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Area deprivation, urbanicity, severe mental illness and social drift — A population-based linkage study using routinely collected primary and secondary care data

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ABSTRACT

We investigated whether associations between area deprivation, urbanicity and elevated risk of severe mental illnesses (SMIs, including schizophrenia and bipolar disorder) is accounted for by social drift or social causation. We extracted primary and secondary care electronic health records from 2004 to 2015 from a population of 3.9 million. We identified prevalent and incident individuals with SMIs and their level of deprivation and urbanicity using the Welsh Index of Multiple Deprivation (WIMD) and urban/rural indicator. The presence of social drift was determined by whether odds ratios (ORs) from logistic regression is greater than the incidence rate ratios (IRRs) from Poisson regression. Additionally, we performed longitudinal analysis to measure the proportion of change in deprivation level and rural/urban residence 10 years after an incident diagnosis of SMI and compared it to the general population using standardised rate ratios (SRRs).

Prevalence and incidence of SMIs were significantly associated with deprivation and urbanicity (all ORs and IRRs significantly >1). ORs and IRRs were similar across all conditions and cohorts (ranging from 1.1 to 1.4). Results from the longitudinal analysis showed individuals with SMIs are more likely to move compared to the general population. However, they did not preferentially move to more deprived or urban areas.

There was little evidence of downward social drift over a 10-year period. These findings have implications for the allocation of resources, service configuration and access to services in deprived communities, as well as, for broader public health interventions addressing poverty, and social and environmental contexts.

1. Introduction

The higher rate of severe mental illness (SMI) associated with urban neighbourhoods characterised by higher levels of deprivation, poverty and ethnic heterogeneity is well evidenced (Allardyce and Boydell, 2006; Faris and Dunham, 1939; Heinz et al., 2013; Kaymaz et al., 2006; March et al., 2008). Since the 1930s there has been considerable debate about the causes of this finding, classically articulated in the so-called "breeder" versus "social drift" hypotheses (Faris and Dunham, 1939; Goldberg and Morrison, 1963). The social causation theory proposes that the accumulation of exposure to environmental risk factors such as lack of social support, higher poverty and crime rates as well as reduced access to health care in deprived and urban areas over time increases risk of these illnesses, particularly for individuals with familial and genetic predisposition (Collip et al., 2008; Sariaslan et al., 2016; Selten et al., 2013; Van Os et al., 2008). The social selection or drift theory proposes that the symptoms and deterioration of cognitive functioning associated with these SMIs leads to increasing difficulties in function and maintenance of living standards, thus individuals drift progressively into lower socioeconomic status (SES) or more deprived areas (Dunham, 1965; Goldberg and Morrison, 1963; Hudson, 2012, 2005). Some consensus has been reached that social drift alone cannot explain the association of deprivation and urbanicity with these elevated rates of SMIs (Heinz et al., 2013; Hudson, 2005; March et al., 2008) because, for example, individuals with schizophrenia are more likely to be born in deprived areas (Werner et al., 2007). The

Abbreviations: CI, confidence interval; 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; OR, odds ratio; PEDW, Patient Episode Database for Wales; pyar, person-years at risk; SES, socioeconomic status; SAIL, Secure Anonymised Information Linkage; SMI, severe mental illness; SRR, standardised rate ratio; WDS, Welsh Demographic Service; WIMD, Welsh Index of Multiple Deprivation.

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available evidence for social drift after illness onset is not compelling (Hudson, 2012, 2005). However, recent evidence from molecular population level genetic studies suggests that the association may be subject to confounding by familial and genetic factors (Sariaslan et al., 2016, 2015) in addition to other possible interactions of personal- and area-level factors (Allardyce and Boydell, 2006; Heinz et al., 2013; March et al., 2008).

We aimed to compare the prevalence and incidence of SMIs (schizophrenia-related disorders and bipolar disorders) at an area level by deprivation and urbanisation to examine social drift, using both anonymised primary and secondary care routinely collected data. We performed a longitudinal analysis over 10 years to examine the change in level of deprivation and urban/rural residence associated with each individual after an incident diagnosis of SMI. We hypothesised that the presence of downward social drift would result in a stronger association between higher level of deprivation/urbanicity and prevalence but not incidence rates of SMIs following first recorded diagnosis within the follow-up period and that higher proportions of individuals would move to more deprived areas over time. We also examined social drift preceding the first recorded diagnosis.

2. Methods

2.1. Study design

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

2.2. Study population and setting

Approximately 3.9 million individuals aged 15 years or above who continuously resided in Wales, UK, between 01/01/2004 and 31/12/2015 were included in this study.

2.3. Data source

The Secure Anonymised Information Linkage (SAIL) databank (www.saildatabank.com) was used in this study. SAIL is an expanding databank of anonymised privacy protecting person-based linkable data from healthcare and public settings to support research (Ford et al., 2009; Lyons et al., 2009). The following datasets were utilised:

1. General Practice Database (GPD), which contains diagnoses, symptoms, investigations, prescribed medication, referrals, coded hospital contacts and test results. At time of analysis, 77% (333/432) of all general practices in Wales were supplying data to SAIL.
2. Patient Episode Database for Wales (PEDW), an NHS Wales hospital admissions dataset that contains types of admissions, diagnostic information, discharge and transfer information covering the whole population of Wales.
3. Welsh Demographic Service (WDS), an administrative register of all individuals in Wales that use NHS services, including anonymised demographics and practice registration history.
4. The Office for National Statistics (ONS) deaths register, documenting nationwide information on deaths and causes of deaths covering the whole population of Wales.

2.4. Ethical approval

This study forms part of the "PsyCymru study" (Lloyd et al., 2015). Ethical approval was granted by the Information Governance Review Panel (IGRP), an independent body consisting of a range of government, regulatory and professional agencies (approval number 0093). The IGRP oversees 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 (SMIs diagnoses)

Diagnoses of SMIs were categorised as schizophrenia-related disorders (schizophrenia, schizotypal, delusional and schizoaffective disorders) and bipolar disorder (see Supp. Table 1). To identify these mental disorders, Read Code version 2 (5-byte) was used in the GPD (primary care cohort) and the International Classification of Diseases (ICD) version 10 was used in PEDW (secondary care cohort) for both planned and emergency admissions. Diagnostic codes used to identify individuals with SMIs have been previously described and externally validated (Economou et al., 2012; Ford et al., 2009; John et al., 2018; Lloyd et al., 2015), involving mapping between Read codes and ICD-10 codes. We also included Read codes that have been cross-mapped to the corresponding ICD-10 codes by the NHS to maintain the consistency of diagnoses sourced from two datasets (see Supp. Table 1).

2.5.2. Exposures (area deprivation and urbanicity measures)

We adopted the Welsh Index of Multiple Deprivation (WIMD) 2011 as a measure of area deprivation at lower-layer super-output area (LSOA) level, the geographic units used in the calculation of WIMD and the reporting of small area statistics comprised of approximately 1500 individuals (Welsh Government, 2017). Eight different domains of deprivation were assessed, namely, income, housing, employment, geographical access to services, education, health, community safety and physical environment. Weighted scores were calculated from these domains and aggregated to become WIMD for each LSOA. The resulting WIMD scores were then ranked and grouped into quintiles from most (Q5) to least (Q1) deprived areas.

For categorising urban and rural areas, the urban/rural indicator for England and Wales first introduced in the 2005 Labour Force Survey was used (Barham and Begum, 2006). The classification was based on hectare grid squares, postcodes and settlement polygons defined by Department for Communities and Local Government. Settlement form and sparsity were the two measurement criteria for the classification. For settlement form, each hectare grid square was associated with a settlement type: dispersed dwellings, hamlet, village, small town and fringe as well as urban (population ≥ 10,000). For sparsity, each hectare grid square was assigned a sparsity score based on the number of households in surrounding hectare squares within 30 km. We used the accepted definition of rural and urban areas to classify LSOAs (Barham and Begum, 2006): rural areas were town and fringe, villages, hamlets and isolated dwellings; urban areas were all urban settlement types with a population of 10,000 or more. Similar to WIMD, urban/rural indicators were documented for all individuals based on the LSOAs at periods they resided in Wales.

2.5.3. Prevalence and incidence of SMIs by deprivation and urban/rural indicator

We computed annual prevalence and first recorded incidence of SMIs between 01/01/2004 and 31/12/2015. Annual prevalence was defined as the number of individuals with a relevant diagnosis in or before the current year divided by the total population within a WIMD quintile or urban/rural group each year. WIMD quintile and urban/rural group were assigned as the date of recorded diagnoses for cases. For individuals without SMIs, WIMD quintile and urban/rural group were assigned at the beginning of each year (1st January) for prevalence. Individuals were not included in calculating annual prevalence at particular year (s) if the LSOA was not available on 1st January at the corresponding year(s). We defined incidence as the number of new diagnoses (first diagnosis with no previous recorded schizophrenia-related and bipolar disorders) over the whole 12-year period divided by the number of person years at risk within each WIMD quintile or urban/rural group. Individuals and time at risk were not included in the incidence calculations if the LSOA was not available on the corresponding date of incident diagnosis. We used first ever recorded incidence to capture the time for

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first ever recorded diagnosis within the observation period and to avoid small sample size due to stratification by calendar year.

Annual prevalence and incidence over the 12-year study period of SMIs were calculated for the primary and secondary care cohorts separately:

Given that coverage of the GPD was for 77% of the population for the primary care cohort, an algorithm (Davies et al., 2018) was used to identify periods of valid GP data coverage within the study period and the denominator and all relevant contacts were extracted only within these valid periods for prevalence and incidence calculations. The population used to calculate prevalence was all individuals who supplied valid data to the GPD in SAIL within the study period. For incidence calculations, the person year at risks of an individual within this GP population was the sum of all valid periods of data provided – each period defined by the GP registration start and end dates – within the study period.

For the secondary care cohort, the whole population in Wales within the study period contributed to the denominator of the prevalence calculation and the corresponding person years at risk the denominator for incidence calculation.

2.5.4. Confounders

We included sex, age (as group: 15–24, 25–34, 35–44, 45–54; 55–64, 65–74, and ≥75 years) and calendar year (2004–2015) as measured confounders. These variables were chosen because they were documented as major confounders by other studies of prevalence and incidence of SMIs (Hardoon et al., 2013).

2.6. Statistical analysis

Linked data in SAIL were interrogated using structured query language (SQL DB2). Descriptive statistics were summarised for demographic, social and clinical characteristics, including means for continuous variables, counts, rates and percentages for binary and categorical variables together with 95% confidence intervals (CIs). All CIs for counts, rates and rate ratios were two-tailed mid-p exact CIs (assuming Poisson distribution) calculated as previously described (Rothman and Boice, 1979). CIs for proportions and percentages were estimated by Wilson score with continuity correction (Newcombe, 1998). CIs for continuous responses were approximated by normal distribution. With the exception of two-by-two contingency tables where Fisher's exact test was used, chi-square test of association and the Cochran-Armitage trend test for linearity were performed for contingency tables (Agresti, 2002), with CIs for relative risks estimated as proposed elsewhere (Altman, 1991). For All statistical analyses were performed using SPSS version 25.0 for Windows and the level of statistical significance was set at $p = 0.05$.

We then: 1) estimated and compared prevalence and incidence of SMIs by WIMD quintile and urban/rural indicator over a 12-year period (2004–2015) and 2) performed a longitudinal analysis of change in WIMD quintile and urban/rural indicator over a 10-year follow-up for each individual in a cohort who were diagnosed with an SMI between 1st January 2004 and 31st December 2005. We calculated prevalence and incidence for the primary and secondary care cohorts separately due to the different extent of data coverage between cohorts. Prevalence, incidence, change in prevalence (prevalence gradient) by deprivation and urban/rural indicator, as well as change in incidence (incidence gradient) by deprivation and urban/rural indicator were estimated using generalised linear modelling with adjustments for potential confounders. We studied social drift by examining a) the difference between prevalence gradients and incidence gradients, and b) the difference between proportions of individuals moving towards more and less deprived areas in the longitudinal analysis.

Prevalence and incidence, expressed as a percentage of population and counts per 100,000 pyar respectively, were estimated using generalised estimating equations with unstructured within-subject correlation structure, using robust variance for parameter estimation (Agresti, 2007; Heck et al., 2012). Prevalence was modelled using binomial distribution with logit link function while incidence was modelled using Poisson distribution with log link function.

For modelling gradients of prevalence and incidence by deprivation, the independent variable was WIMD quintile as ranked categories, where WIMD quintile was coded as 1 (Q1, least deprived) to 5 (Q5, most deprived). With this coding scheme, odds ratios (ORs for prevalence) and incidence rate ratios (IRRs for incidence) represented ratios per unit quintile increase of level of deprivation. ORs or IRRs greater than one represent higher prevalence or incidence in more deprived compared to less deprived areas.

Equivalent modelling for estimating gradients of prevalence and incidence by urban/rural indicator was conducted. The independent variable was urban/rural indicator as ranked categories, where rural was coded as 1 and urban as 2. ORs or IRRs greater than unity indicates higher prevalence or incidence in urban compared to rural areas.

All prevalence and incidence were adjusted for sex (male as the reference category) and age group (15–24 years as reference category). Both WIMD quintile and urban/rural indicator were also jointly adjusted in all models. We included calendar year (2004 as reference category) as a within-subject factor in the prevalence model only. In the incidence model, WIMD quintile and urban/rural group were entered as within-subject covariate.

2.7. Longitudinal analysis

We further examined potential social drift at area level after an SMI diagnosis (as exposure) by analysing the difference in WIMD quintile (as outcome) for an individual as a proxy for social drift. We also examined whether these changes are associated with change in urban and rural settlement (as outcome). Thus, we calculated the difference in WIMD quintile and urban/rural indicator between start and end of the follow up period. We compared these differences over a 10-year period between individuals with SMIs (with an SMI diagnosis in either GPD or PEDW between 01/01/2004 and 31/12/2005) and the whole population of Wales (at a random date between 01/01/2004 and 31/12/2005). For individuals with SMIs, we extracted WIMD quintile and urban/rural indicator at the date of diagnosis and 10 years later (or date of death, whatever came first). For the Wales population, we extracted WIMD quintile and urban/rural indicator on a date randomly assigned to each individual (between 01/01/2004 and 31/12/2005) and 10 years later (or date of death, whatever came first). We then computed the change (earlier minus later) in WIMD quintile and change in urban/rural indicator (categories rural to urban, no change and urban to rural) for each individual.

To compare distributions of change in deprivation and rural/urban indicator between those with SMIs and the general population, we calculated standardised rate ratios (SRR), a method similar to the calculation of standardised mortality ratios using the indirect method with the whole cohort as the standard population. We divided the observed counts of change from the SMI sub-population by the expected counts of change from the general population. For deprivation, we calculated SRRs for 3 categories of change in WIMD quintile: individuals who moved to more deprived areas (change in WIMD quintile < 0), less deprived areas (change in WIMD quintile > 0) or areas with the same WIMD quintile (change in WIMD quintile $= 0$). For urbanicity, we calculated SRRs for 3 categories of change in urban/rural indicator (rural to urban, no change and urban to rural). SRRs were standardised by age bands (15–34, 35–54, 55–74 and ≥75 years), sex and whether an individual was alive or dead within the 10-year period (live and dead). The presence of downward social drift would be reflected by the SRR for individuals who moved to more deprived/urban areas >1 as well as greater than the SRR for individuals moved to less deprived/rural areas. Passive social drift – individuals with SMIs in areas with the same level of deprivation while the general population moved to less

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deprived areas – would also be reflected in the SRR i.e., by having larger values of the denominators (expected counts) for the less deprived compared with those for the more deprived category. In addition to the SRRs at 10 years of follow-up, we reported the SRRs at intervals of one year from the start of follow-up to identify any short-term drift and possible compensation (e.g., by health care) within 10 years. We also compared the characteristics for the individuals within deprivation/urbanicity change categories at the end of the follow-up (10 years).

In addition to the analysis of the change in WIMD quintile and urban/rural indicator within the 10-year follow-up period, we also tracked both WIMD quintile and urban/rural indicator for these individuals before the date of the incident diagnosis (index date). The tracking period varied for individuals depending on data availability from the WDS administrative register and was accounted for in pyar analyses. SRRs were calculated based on the WIMD quintile and urban/rural indicator at the first day with available WDS administrative data to the day before the index date (date of diagnosis for individuals with SMIs or 31/12/2005 for the general population).

3. Results

3.1. Study population

There were 5,019,602 individuals in total found in the WDS administrative register and we identified 2,898,382 eligible individuals (57.4%) who were 15 years or older and continuously registered in Wales between 01/01/2004 and 31/12/2015 (Fig. 1). For the primary care cohort, 2,114,777 individuals (73.0% of 2,898,382) supplied data to the GPD. 8709 (out of 2,114,777, overall 12-year-period prevalence: 0.4% out of 2,114,777, 95% CI: 0.4%–0.4%) of these individuals had at

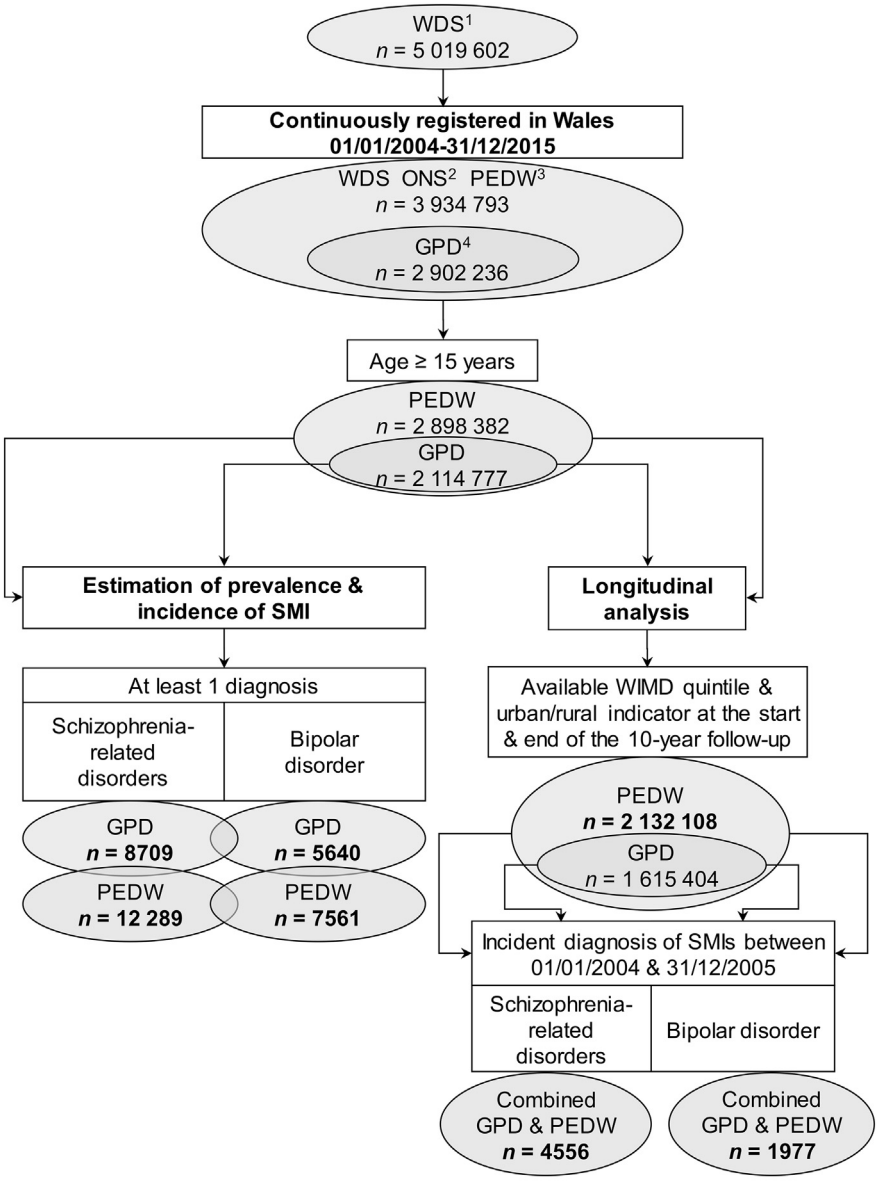

Fig. 1. Study flow diagram.

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least one diagnosis of schizophrenia-related disorders, while 5640 individuals (out of 2,114,777, overall 12-year-period prevalence: 0.3% out of 2,114,777, 95% CI: 0.3%–0.3%) had at least one diagnosis of bipolar disorder. For the secondary care cohort, 12,289 individuals (out of 2,898,382, overall 12-year-period prevalence: 0.4% out of 2,898,382, 95% CI: 0.4%–0.4%) had at least one diagnosis of schizophrenia-related disorders. 7561 individuals (out of 2,898,382, overall 12-year-period prevalence: 0.2% out of 2,898,382, 95% CI: 0.3%–0.3%) had at least one diagnosis of bipolar disorder. Table 1 shows demographics of the study cohort, distribution of WIMD quintiles and urban/rural indicator for the primary and secondary care cohorts at 01/01/2010.

Distribution of rural and urban areas by WIMD quintiles for all 1896 LSOAs documented in this study is tabulated in Supp. Table 2. The Cochran-Armitage trend test for linearity was statistically significant (Cochran-Armitage chi-squared = 63.8, $p < 0.001$), suggesting a strong linear association between more deprived and urban LSOAs (refer Supp. Figs. 1 and 2 for the geographical distribution of WIMD quintile and urban/rural indicator of LSOAs respectively).

3.2. Prevalence and incidence gradient of SMIs by deprivation and urban/rural indicator

For the primary care cohort, the mean annual prevalence of schizophrenia-related disorders and bipolar disorder was 0.3% (95% CI: 0.3%–0.3%) and 0.2% (95% CI: 0.2%–0.2%) respectively. We identified 8569 incident cases of schizophrenia-related disorder (incidence rate per 100,000 pyar = 45.8, 95% CI: 44.8–46.8) and 5563 incident cases of bipolar disorder (incidence rate per 100,000 pyar = 29.7, 95% CI: 28.9–30.5). For the secondary care cohort, the mean annual prevalence of schizophrenia-related disorders and bipolar disorder was 0.3% (95% CI: 0.3%–0.3%) and 0.2% (95% CI: 0.1%–0.2%) respectively. There were 11,884 incident cases of schizophrenia-related disorders (incidence rate per 100,000 pyar = 45.0, 95% CI: 44.1–45.8) and 7375 incident cases of bipolar disorder (incidence rate per 100,000 pyar = 27.9, 95% CI: 27.3–28.5). Table 2 summarises the 12-year-period prevalence and incidence sourced from primary and secondary care cohorts by WIMD quintile and urban/rural indicator. Geographical variations of prevalence and incidence of SMIs for primary and secondary care cohort are illustrated in Supp. Figs. 1 and 2 respectively.

Table 1
Demographics and characteristics of the study population at the mid-point of study period (01/01/2010).

		Primary care cohort		Secondary care cohort	
		Number†	%	Number†	%
Total		1,636,280	100.0	2,251,777	100.0
Sex	Male	804,110	49.1	1,109,151	49.3
	Female	832,170	50.9	1,142,626	50.7
Age (years)	15–24	302,251	18.5	403,399	17.9
	25–34	278,449	17.0	381,016	16.9
	35–44	315,028	19.3	434,753	19.3
	45–54	268,506	16.4	373,862	16.6
	55–64	240,396	14.7	333,755	14.8
	65–74	148,870	9.1	208,189	9.2
	≥75	82,780	5.1	116,803	5.2
Deprivation (WIMD quintile*)	Q5	315,717	19.3	429,727	19.1
	Q4	303,086	18.5	445,082	19.8
	Q3	327,628	20.0	452,776	20.1
	Q2	288,387	17.6	445,406	19.8
	Q1	345,187	21.1	450,718	20.0
Urbanicity	Urban	1,107,881	67.7	1,476,416	65.6
	Rural	472,124	28.9	747,293	33.2
Unknown LSOA		56,275	3.4	28,068	1.2

* Q5: most deprived.
† The numbers are the individual counts for the cohort as at 01/01/2010. They are different from the total counts from the whole study period between 01/01/2004 and 31/12/2015 as shown in the study flow chart (Fig. 1).

Higher prevalence and incidence in more deprived and urban areas (ORs or IRRs > 1, Fig. 2 and Supp. Tables 3 and 4) was evident. While ORs and IRRs were significantly larger than unity for schizophrenia-related disorders and bipolar disorder (all p-values < 0.05, Supp. Tables 3 and 4), schizophrenia-related disorders showed greater prevalence and incidence gradients than bipolar disorder. Overall, prevalence and incidence of schizophrenia-related disorders for individuals resident in the most deprived areas were approximately 2.5–3.1 times (by taking the ORs or IRRs to the fourth power) of those resident in the least deprived areas and these ratios were 1.4–1.9 for bipolar disorders. These patterns were similar for the prevalence and incidence gradients by urban/rural indicator. Prevalence and incidence of schizophrenia-related disorders and bipolar disorder at urban areas were approximately 1.2–1.3 and 1.1 times of those at rural areas respectively. All ORs and IRRs were higher for the secondary care cohort than for the primary care cohort, except that OR by urban/rural indicator for schizophrenia-related disorders was greater for the primary care cohort (Fig. 2E and F). This suggests a steeper gradient of prevalence and incidence by deprivation in the secondary compared with primary care cohort. Most importantly, we found similar effect sizes for prevalence and incidence for both cohorts.

3.3. Longitudinal analysis of social drift

We identified 2,132,108 eligible individuals for the longitudinal analysis (Fig. 1 and Supp. Table 5). Within the case ascertainment period between 01/01/2004 and 31/12/2005, there were 4556 individuals (0.2%, 95% CI: 0.2%–0.2%) who had an incident diagnosis of schizophrenia-related disorders and 1977 individuals (0.1%, 95% CI: 0.1%–0.1%) who had an incident diagnosis of bipolar disorder. The corresponding incidence over the two-year period for schizophrenia-related disorders and bipolar disorder was 53.7 (95% CI: 50.2–57.3) and 33.3 (95% CI: 29.3–37.8) per 100,000 pyar respectively. For schizophrenia-related disorders, 33.6% (out of 4556, 95% CI: 32.3%–35.0%) and 10.2% (95% CI: 9.4%–11.1%) moved to areas with different WIMD quintiles and urban/rural indicators respectively during the follow-up period. For bipolar disorder, we found 29.6% (out of 1977, 95% CI: 27.6%–31. 7%) and 9.7% (95% CI: 8.4%–11.1%) moved to area with different WIMD quintile and urban/rural indicator respectively during the follow-up period.

SRRs were significantly >1 (1.3–1.7, Fig. 3 and Supp. Table 6) for deprivation and urban/rural indicators depicting change while SRRs are significantly smaller than 1 (0.8–1.0, Fig. 3 and Supp. Table 6) for categories depicting no change in deprivation or urban/rural indicator. SRRs were similar between individuals who moved to more and less deprived areas, as well as between those who moved from rural to urban and urban to rural areas. SRRs for both sexes were similar whereas older individuals (except for those whose age ≥ 75 years) had SRRs more deviated from unity (Supp. Table 6). SRRs by year of follow-up were significantly >1 for groups with changes in deprivation and urban/rural indicators although they decreased gradually with time (Supp. Fig. 3). SRRs were still similar between individuals who moved to more or less deprived areas for both schizophrenia-related disorders and bipolar disorder. They were also similar for those who moved between rural and urban areas in either direction for bipolar disorder but not schizophrenia-related disorders. Interestingly, during the first four years after an incident diagnosis of schizophrenia-related disorders, SRRs for moving to urban areas were higher than that of rural areas. However, this difference decreased in subsequent years.

There were no significant differences in all measured characteristics between individuals moving towards more and less deprived areas, as well as, between urban to rural and rural to urban areas (Supp. Table 7). However, individuals in all the 'no change' groups for deprivation groups were older than those who moved to areas with different levels of deprivation. A significantly higher proportion of individuals who had schizophrenia-related disorders in the no change deprivation

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Table 2
Prevalence and incidence of schizophrenia-related disorders and bipolar disorder by WIMD quintile and urban/rural indicator.

				Mean annual prevalence 2004–2015				Incidence 2004–2015			
				Mean number of counts	Mean population	Period prevalence (%)	95% CI	Number of new cases	Person-years at risk	incidence (/100,000/year)	95% CI
Primary care	Schizophrenia-related disorders	Deprivation (WIMD quintile*)	Q5	1483	314,007	0.5	0.4–0.5	2804	3,747,882	74.8	72.1–77.6
			Q4	963	300,087	0.3	0.3–0.3	1849	3,585,788	51.6	49.3–54.0
			Q3	825	325,249	0.3	0.2–0.3	1656	3,884,584	42.6	40.6–44.7
			Q2	547	285,381	0.2	0.2–0.2	1105	3,406,872	32.4	30.6–34.4
			Q1	544	342,700	0.2	0.1–0.2	1155	4,088,931	28.2	26.7–29.9
		Urban/rural indicator	Urban	3448	1,096,770	0.3	0.3–0.3	6626	13,088,074	50.6	49.4–51.9
			Rural	916	470,657	0.2	0.2–0.2	1943	5,625,983	34.5	33.0–36.1
	Bipolar disorder	Deprivation (WIMD quintile*)	Q5	657	314,007	0.2	0.2–0.2	1397	3,751,890	37.2	35.3–39.2
			Q4	549	300,087	0.2	0.2–0.2	1135	3,588,070	31.6	29.8–33.5
			Q3	540	325,249	0.2	0.2–0.2	1089	3,886,234	28.0	26.4–29.7
			Q2	424	285,381	0.1	0.1–0.2	902	3,407,693	26.5	24.8–28.2
			Q1	494	342,700	0.1	0.1–0.2	1040	4,088,773	25.4	23.9–27.0
		Urbanicity	Urban	1950	1,096,770	0.2	0.2–0.2	4036	13,095,794	30.8	29.9–31.8
			Rural	715	470,657	0.2	0.1–0.2	1527	5,626,866	27.1	25.8–28.5
Secondary care	Schizophrenia-related disorders	Deprivation (WIMD quintile*)	Q5	1897	431,387	0.4	0.4–0.5	3793	5,116,985	74.1	71.8–76.5
			Q4	1405	444,996	0.3	0.3–0.3	2798	5,286,482	52.9	51.0–54.9
			Q3	1131	452,840	0.2	0.2–0.3	2319	5,385,454	43.1	41.3–44.8
			Q2	815	444,368	0.2	0.2–0.2	1707	5,284,736	32.3	30.8–33.9
			Q1	584	451,090	0.1	0.1–0.1	1267	5,364,821	23.6	22.3–24.9
		Urban/rural indicator	Urban	4358	1,475,838	0.3	0.3–0.3	8629	17,525,508	49.2	48.2–50.3
			Rural	1475	748,845	0.2	0.2–0.2	3255	8,912,970	36.5	35.3–37.8
	Bipolar disorder	Deprivation (WIMD quintile*)	Q5	826	431,387	0.2	0.2–0.2	1930	5,122,301	37.7	36.0–39.4
			Q4	742	444,996	0.2	0.2–0.2	1653	5,289,352	31.3	29.8–32.8
			Q3	627	452,840	0.1	0.1–0.1	1442	5,387,991	26.8	25.4–28.2
			Q2	543	444,368	0.1	0.1–0.1	1233	5,285,919	23.3	22.1–24.7
			Q1	477	451,090	0.1	0.1–0.1	1117	5,364,730	20.8	19.6–22.1
		Urbanicity	Urban	2235	1,475,838	0.2	0.1–0.2	5130	17,535,392	29.3	28.5–30.1
			Rural	982	748,845	0.1	0.1–0.1	2245	8,914,901	25.2	24.2–26.2

* Q5: most deprived.

group died within the 10-year follow-up period compared with the other two groups.

Before the date of first recorded diagnosis, we identified 1,084,912 (out of 2,132,108, 50.9%, 95% CI: 50.8%–51.0%) individuals with WIMD quintile and urban/rural indicator available at the onset of the WDS administrative records. The mean years of follow-back was 18.0 years (95% CI: 18.0–18.0). Totally 2208 (out of 1,084,912, 0.2%, 95% CI: 0.2%–0.2%) and 1035 (0.1%, 95% CI: 0.1%–0.1%) individuals were identified respectively with schizophrenia-related disorders and bipolar disorder respectively. For schizophrenia-related disorders, only 4.4% (out of 2208, 95% CI: 3.6%–5.4%) and 0.8% (95% CI: 0.5%–1.3%) moved to area with different WIMD quintile and urban/rural indicator respectively before the date of first record diagnosis. For bipolar disorder, we found only 4.6% (out of 1035, 95% CI: 3.5%–6.2%) and 1.6% (95% CI: 1.0%–2.7%) moved to area with different WIMD quintile and urban/rural indicator respectively before the date of first record diagnosis. The corresponding SRRs are summarised in Supp. Table 8 and Supp. Fig. 4. It shows individuals with schizophrenia-related disorders or bipolar disorder were less likely to move to areas with different WIMD quintiles and urban/rural indicators compared with the general population from the beginning of the available records to the date of first recorded diagnosis. Prior to diagnosis, although individuals with schizophrenia-related disorders were more likely to remain in areas with the same level of deprivation (SRR: 1.0, 95% CI: 1.0–1.1) and equal likely to move to more deprived areas (SRR: 0.9, 95% CI: 0.6–1.2) compared with the general population, they were less likely to move to less deprived areas (SRR: 0.6, 95% CI: 0.4–0.9, see Supp. Table 8 and Supp. Fig. 3A).

4. Discussion

This study revisited aspects of the social drift and causation hypotheses by examining associations between increased risks of SMIs (schizophrenia-related disorders and bipolar disorder) and area deprivation and urbanicity. We compared gradients of prevalence and incidence by deprivation and urban/rural indicator from 2004 to 2015, and analysed the proportion of individuals drifting longitudinally using the change in WIMD quintiles and urban/rural indicator within the cohort between 2006 and 2015. We found robust associations between increasing prevalence and incidence of SMIs in more deprived and urban areas. These gradients remained when the prevalence and incidence were adjusted for sex, age, time, as well as when level of deprivation and urbanicity were jointly adjusted. By comparing prevalence and incidence concurrently for the same population, we found similar prevalence and incidence gradients of SMIs by deprivation and urban/rural indicator, suggesting the absence of downward social drift indicated by people with SMI moving to more deprived neighbourhoods. Similar methods have been used to examine downward social drift for individuals with epilepsy using routinely collected data (Pickrell et al., 2015) but to our knowledge, this is the first time these have been used to study SMIs with data sourced from both primary and secondary care cohorts.

Our incidence rates of SMIs are comparable to others reported in the UK (Hardoon et al., 2013; Kirkbride et al., 2012) and other developed regions (Jongsma et al., 2019, 2018). Overall prevalences by disorder are also consistent with systematic reviews (Saha et al., 2005; Simeone et al., 2015). Our results for deprivation fall within the range of values for developed countries or regions reported by others. A systemic review on area level social deprivation and the risk of schizophrenia, psychosis and non-affective psychotic disorders revealed the adjusted relative risks of most to least deprived areas ranged from 1.0 to 4.8 (O'Donoghue et al., 2016). When the Townsend Score 2001 (Yousaf and Bonsall, 2017) was used for the UK population, it was reported that the adjusted (for gender and urbanicity) relative risks of the most to least deprived quintiles was 4.75 (95% CI: 3.98–5.67) for schizophrenia and 2.93 (95% CI: 2.64–3.25) for other psychosis (Hardoon et al., 2013). For bipolar disorder, the adjusted (for gender and urbanicity)

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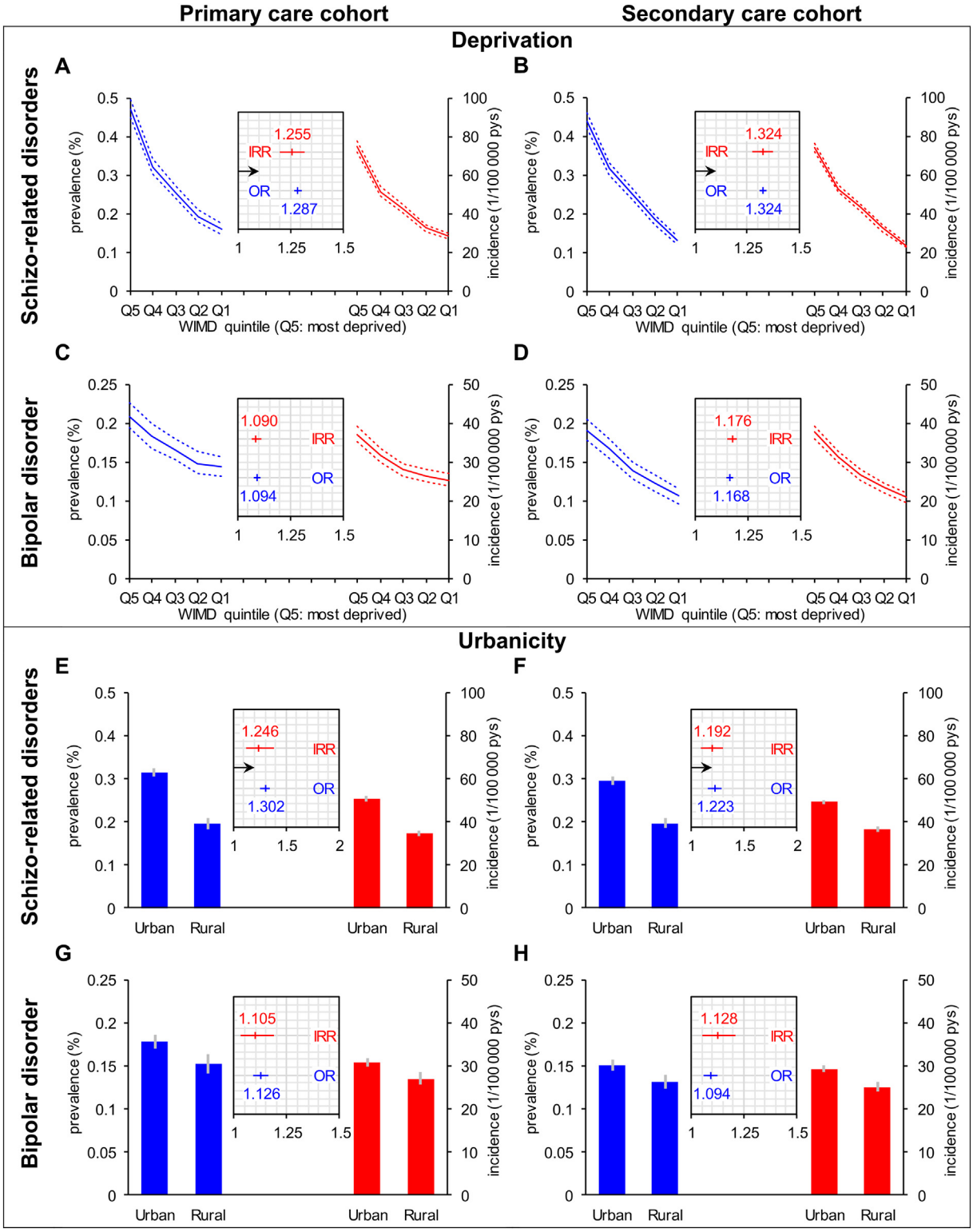

Fig. 2. Prevalence (light grey) and incidence (dark grey) of schizophrenia-related disorders (schizo-related disorders, A, B, E & F) and bipolar disorder (C, D, G & H) by WIMD quintile (A–D) and urban/rural indicator (E–H). Insets show ORs (blue) and IRRs (red) per unit WIMD quintile (A–D) or per urban/rural indicator (E–H) representing gradients of prevalence and incidence by deprivation and urban/rural indicator. Black arrows denote direction towards steeper gradients, i.e., greater differences of prevalence or incidence between most and least deprived or between urban and rural areas. Error bars and dash lines: 95% CIs. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

IRR comparing the most to least deprived Townsend quintile was found to be 1.84 (95% CI: 1.61–2.12) in a UK primary care cohort study (Hardoon et al., 2013).

For urbanicity, our relative risks of schizophrenia-related disorders comparing urban with rural areas are close to the values (1.40–1.97) reported in studies that examined urban residence at time of illness onset and psychoses using binary (rural vs. urban) measures (Kelly et al., 2010). Higher relative risks (>2) were reported in studies focused on urban birth or upbringing as well as using multi-level (≥3 levels) measures for urban/rural classification (Radua et al., 2018; Vassos

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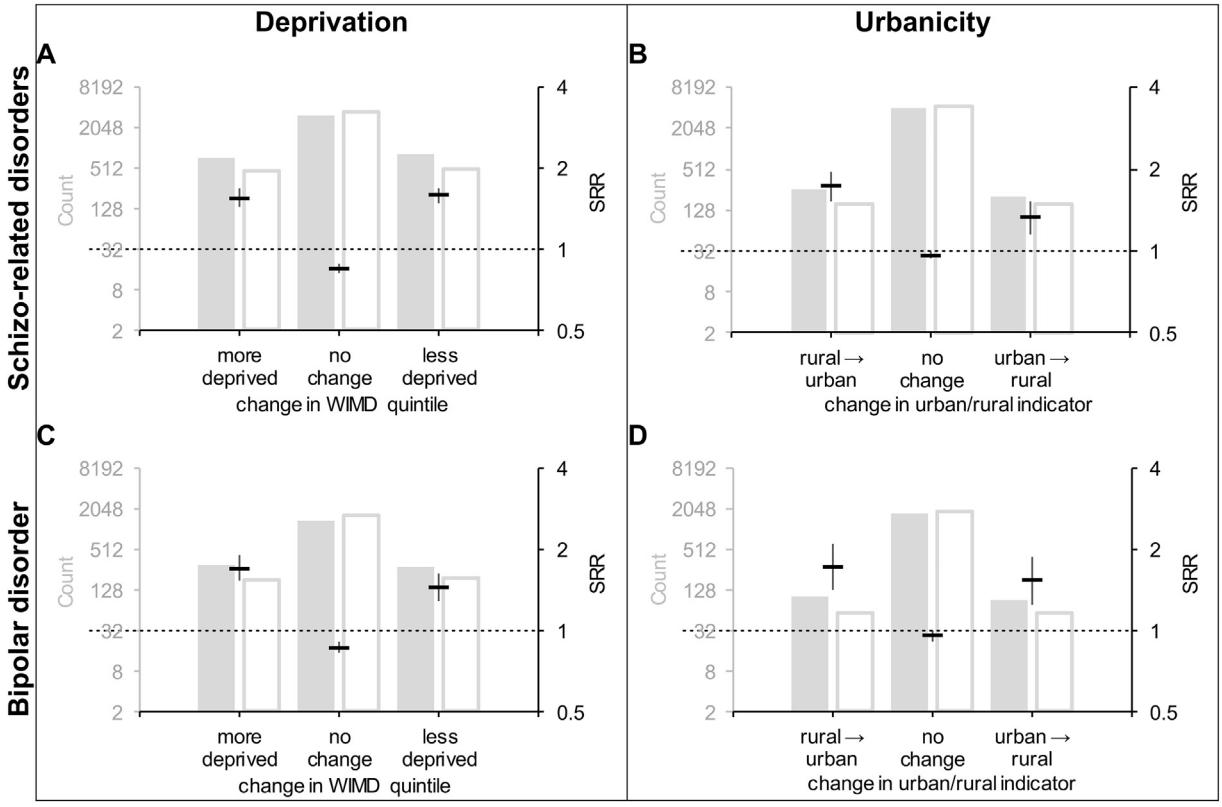

Fig. 3. Observed (filled bars), expected (open bars) count and the standardised rate ratio (SRR) of the change in WIMD quintile (A and C) and rural-urban residence (B and D) over 10-year follow-up period after incident diagnosis of schizophrenia-related disorders (schizo-related disorders, A and B) and bipolar disorder (C and D) between 2004 and 2005. For deprivation, data are stratified by 3 groups with individuals moved towards more deprived (change of WIMD quintile < 0), less deprived (change of WIMD quintile >0) areas or areas with the same WIMD quintile (no change in WIMD quintile). Rural → urban: change from rural to urban areas, urban → rural: change from urban to rural areas. Error bars: 95% CIs. Dash line: SRR = 1. Note that all data are plotted in log scale.

et al., 2012). For bipolar disorder, a significant adjusted (age sex, education level and cannabis use) linear OR trend of 1.18 (95% CI: 1.03–1.35) was reported in a Dutch study (Kaymaz et al., 2006) comparing cumulative incidence between areas with the most and least population density as a proxy for urbanicity. This is in consistence with the adjusted OR/IRR (~1.1) for bipolar disorder.

Effects of deprivation and urbanicity across studies are not directly comparable due to different settings, diagnostic criteria, outcome measures used and control for confounding variables among studies. Nevertheless, we found non-overlapping CIs of ORs and IRRs between schizophrenia-related disorders and bipolar disorder, suggesting difference in gradients of prevalence and incidence between these two conditions. Such difference in the strength of association between conditions to area deprivation and urbanicity was reported elsewhere (Gruebner et al., 2017; Heinz et al., 2013; Laursen et al., 2007; March et al., 2008).

Our data showed strong effects of deprivation and urbanicity when measures of deprivation and urbanicity were jointly controlled for although such associations were weaker compared to the effects when deprivation and urbanicity are treated as separate exposures (Hardoon et al., 2013). Indeed, we showed among all available LSOAs that more deprived LSOAs are predominantly urban areas. All these support the existence of factors such as poor social cohesion, availability of social services, crime and other environmental risks shared between more deprived and urban areas that may explain the elevated risks (Allardyce and Boydell, 2006; Sariaslan et al., 2015; Werner et al., 2007).

Results from the longitudinal analysis showed that individuals with SMIs tended to move to areas with different levels of deprivation and urban/rural indicators compared to the general population after SMIs diagnoses. Although calculating SRRs using indirect standardisation preclude statistical comparisons of SRRs between groups, our data revealed that individuals with SMI did not preferentially move towards more deprived or urban areas. We identify that up to four years after an incident diagnosis individuals with schizophrenia-related disorders might preferentially move to urban areas. While a potential explanation of this could be the compensating effect by treatments and social care for the gap closing between moving to urban areas and to rural areas over time, further research is warranted. In terms of demographic characteristics, individuals who moved to more and less deprived areas, as well as between urban to rural and rural to rural areas had similar sex, age and mortality distribution.

We found prior to SMI diagnosis, <5% of the individuals moved to areas with different level of deprivation and urbanisation compared to ~30% after diagnoses. Hence, social drift prior to illness onset seemed unlikely within the limits of data coverage on documenting individual movement or migration throughout lifespan. Our results generally do not support the downward social drift hypothesis. However, we cannot exclude the possibility that prior to illness onset, individuals with schizophrenia-related disorders might not move to less deprived areas similarly to the general population, reflecting a passive form of social drift or "failure to thrive".

While the social causation/drift debate is still ongoing, more evidence is emerging for the social causation hypothesis (Heinz et al., 2013; March et al., 2008). Research shows that higher incidence is found for individuals who are either born or brought up in more deprived and urban areas before illness onset (Eaton et al., 2000; Lewis et al., 1992; Marcelis et al., 1998; Pedersen and Mortensen, 2001; Sundquist et al., 2004; Werner et al., 2007). On the other hand, results from longitudinal examination of intra-generational social drift were not conclusive (Hudson, 2012, 2005). In an analysis of hospitalised individuals with mental illness including schizophrenia, it was found that only a slight downward social drift, measured by an index of SES for communities in the USA, was observed for individuals with schizophrenia during the

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course of 7-year hospitalisation (Hudson, 2005). Such drift was absent for individuals with other mental illnesses. Although the small magnitude of downward drift for schizophrenia could be replicated in a subsequent analysis for the same region (Hudson, 2012), the effects were confounded by the level of SES at the time of illness onset. On the contrary, a recent Canadian study examined the pattern of first migration after onset of schizophrenia and found evidence of geographical and social drift given the presence of migration from non-metropolitan to metropolitan areas as well as from less socially to more socially deprived areas (Ngui et al., 2013b).

Nevertheless, the presence of downward drift subsequent to the illness onset may not necessarily support the notion that the illness alone causes any subsequent downward drift. It has been proposed that social drift involves inter- and intra-generational processes and therefore familial and/or genetic influences cannot be ruled out (Plomin and Deary, 2015; Rodgers and Mann, 1993). A recent study using Genome-wide association analysis and mendelian randomization revealed that individuals with elevated genetic risk of schizophrenia tend to reside in urban or densely populated areas regardless of SES, suggesting that genetic susceptibility to schizophrenia might associate with individuals drifting to urban and more deprived areas (Colodro-Conde et al., 2018). While both genetic susceptibility and shared-environmental risk factors can pass onto children, parents can make choices to raise children preferably in more deprived/urban areas due to their own and/or children's genetically influenced traits (Paksarian et al., 2018). Nonetheless, recent studies found only modest association between polygenic risk scores for schizophrenia and urban birth (Paksarian et al., 2018; Solmi et al., 2019). The presence of inter-generational social drift seemed unsupported since controlling for both familial factors and polygenic risk scores for schizophrenia do not attenuate the association between deprivation/urbanicity at birth and the risk of having psychotic experiences later in life (Solmi et al., 2019).

Nonetheless, our findings on longitudinal drift after onset of SMIs are in consistence with others (Lix et al., 2007, 2006; Ngui et al., 2013a, 2013b) where individuals with SMIs have higher residential mobility albeit with similar migration between urban to rural and rural to urban regions. Our results are also in agreement with others showing that younger individuals with schizophrenia have higher residential mobility after illness onset in order to search for better access to mental health services (Ngui et al., 2013b). This might also explain the contrast of having lower than expected chances of changing deprivation or urbanicity category before but higher after illness onset. Interestingly, a recent study revealed residential mobility during childhood and adolescence are more likely to occur for individuals who later develop non-affective psychosis (Price et al., 2018). Although our data shows that individuals with SMIs are more likely to stay in areas with the same level of deprivation and urbanicity before illness onset compared with the general population, we could not rule out that these individuals moved more frequently than the unaffected individuals did.

4.1. Strength and limitations

This study evaluated the effect of area deprivation and urbanicity on the risks of SMIs drawn from primary care and secondary inpatient care settings in population-based linked datasets. One of the advantages of our study is that our data covered high proportion of the whole studied population (Wales) given the complete coverage of the hospital admission dataset and population level coverage of the GP dataset (>70%). We adopted previous approaches (Pickrell et al., 2015) to estimate and compare prevalence and incidence of SMIs concurrently alongside longitudinal observations of the change in deprivation, thus providing multiple evidence for the associations between SMIs and deprivation and urbanicity. We used previously validated diagnostic codes for SMIs to identify affected individuals (Economou et al., 2012; John et al., 2018; Lloyd et al., 2015). By linking demographic parameters with diagnoses, we were able to compare the effects of deprivation and urbanicity between conditions and between primary and secondary care cohorts.

One major limitation of the present study is that we cannot rule out social drift before an incident SMIs-related contact using routinely collected data. We therefore conducted the longitudinal analysis before the first record diagnosis to capture any social drift. Our results in general do not show downward social drift before the first record diagnosis. Thus, we are able to draw conclusions on the presence of social drift by comparing prevalence and incidence of SMIs provided that drift before the first record diagnosis was absent or minimal.

Level of deprivation cannot be easily summarised into a single measure because of its multifaceted nature (Welsh Government, 2017). Indeed, other alternative measures have been proposed to assess deprivation (Page et al., 2018). We used WIMD, an index that aggregates more than one domain of deprivation for small areas defined in the Census, to represent deprivation for all inhabitants in LSOAs (Welsh Government, 2017). Since WIMD and urban/rural indicator are area- rather than individual-level measures, we could misclassify individuals who are more (less) individually deprived but reside in less (more) deprived areas. As a result, using ecological data to estimate social drift may underestimate the amount of social drift at individual level (Goldberg and Morrison, 1963; Pickrell et al., 2015). In future studies, we could link data at individual level, e.g., income and employment to assess deprivation.

Similarly to deprivation, there is no standardised definition of urban and rural areas and various criteria such as number of inhabitants and population density have been used (Pedersen, 2006). We categorised rural and urban areas in accordance with a system used by government departments, which is based on the number of populations in settlement and sparsity types. Compared with studies using multilevel measure for the degree of urbanisation (Vassos et al., 2012), the effect upon the risks of SMIs in our study is smaller. This could be explained by the dichotomous measure used in our study since our rural category contains more heterogeneous settlement types (town and fringe, village, hamlet and isolated dwellings) in contrast to our urban category including only urban settlement types. Nonetheless, the urban/rural difference in the risks of SMIs were still robust regardless of the measure being used.

Due to data availability, we could not measure potential confounding on SMI-deprivation/urbanicity associations by individuals' marital status, education level and income. Nor could we extract data regarding individuals' genetic liability to SMIs and familial background. It has been documented that disadvantage in childhood, e.g., family history of psychosis, parental unemployment, low parental education level and income increased the risk of psychosis in urban areas (Heinz et al., 2013). More data linkage studies gathering these data are necessary.

Other limitations include the use of routinely collected clinical health care data for research purposes where information and selection bias may be present. Since we could not document individuals with SMIs who do not present to the healthcare services or who have symptoms but do not reach diagnostic thresholds, contact rates to services regarding SMIs might be underestimated and misclassification of SMIs cannot be ruled out. Although this is a common feature of all studies utilising routinely collected data, we used externally validated diagnostic codes of SMIs and allowing for cross mapping between Read codes and ICD-10 codes to maintain validity and consistency of SMI diagnoses for both primary and secondary care datasets. Since remission and relapse of SMIs cannot be easily defined in routinely collected data, we used the definition of annual prevalence as all individuals in contact with health services in or before the given year. Nonetheless, our patterns of incidence rates across age for schizophrenia-related disorders and bipolar disorder are consistent with those reported in a study using a UK-wide primary care database (Hardoon et al., 2013). Our data may also subject to selection bias, particularly the loss of follow-up and missing data. For instances, we only analysed individuals who continuously registered in Wales within the follow-up period (and

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before the first recorded diagnosis in the longitudinal analysis) with both WIMD and urban/rural indicator available during these periods. As a result, data from individuals who intermittently moving in/out Wales as well as homeless individuals were not analysed. In prevalence and incidence estimation, we were unable to adjust for time in the incidence models due to failure of convergence. For the same modelling convergence issue, we did not study deprivation by urbanicity interaction.

Although this study was based on the Wales population only, our results are generalisable to other developed regions. In contrast, the present results may not be generalisable to developing regions. It has been recently suggested that urban living does not increase the risks of psychoses in low- and middle-income countries (Chan et al., 2015; DeVylder et al., 2018) since wider income inequalities in developed countries could contribute to the elevated risks of psychoses. Socioeconomic inequality, as well as, social and familial isolation may be less salient in low- and middle-income countries (Burns et al., 2014; DeVylder et al., 2018; Johnson et al., 2015). However, caution is needed in the interpretation of these findings based on the validity of the mental health outcomes used, variations in the pace of urbanisation, individuals' interpretation of severe mental health, rural and urban living within their sociocultural and historical context, and finally patterns of exposure to risks factors within and between developed and low- and middle-income regions (Kirkbride et al., 2018). Future research should focus on the analysis of worldwide data to untangle how and how well these variations could explain the heterogeneity of the social inequality in SMIs.

4.2. Implications for policy and practice

This study provides an opportunity to identify area-related risk factors associated with SMIs and thus facilitates effective allocation of resources for policy, management of individuals with SMIs, further research and investment. Although recently there have been tools available to predict first episode of psychosis at community level (Kirkbride et al., 2013), strategies and priorities on where resources and interventions for psychotic disorders should be allocated, for example redistributed to areas and communities where SMIs are more prevalent, were not commonly discussed (O'Donoghue et al., 2016). In light of the present findings, we suggest, in line with previous studies, that urban areas and/or areas associated with higher level of deprivation should receive more targeted focus in terms of prevention and management. Accordingly, appropriate and timely interventions would be delivered to the most vulnerable communities and individuals (Kirkbride and Jones, 2014).

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Contributors

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

Role of the funding source

The funders had no role in study design, data, collection, data analysis, data interpretation, or writing of the manuscript.

Declaration of competing interest

None.

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None.

Data statement

Data analysed for this study were obtained under the IGRP approval from the SAIL databank (www.saildatabank.com). Raw data are not available for sharing but can be applied for access through SAIL. Relevant data are also available in the paper and its Supplementary files.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.schres.2020.03.044.

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