, 1939; Heinz et al., 2013; March et al., 2008; Norman, 2018; Paksarian et al., 2018; Plomin and Deary, 2015). These processes not only involve socioeconomic factors, but also familial and genetic factors (Colodro-Conde et al., 2018; Paksarian et al., 2018; Sariaslan et al., 2016, 2015) that could remain stable over generations.

We used annual total number of available diagnoses as a measure of change in health services provision in two of our sensitivity analyses. However, number of available diagnoses is not a direct measure of health services provision (e.g., number of hospital available). Neither could we assess the effect of policy change in health care provision (e.g., Home Treatment teams) on identifying SMIs using GPD and hospitalisation datasets only. We used annual proportion of SMIs to overall diagnose as alternative outcome. An important caveat of interpreting results from proportion is that it measures socioeconomic inequality of SMIs relative to socioeconomic inequality in health, instead of absolute inequality based on incidences.

Other limitations include those shared by other studies using routinely collected data for research. Information bias can occur on underestimating rates and misclassify SMIs for individuals who do not contact to health services or have non-detectable symptoms. Selection bias due to loss of follow-up and missing data may reduce validity. In keeping with our previous study (Lee et al., 2020), we only included individuals with continuous registration in Wales within the follow-up period so that both WIMD and urban/rural indicator were available for analyses. However, this may bias incidence calculation by excluding e.g., the homeless populations and individuals moving in/out Wales intermittently. We analysed first recorded

incidence instead of prevalence because of the difficulty in defining remission and relapse of SMIs from routinely collected data (Lee et al., 2020). Given the incidence gradients of SMIs by deprivation/urbanicity are similar as previously shown (Lee et al., 2020), we would obtain similar results if prevalence was used. Other limitations include the presence of unmeasured confounding due to data unavailability (e.g., ethnicity, employment, genetic liability and familial background, status of substance use). Age-specific trends of gradients were not analysed due to sample size issues. Due to sample size issues, we did not perform analyses separately for individuals with both schizophrenia-related disorders and bipolar disorder.

4.3 Implications for policy and practice

This study makes an integral contribution to policy makers concerning the effects of economic downturn and subsequent policies such as austerity on socioeconomic gap in individuals with SMIs. Our findings not only identify an increase in risk (incidences) of SMIs associated with the economic recession/austerity, but also groups (individuals with bipolar disorder requiring hospitalisation) exhibiting widening of inequalities over the 18-year period. Taking our results together, we highlighted that the impact of recession/austerity on SMIs was similar among socioeconomic levels and these findings were crucial on formulating intervention policies in similar situations. Although socioeconomic gap was not shown as widening in times of recession, our findings do not argue against the potential benefits of providing social protection systems and programmes to fend off risks associated with economic downturn. Recent research suggested that disadvantaged social groups indeed benefit most from increases in spending on social protection following recession (Niedzwiedz et al., 2016). While the debate on how recession/austerity affects inequalities in mental health remains controversial and unsettled, analysis similar to the current study could help identify subtle changes in socioeconomic inequalities in mental illnesses linked to both short- and long-term social and economic changes and help facilitate timely planning of relevant infrastructure.

5. Competing Interest

None declared.

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7. Contributors

All authors conceived the study; AJ and SCL designed the study; AJ supervised the study; SCL conduct the analysis; SCL and AJ wrote the initial draft and all authors commented on the manuscript.

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