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5 **The epidemiology of first episode psychosis in early intervention in psychosis services: findings**  
6 **from the Social Epidemiology of Psychoses in East Anglia [SEPEA] study**

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1 **Abstract**

2 *Objective:* Few studies have characterized the epidemiology of first episode psychoses in rural or  
3 urban settings since the introduction of Early Intervention Psychosis services. To address this, we  
4 conducted a naturalistic cohort study in England, where such services are well-established.

5 *Method:* We identified all new first episode psychosis cases, 16-35 years old, presenting to Early  
6 Intervention Psychosis services in the East of England, during 2 million person-years follow-up.  
7 Presence of International Classification of Diseases, Tenth Revision, F10-33 psychotic disorder was  
8 confirmed using OPCRIT. We estimated incidence rate ratios [IRR] following multivariable Poisson  
9 regression, adjusting for age, sex, ethnicity, socioeconomic status, neighborhood-level deprivation  
10 and population density.

11 *Results:* Of 1,005 referrals, 687 participants (68.4%) fulfilled epidemiological and diagnostic criteria  
12 for first episode psychosis (34.0 new cases per 100,000 person-years; 95%CI: 31.5-36.6). Median  
13 age-at-referral was similar ( $p=0.27$ ) for men (22.5 years; interquartile range: 19.5-26.7) and women  
14 (23.4 years; 19.5-29.1); incidence rates were highest for men and women before 20 years old. Rates  
15 increased for ethnic minority groups (IRR: 1.4; 95%CI: 1.1-1.6), with lower socioeconomic status (IRR:  
16 1.3; 95%CI: 1.2-1.4) and in more urban (IRR: 1.4; 95%CI: 1.0-1.8) and deprived neighborhoods (IRR:  
17 2.1; 95%CI: 1.3-3.3) after adjustment for confounders.

18 *Conclusions:* Pronounced variation in psychosis incidence, peaking before 20 years old, exists in  
19 populations served by Early Intervention Psychosis services. Excess rates were restricted to urban  
20 and deprived communities, suggesting a threshold of socioenvironmental adversity may be  
21 necessary to increase incidence. This robust epidemiology can inform service development in various  
22 settings about likely population-level need.

## 1 **Background**

2 Early Intervention in psychosis now arguably represents the gold standard of care for people in their  
3 first episode of psychosis (1). This care model incorporates pharmacological and psychological  
4 interventions, family and social support, supported employment and physical healthcare checks,  
5 delivered by a multidisciplinary team for up to 5 years. The rationale for early intervention derives  
6 from observations that reducing the duration of untreated psychosis may improve clinical, functional  
7 and social outcomes in the short- to medium-term (2–8). This effect is most robust for schizophrenia  
8 spectrum disorders (2–4), with much less evidence in regard to the affective psychoses (9). Since  
9 Early Intervention Psychosis service provision is founded on evidence-based healthcare (10), this  
10 should include the provision of robust estimates of incidence of psychotic disorders to inform  
11 healthcare commissioners about local variation in service need. Unfortunately, psychosis  
12 epidemiology is predominantly informed by an older literature, conducted prior to the widespread  
13 introduction of these services (11; 12), almost exclusively based in urban settings (13). This research  
14 has revealed important heterogeneity in incidence by person (14–18) and place (19; 20), generating  
15 new directions for etiological research (21–23). However, national implementation efforts being  
16 developed in countries such as Denmark (24), Australia (25) and Canada (26), and currently  
17 undergoing revision in the UK (27), require accurate, relevant estimates about the epidemiology of  
18 psychotic disorders in populations served by Early Intervention Psychosis services. Such data will also  
19 be critical in countries such as the USA, where early intervention initiatives are gaining traction (28–  
20 31), but where little recent epidemiological data exists to inform service provision.

21

22 To address this gap, we established a naturalistic cohort study, known as the Social Epidemiology of  
23 Psychoses in East Anglia [SEPEA] study, in a diverse, mixed rural and urban setting in the East of  
24 England. We sought to precisely delineate the epidemiology of psychotic disorders since the  
25 introduction of Early Intervention Psychosis services. Consistent with earlier epidemiology (11; 13),  
26 we hypothesized that the incidence of psychotic disorders, including non-affective psychoses, would  
27 decline with age and greater socioeconomic status, and be higher amongst men, black and minority  
28 ethnic groups and in more deprived, urban neighborhoods. In line with previous findings (13; 20), we  
29 also hypothesized that affective psychoses would show less variation across these domains.

30

## 31 **Method**

32 *Design & setting*

1 We identified all people aged 16-35 years old who presented to six Early Intervention Psychosis  
2 services in a defined catchment area, over 3.5 years from 1 August 2009. These services were  
3 implemented on the basis of a national implementation guide (32) as the sole referral point for  
4 suspected psychosis for people up to 35 years old. Services accepted referrals from several sources,  
5 including self-referral, primary care, schools, universities, police and judicial services and other  
6 mental health services. The catchment area was concomitant with the boundaries of the  
7 Cambridgeshire and Peterborough NHS Foundation Trust and Norfolk and Suffolk NHS Foundation  
8 Trust (Supplemental Figure 1). In 2011, the catchment area had an estimated population of 2.4m  
9 people (4.5% of the English population) (33), of whom 24.0% were 16-35 years old. The catchment  
10 area contained 530 administrative neighborhoods with a median population of 3,992 people  
11 (interquartile range [IQR]: 2,426-5,935). The region is varied in terms of its sociodemographic  
12 characteristics and population density (Supplemental Figure 1).

13

#### 14 *Inclusion criteria*

15 We applied the following inclusion criteria to all participants referred to Early Intervention Psychosis  
16 services in our study:

17

- 18 1. Acceptance into care due to suspected psychosis
- 19 2. 16-35 years old (17-35 in “Cambridgeshire North” and “Cambridgeshire South” services)
- 20 3. Resident in the catchment area, including those of no fixed abode
- 21 4. Absence of moderate or severe learning disability, or an organic basis to disorder
- 22 5. No previous contact with health services for psychotic disorder

23

24 We collected baseline sociodemographic data on all participants who met these criteria (henceforth,  
25 the “*incepted sample*”), irrespective of later diagnosis. We followed incepted participants from  
26 referral until receipt of 3 years of standard care, or discharge from the service, if earlier.

27

#### 28 *Diagnostic outcomes*

29 We used a two-stage diagnostic procedure to confirm presence of an International Classification of  
30 Diseases, Tenth Revision, psychotic disorder (ICD-10 F10-33). In the first stage, we asked the clinician  
31 responsible for care to provide a clinical diagnosis six months after acceptance into care, and at  
32 service discharge (median follow-up: 2.3 years; IQR: 1.2-3.0). In the second stage, we obtained

1 research-based diagnoses at these time points using OPCRIT (34), a reliable diagnostic instrument  
2 (34; 35), which produces ICD-10 diagnoses according to 90 standardized symptom items (36). We  
3 trained a panel of clinicians (N=25) to rate OPCRIT items from available case note information.  
4 Excellent inter-rater reliability was achieved for any clinically-relevant psychotic disorder (F10-33:  
5 92% agreement; IQR:92-100) and specific diagnoses (85%; IQR=81-90), based on completion of 20  
6 case vignettes. Incepted participants were included in our *incidence sample* if they received an ICD-  
7 10 clinical diagnosis of psychotic disorder (F10-33) at either time point, confirmed by OPCRIT  
8 assessment.

9

10 We classified participants according to their final OPCRIT diagnosis, as follows: all clinically-relevant  
11 psychotic disorders (F10-33), non-affective psychoses (F20-29), schizophrenia (F20), other non-  
12 affective psychoses (F21-29), substance-induced psychoses (F10-19), affective psychoses (F30-33),  
13 bipolar disorder (F30-31) and psychotic depression (F32-33). Since OPCRIT does not distinguish  
14 substance-induced psychoses from other non-affective psychoses, we relied on a clinical diagnosis of  
15 substance-induced psychosis at 6 months after acceptance (n=8), discharge (n=2) or both (n=19) for  
16 people who received an OPCRIT diagnosis of “ICD-10 other non-organic psychoses” (i.e. F21-29 &  
17 F1X.5). Incepted participants without any OPCRIT-confirmed psychotic disorder were excluded from  
18 the *incidence sample* (Figure 1).

19

#### 20 *Exposure and confounder variables*

21 Sociodemographic information, including birthdate, sex, ethnicity, marital status, birth country,  
22 postcode, employment status, and main, current or last occupation and parental occupations was  
23 collected at first referral, using a standardized form. We classified age into seven categories (16-17,  
24 18-19, 20-22, 23-25, 26-28, 29-31, 32-35) to permit fine-grained estimation of incidence by age and  
25 sex. Marital status was classified as single, married/civil partnership or widowed/divorced/dissolved.  
26 Ethnicity was self-ascribed to one of 18 categories from the 2011 Census of Great Britain. Here, we  
27 created a dichotomous ethnicity variable (black and minority ethnic groups versus white British) to  
28 examine initial variation. We classified birth country as UK- or foreign-born. We classified participant  
29 socioeconomic status according to current, or if unemployed for less than two years, main or last  
30 occupation, according to a standard methodology (37; 38) as follows: professional & managerial  
31 occupations; intermediate occupations (including small employers & self-employed); routine &  
32 manual occupations, and; those not in employment (long-run unemployed, never worked, students,

1 otherwise unclassifiable). We coded parental socioeconomic status similarly, taking the higher  
2 occupation of both parents, where available.

3

4 We geocoded participants to their neighborhood at initial referral to obtain measures of their social  
5 environment. We defined multiple deprivation as the proportion of households in each  
6 neighborhood classified as deprived on at least two of four indicators from the 2011 census  
7 (employment, education, health, living environment; Supplemental Table 1). We categorized  
8 multiple deprivation on an equal-interval scale (7.7-18%; 18.1-28%; 28.1-38%; 38.1-47.1%). We  
9 estimated population density for each neighborhood based on the total 2011 census population  
10 divided by area, expressed as people per square mile. We categorized population density according  
11 to the proportion of neighborhoods: below the median (48-587 people per square mile); in the 50<sup>th</sup>-  
12 75<sup>th</sup> percentile (588-4653); 76<sup>th</sup>-95<sup>th</sup> percentile (4,654-11,099); 96<sup>th</sup>-100<sup>th</sup> percentile (11,100-21,970).

13

#### 14 *Population at-risk*

15 The usual resident population at-risk, including students, was estimated from the 2011 Census,  
16 conducted 1<sup>st</sup> April 2011, which coincided with the mid-point of case ascertainment. We multiplied  
17 population estimates by 3.5 to obtain person-years at-risk over the study period, and stratified the  
18 data by age group (16-24,25-29,30-35 years), sex, ethnicity and participant socioeconomic status.

19

#### 20 *Statistical analyses*

21 We first reported descriptive epidemiological characteristics of the sample, including crude  
22 incidence rates for each psychotic outcome and 95% confidence intervals [95%CI]. We used two-  
23 tailed Chi<sup>2</sup> [ $\chi^2$ ], Mann-Whitney U and Kruskal-Wallis  $\chi^2$  tests to analyze differences in  
24 sociodemographic characteristics between cases and the population at-risk. For all psychotic  
25 disorders (F10-33), non-affective psychoses (F20-29) and affective psychoses (F30-33), we then fitted  
26 multivariable Poisson regression models to examine potential differences in incidence by age group  
27 (three-category), sex, ethnicity, participant socioeconomic status and Early Intervention Psychosis  
28 service setting, after mutual adjustment for all remaining variables. Forward-fitting modelling was  
29 used to determine the most parsimonious model, assessed via likelihood ratio test [LRT- $\chi^2$ ]. Where  
30 variation in incidence between services was detected, we then examined whether this was  
31 attributable to multiple deprivation or population density, using multilevel Poisson models, fitted  
32 with neighborhood-level random intercepts. In these analyses, we excluded participants of no fixed

1 abode (n=28). Incidence rates were presented per 100,000 person-years. Analyses were conducted  
2 using Stata (version 13).

3

#### 4 *Ethics*

5 Ethical approval was granted by Cambridgeshire III Local Research Ethics Committee (09/H0309/39).

6

### 7 **Results**

#### 8 *Case ascertainment and crude rates, by contact type*

9 Over one thousand people (n=1,005) were initially referred to six Early Intervention Psychosis  
10 services with a suspected first episode of psychosis during 2.02m person-years at-risk, of whom 899  
11 (89.5%) were accepted into care (Figure 1). This corresponded to crude referral and acceptance rates  
12 of 49.7 (95%CI: 46.7-52.9) and 44.5 (95%CI: 41.7-47.5) per 100,000 person-years, respectively  
13 (Supplemental Figure 2). One-hundred-and-one participants (10.0%) did not meet epidemiological  
14 criteria (Figure 1), leaving 798 people in our incepted sample, of whom 687 (86.1%) were diagnosed  
15 with an OPCRIT-confirmed ICD-10 psychotic disorder (F10-33). This corresponded to a crude  
16 incidence of 34.0 new cases per 100,000 person-years (95%CI: 31. 5-36. 6). Most incidence cases  
17 received a diagnosis of schizophrenia (F20; 50.9%) or other non-affective psychotic disorder (F21-29;  
18 32.5%), giving a crude incidence of 28.3 per 100,000 person-years (95%CI: 26.1-30.8) for non-  
19 affective psychotic disorders. The incidence of affective psychotic disorders (F30-33) was lower (4.2  
20 per 100,000 person-years; 95%CI: 3.4-5.1); the majority of these (77.4%) were bipolar affective  
21 psychoses (Figure 1). The incidence of probable substance-induced psychosis was low (1.5 per  
22 100,000 PYAR; 95%CI: 1.0-2.1).

23

#### 24 *Baseline characteristics and descriptive epidemiology*

25 In our incidence sample, median age-at-referral did not differ between men (22.5; IQR: 19.5-26.7)  
26 and women (23.4; IQR: 19.5-29.1; Mann-Whitney U-test: Z=1.1; p=0.27). We observed weak  
27 evidence (Kruskal-Wallis  $\chi^2=5.0$  on 2 degrees of freedom [df]; p=0.08) of differences in median age-  
28 at-referral between affective (23.6 years; IQR: 20.0-27.3), non-affective (22.6 years; IQR: 19.6-27.4)  
29 and probable substance-induced psychoses (21.0 years; IQR: 17.7-24.7). Two-thirds of cases (n=459;  
30 66.8%) were men (Table 1), although there was also weak evidence that this pattern differed  
31 between non-affective (67.7% men), affective (57.1% men) and probable substance-induced



1 psychoses (76.7% men) ( $\chi^2$ -test on 2df=5.1; p=0.08). Compared with the population at-risk, cases  
2 were more likely to be men, younger, from an ethnic minority background, single, unemployed, of  
3 lower socioeconomic status and from more deprived and densely populated neighborhoods (all  
4 p<0.01), reflecting corresponding variation in crude incidence (Table 1). Further examination of  
5 incidence by age revealed classic effect modification by sex (Figure 2A; LRT- $\chi^2$  on 6df=21.1: p<0.01),  
6 such that rates were higher for men than women until 29-31 years old, with a decline in incidence  
7 for both sexes from initial peak rates at 18-19 years in men and 16-17 years old in women. These  
8 patterns were similar for non-affective psychoses (Figure 2B; LRT- $\chi^2$  on 6df=15.4; p=0.02), but  
9 differed for affective psychoses (LRT- $\chi^2$  on 6df=9.5 p=0.15), which were similar for men and women  
10 at all ages (Figure 2C).

11

#### 12 *Variation in the incidence of all clinically-relevant psychotic disorders*

13 Incidence varied by age, sex, ethnicity, socioeconomic status and setting, following mutual  
14 adjustment for each other (Table 2, Adjustment 1). For example, rates were 1.47 times higher in  
15 ethnic minority participants (95%CI: 1.23-1.76) compared with the white British group, increased  
16 with lower socioeconomic status and varied between Early Intervention Psychosis services. Further  
17 multilevel modelling suggested that variation in incidence across the region was associated with  
18 both neighborhood-level population density and multiple deprivation, after adjustment for all other  
19 covariates (Table 2, Model 2). We observed evidence that this relationship was nonlinear, with  
20 excess rates restricted to the most densely populated (IRR 1.37; 95%CI: 1.02-1.84) and deprived  
21 neighborhoods (IRR: 2.11; 95%CI 1.34-3.32) in the study.

22

#### 23 *Variation in the incidence of non-affective and affective psychotic disorders*

24 Incidence of non-affective psychoses followed similar patterns to those described above with  
25 respect to individual-level risk factors (Supplemental Table 2). However, only multiple deprivation  
26 (IRR in most versus least deprived neighborhoods: 2.74; 95%CI: 1.71-4.39) remained consistently  
27 associated with neighborhood-level incidence (Supplemental Table 3). There was some evidence  
28 that patterns of risk differed for the affective psychoses, despite a smaller sample (N=84). Rates  
29 were more similar for men and women (IRR for men: 1.27; 95%CI: 0.82, 1.96) and less strongly  
30 associated with socioeconomic status, after adjustment for other confounders (Supplemental Table  
31 2). While affective psychoses rates varied between services, this was not associated with either  
32 neighborhood-level variable (Supplemental Table 3).

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## Discussion

In this, the largest epidemiological study of first episode psychosis conducted since Early Intervention Psychosis services were introduced in England, we have precisely delineated heterogeneity in incidence in a mixed rural and urban population. Our findings should provide timely evidence for mental healthcare policymakers in various settings about the current burden of psychotic disorders in young people. In particular, our findings (i) reveal substantial incidence rates of all clinically-relevant psychotic disorders in young people; (ii) demonstrate that median age-at-first-referral is similar for young men and women before 35 years old, with 50% of cases presenting by 23 years old, and; (iii) we extend previous knowledge to show that incidence in more rural populations in England, which have received less research, varies by classic individual- and neighborhood-level social and economic determinants of health, particularly for non-affective disorders; affective psychoses showed less variation overall.

### *Methodological considerations*

Our study was based on referrals to Early Intervention Psychosis services from multiple sources, including other mental health services within the National Health Service, and self-referrals. Our findings should therefore be interpreted based on administrative or first contact incidence. We were unable to perform a leakage study to detect potentially missed cases, which could have led us to under-estimate the true incidence in the catchment area. Nonetheless, Early Intervention Psychosis services are the sole referral point for young people with suspected psychotic symptoms, and actively engaged in outreach and promotion in the East of England. In England, there is very little private mental healthcare for psychosis, reducing risk of leakage. The epidemiological characteristics of our sample were consistent with other major first episode psychosis studies (39; 40), implying that our study design did not introduce substantial under-ascertainment overall, or differentially by sociodemographic subgroups. Although the excess incidence in black and minority ethnic groups was smaller than normally reported (13), there is no evidence that such groups are less likely to be referred to Early Intervention Psychosis services, despite differing care pathways (41–43). Furthermore, a separate paper from our study (*in submission*) demonstrates that rates for specific ethnic groups are in line with excesses more typically observed (13). Our modest IRRs for this group, overall, are probably driven by the large proportion of non-British white migrants in this population (52.2%), whose overall psychosis risk is similar to the white British population (40). We did not measure the duration of untreated psychosis in our sample, but this could only have affected the

1 estimation of incidence rates if it had changed rapidly over the short follow-up period of our study  
2 (3.5 years); this is unlikely, particularly given services were well-established in our catchment area.

3

4 We cannot generalize our findings to people younger than 16 years old. This remains an important,  
5 underexplored epidemiological research issue, given that early intervention and more general youth  
6 mental health services, often accept cases from 14 years old or younger; limited evidence suggests  
7 incidence is very rare (44; 45). Our catchment area was considerably more rural than those  
8 previously studied in England. Generalizability to other settings will depend on the exact  
9 composition of their catchment areas, and we did not have data on very rural areas (i.e. less than 48  
10 inhabitants per square mile). Nonetheless, variation in population density across our catchment area  
11 included the values for median population densities of 37 of 50 U.S. states (46).

12

13 We obtained denominator data from the 2011 Census. While the true population at-risk is dynamic,  
14 any demographic changes in East Anglia over the 3.5-year period of our study would have been  
15 small, and unlikely to have substantially biased our results given the absolute rarity of psychotic  
16 disorders. The 2011 Census methodology minimized and adjusted estimates for non-response prior  
17 to publication (47). We could not adjust or inspect variation by factors including family history of  
18 psychiatric disorders or substance use, which are not routinely collected for the denominator.

19

20 We used a two-stage diagnostic procedure to apply research-based criteria for psychotic disorder to  
21 our initial sample. OPCRIT diagnoses were assessed by trained clinicians, with good inter-rater  
22 reliability based on a small sample of twenty real-world case vignettes. The proportion of people  
23 who received a clinical diagnosis in the inception sample, who also met OPCRIT-criteria for psychotic  
24 disorder was high (positive predictive value = 687/722 i.e. 95.2%), demonstrating good concurrent  
25 validity in line with previous research (36). We presented results for all clinically-relevant disorders  
26 given current interest in this broad psychosis phenotype. Rates of affective psychotic disorders were  
27 lower than typically reported in adults (i.e. up to 64 years old) in England (13), though were  
28 consistent with observations elsewhere in Europe (48). Given that the incidence of such disorders  
29 show less decline with age, and may even peak after 45 years old (13; 49), lower rates reported in  
30 our young sample may be consistent with the underlying epidemiology.

31

32 *Meaning of findings: implications for mental health services provision*

1 Our findings highlight substantial demand for Early Intervention Psychosis services in a large, diverse  
2 rural and urban population in the East of England. Referral rates to such services approached 50  
3 people per 100,000 person-years, with services subsequently accepting nearly nine out of ten  
4 referrals onto caseloads. We estimated that the true incidence of psychotic disorder seen through  
5 these services was closer to 34 new cases per 100,000 person-years. This difference highlights  
6 important challenges faced by policymakers, commissioners and practitioners in developing,  
7 deploying and delivering effective early intervention services.

8

9 Previous influential commissioning guidelines have used uniform estimates of narrowly-defined  
10 schizophrenia incidence – closer to 15 per 100,000 person-years – based on an older epidemiology,  
11 as a basis for caseload and workforce calculations (32). However, in practice, Early Intervention  
12 Psychosis services may be mandated to intervene on a broader spectrum of psychoses, including  
13 other non-affective and affective psychotic disorders, as well as other mental health disorders where  
14 psychotic-like symptoms can present. In a US context, where Early Intervention Psychosis services  
15 are currently gaining momentum (29; 30), service provision is primarily predicated on the treatment  
16 of non-affective psychoses. If, however, earlier intervention in the critical period for psychosis  
17 generates greater diagnostic uncertainty (50), this will inevitably result in a higher proportion of  
18 undifferentiated psychopathologies at first referral. Our data highlight some of the pragmatic  
19 realities in implementing Early Intervention Psychosis services, which will accept a proportion of  
20 people who do not meet full research-based criteria for non-affective psychotic disorder (29.1% of  
21 the incepted sample), in addition to 10.5% of people referred to but not accepted by services. Such  
22 groups would still require a degree of psychiatric triage and signposting, for which services need to  
23 be additionally resourced to effectively implement the fidelity criteria upon which they are  
24 predicated (5). We have provided robust estimates of referral, acceptance, inception and incidence  
25 rates in a diverse population, which can be used as part of a wider suite of evidence to inform  
26 service provision across the full spectrum of psychoses (51), not limited to schizophrenia.

27

### 28 *Meaning of the findings epidemiological implications*

29 Our findings extend previous epidemiological research to show that incidence of psychotic disorders  
30 varies by sociodemographic and environmental characteristics in more rural settings than typically  
31 studied (11; 13). As expected, incidence rates were lower, overall, than reported in more urban  
32 populations in England. For example, recent rates for young people presenting to Early Intervention  
33 Psychosis services in highly-urban Southeast London (29,267 people per square mile) were 54.6 per

1 100,000 person-years (95%CI: 49.5-60.2) (52), higher than reported here. Nonetheless, crude rates  
2 of psychotic disorders in our most urban and deprived communities overlapped with such estimates,  
3 which persisted after adjustment for age, sex, ethnicity and individual-level socioeconomic status.  
4 The nonlinear associations we observed between population density, deprivation and psychosis  
5 incidence in our mixed rural and urban population imply that a threshold of exposure to  
6 environmental factors may be necessary to increase risk. These findings accord with limited previous  
7 research on this issue (53). However, it remains unclear whether associations between  
8 environmental characteristics and psychosis risk reflect genuine etiological variance, or arise from  
9 selection factors, including familial aggregation of shared genetic or environmental experiences,  
10 which perpetuate downward social drift (22). These processes may not be mutually exclusive, but  
11 lead to the intergenerational accumulation of deleterious risk factors which subsequently affect a  
12 number of adverse health and social outcomes, including schizophrenia and other psychoses.  
13 Further longitudinal studies are required to disentangle the potential role of social causation from  
14 drift or selection. Although we could not establish causation directly, our results demonstrate that  
15 our most more deprived and urban communities shoulder a disproportionate burden of psychosis  
16 morbidity at the population-level. This should be used to inform the provision of effective early  
17 intervention services for psychosis.

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**Table 1: Socio-demographic characteristics of people with first episode psychosis and the population at-risk**

Variable <sup>1</sup>	Cases		Person-years		Crude incidence <sup>2</sup>	
	N	%	N	%	Rate	(95%CI)
<b>Total</b>	687	(100.0)	2,021,663	(100.0)	34.0	(31.5, 36.6)
<b>Age group</b>						
16-17	78	(11.4)	170,125	(8.4)	45.8	(36.7, 57.2)
18-19	115	(16.7)	201,184	(10.0)	57.2	(47.6, 68.6)
20-22	161	(23.4)	311,294	(15.4)	51.7	(44.3, 60.4)
23-25	118	(17.2)	320,537	(15.9)	36.8	(30.7, 44.1)
26-28	84	(12.2)	311,749	(15.4)	26.9	(21.8, 33.4)
29-31	76	(11.1)	318,756	(15.8)	23.8	(19.0, 29.9)
32-35	55	(8.0)	388,021	(19.2)	14.2	(10.9, 18.5)
$\chi^2$ on 6df: 127.4; p-value:	<i>p</i> <0.01					
<b>Sex</b>						
Women	228	(33.2)	989,434	(48.9)	23.0	(20.2, 26.2)
Men	459	(66.8)	1,032,229	(51.1)	44.5	(40.6, 48.7)
$\chi^2$ on 1df: 68.2; p-value:	<i>p</i> <0.01					
<b>Ethnicity</b>						
White, British	514	(74.8)	1,623,031	(80.3)	31.7	(29.0, 34.5)
Black & minority ethnic groups	173	(25.2)	398,632	(19.7)	43.4	(37.4, 50.4)
$\chi^2$ on 1df: 13.0; p-value:	<i>p</i> <0.01					
<b>Country of birth</b>						
UK-born	578	(84.1)	1,656,512	(81.9)	34.9	(32.2, 37.9)
Foreign-born	109	(15.9)	365,152	(18.1)	29.9	(24.7, 36.0)
$\chi^2$ on 1df: 2.2; p-value:	<i>p</i> =0.14					
<b>Employment status</b>						
Employed	154	(22.4)	1,292,656	(63.9)	11.9	(10.2, 14.0)
Student	119	(17.3)	419,633	(20.8)	28.4	(23.7, 33.9)
Looking after home or family	29	(4.2)	104,727	(5.2)	27.7	(19.2, 39.8)
Long term sick or disabled	164	(23.9)	89,332	(4.4)	183.6	(157.5, 213.9)
Unemployed	218	(31.7)	114,309	(5.7)	190.7	(167.0, 217.8)
Retired	-	-	1,007	(0.05)	-	
Missing	3	(0.4)	-	-	-	
$\chi^2$ on 4df: 1600; p-value: <sup>3</sup>	<i>p</i> <0.01					
<b>Participant socioeconomic status</b>						
Professional & managerial	71	(10.3)	493,675	(24.4)	14.4	(11.4, 18.1)
Intermediate occupation	80	(11.6)	333,806	(16.5)	24.0	(19.2, 29.8)
Routine & manual	272	(39.6)	668,782	(33.1)	40.7	(36.1, 45.8)
Long-term unemployed, students & unclassifiable	264	(38.4)	525,400	(26.0)	50.2	(44.5, 56.7)
$\chi^2$ on 3df: 115.3; p-value:	<i>p</i> <0.01					
<b>Parental socioeconomic status<sup>4</sup></b>						
Professional & managerial	204	(29.7)	-	-	-	
Intermediate occupation	155	(22.6)	-	-	-	
Routine & manual	189	(27.5)	-	-	-	
Long-term unemployed, students & unclassifiable	139	(20.2)	-	-	-	

<b>Marital status<sup>5</sup></b>						
Single	611	(88.9)	109,677	(61.0)	-	
Married or civil partnership	61	(8.9)	54,131	(30.1)	-	
Widowed, divorced or dissolved	15	(2.2)	15,954	(8.9)	-	
$\chi^2$ on 2df: 224.7; p-value:	<i>p&lt;0.01</i>					
<b>Early Intervention Psychosis service</b>						
North Cambridgeshire	91	(13.2)	309,302	(15.3)	29.4	(24.0, 36.1)
South Cambridgeshire	161	(23.4)	443,730	(21.9)	36.3	(31.1, 42.3)
West Norfolk	37	(5.4)	110,989	(5.5)	33.3	(24.2, 46.0)
Central Norfolk	147	(21.4)	498,222	(24.6)	29.5	(25.1, 34.7)
Great Yarmouth & Waveney	80	(11.6)	160,825	(8.0)	49.7	(40.0, 61.9)
Suffolk	171	(24.9)	498,596	(24.7)	34.3	(29.5, 39.3)
$\chi^2$ on 5df: 17.3; p-value:	<i>p&lt;0.01</i>					
<b>Neighborhood population density (People per square mile)<sup>6</sup></b>						
48-587 (Below median)	135	(20.5)	543,010	(26.9)	24.9	(21.0, 29.4)
588-4,653 (50-75 <sup>th</sup> percentile)	181	(27.5)	549,365	(27.2)	32.9	(28.5, 38.1)
4,654-11,099 (76-95 <sup>th</sup> percentile)	218	(33.1)	634,887	(31.4)	34.3	(30.1, 39.2)
11,100-21,970 (96-100 <sup>th</sup> percentile)	125	(19.0)	294,533	(14.6)	42.4	(35.6, 50.6)
$\chi^2$ on 3df: 19.3; p-value:	<i>p&lt;0.01</i>					
<b>Neighborhood multiple deprivation (% households)<sup>6</sup></b>						
7.8-18.0%	161	(24.4)	623,332	(30.8)	25.8	(22.1, 30.1)
18.1-28.0%	288	(43.7)	862,013	(42.6)	33.4	(29.8, 37.5)
28.1-38.0%	159	(24.1)	456,966	(22.6)	34.8	(29.8, 40.6)
38.1-47.1%	51	(7.7)	79,352	(3.9)	64.3	(48.8, 84.6)
$\chi^2$ on 3df: 34.0; p-value:	<i>p&lt;0.01</i>					

<sup>1</sup> $\chi^2$ -test reports evidence that the distribution of people with first episode psychosis differs from population-at-risk for a given variable, based on appropriate Pearson  $\chi^2$  statistics and degrees of freedom (*df*)

<sup>2</sup>Per 100,000 person-years at risk

<sup>3</sup>Test based on all categories except “retired” & “missing” where there was insufficient data

<sup>4</sup>Not available for denominator

<sup>5</sup>Population data only was only available by marital status and age (16-35 years) for the “Household Reference Person”, i.e. head of household, not all individuals in population at-risk. Incidence rates not estimated

<sup>6</sup>N=28 cases of no fixed abode were excluded because they could not be geocoded to a neighborhood

**Table 2: Multivariable Poisson regression of all clinically-relevant psychosis**

Variable	Unadjusted		Adjustment 1		Adjustment 2	
	IRR	95% CI	IRR	95% CI	IRR	95% CI
<b>Sex (men vs women)</b>	1.93	(1.65, 2.26) <sup>†</sup>	1.90	(1.62, 2.22) <sup>†</sup>	1.87	(1.59, 2.20) <sup>†</sup>
<b>Age group</b>						
16-24	Ref		Ref		Ref	
25-29	0.57	(0.47, 0.68) <sup>†</sup>	0.66	(0.54, 0.80) <sup>†</sup>	0.65	(0.53, 0.80) <sup>†</sup>
30-35	0.33	(0.27, 0.41) <sup>†</sup>	0.41	(0.32, 0.52) <sup>†</sup>	0.42	(0.33, 0.53) <sup>†</sup>
<b>Ethnicity</b>						
White British	Ref		Ref		Ref	
Black & minority ethnic groups	1.37	(1.15, 1.63) <sup>†</sup>	1.47	(1.23, 1.76) <sup>†</sup>	1.35	(1.12, 1.63) <sup>†</sup>
<b>Participant socioeconomic status</b>						
Professional & managerial	Ref		Ref		Ref	
Intermediate occupations	1.67	(1.21, 2.29) <sup>†</sup>	1.58	(1.14, 2.17) <sup>†</sup>	1.59	(1.15, 2.19) <sup>†</sup>
Routine & manual occupations	2.83	(2.18, 3.67) <sup>†</sup>	2.28	(1.74, 2.97) <sup>†</sup>	2.09	(1.60, 2.74) <sup>†</sup>
Long-term unemployed, students & unclassifiable	3.49	(2.69, 4.54) <sup>†</sup>	2.26	(1.70, 2.99) <sup>†</sup>	2.19	(1.65, 2.92) <sup>†</sup>
<b>Early Intervention Psychosis service</b>						
North Cambridgeshire	Ref		Ref		Ref	
South Cambridgeshire	1.23	(0.95, 1.59)	1.24	(0.96, 1.61)	1.54	(1.12, 2.12) <sup>†</sup>
West Norfolk	1.13	(0.77, 1.66)	1.14	(0.78, 1.67)	1.21	(0.79, 1.84)
Central Norfolk	1.00	(0.77, 1.30)	1.02	(0.78, 1.33)	1.11	(0.83, 1.50)
Great Yarmouth & Waveney	1.69	(1.25, 2.28) <sup>†</sup>	1.69	(1.24, 2.29) <sup>†</sup>	1.47	(1.05, 2.08) <sup>†</sup>
Suffolk	1.17	(0.90, 1.50)	1.21	(0.94, 1.56)	1.34	(1.00, 1.80) <sup>†</sup>
<b>Neighborhood population density (People per square mile)<sup>‡</sup></b>						
48-587 (Below median)	Ref		-		Ref	
588-4,653 (50-75 <sup>th</sup> percentile)	1.32	(1.04, 1.67) <sup>†</sup>	-		1.25	(0.98, 1.59)
4,654-11,099 (76-95 <sup>th</sup> percentile)	1.36	(1.08, 1.71) <sup>†</sup>	-		1.17	(0.91, 1.49)
11,100-21,970 (96-100 <sup>th</sup> percentile)	1.71	(1.30, 2.26) <sup>†</sup>	-		1.37	(1.02, 1.84) <sup>†</sup>
<b>Neighborhood multiple deprivation (% households)<sup>‡</sup></b>						
7.8-18.0%	Ref		-		Ref	
18.1-28.0%	1.27	(1.04, 1.56) <sup>†</sup>	-		1.36	(1.08, 1.72) <sup>†</sup>
28.1-38.0%	1.36	(1.07, 1.72) <sup>†</sup>	-		1.37	(1.02, 1.83) <sup>†</sup>
38.1-47.1%	2.46	(1.71, 3.54) <sup>†</sup>	-		2.11	(1.34, 3.32) <sup>†</sup>

IRR: incidence rate ratio

<sup>†</sup>p<0.05

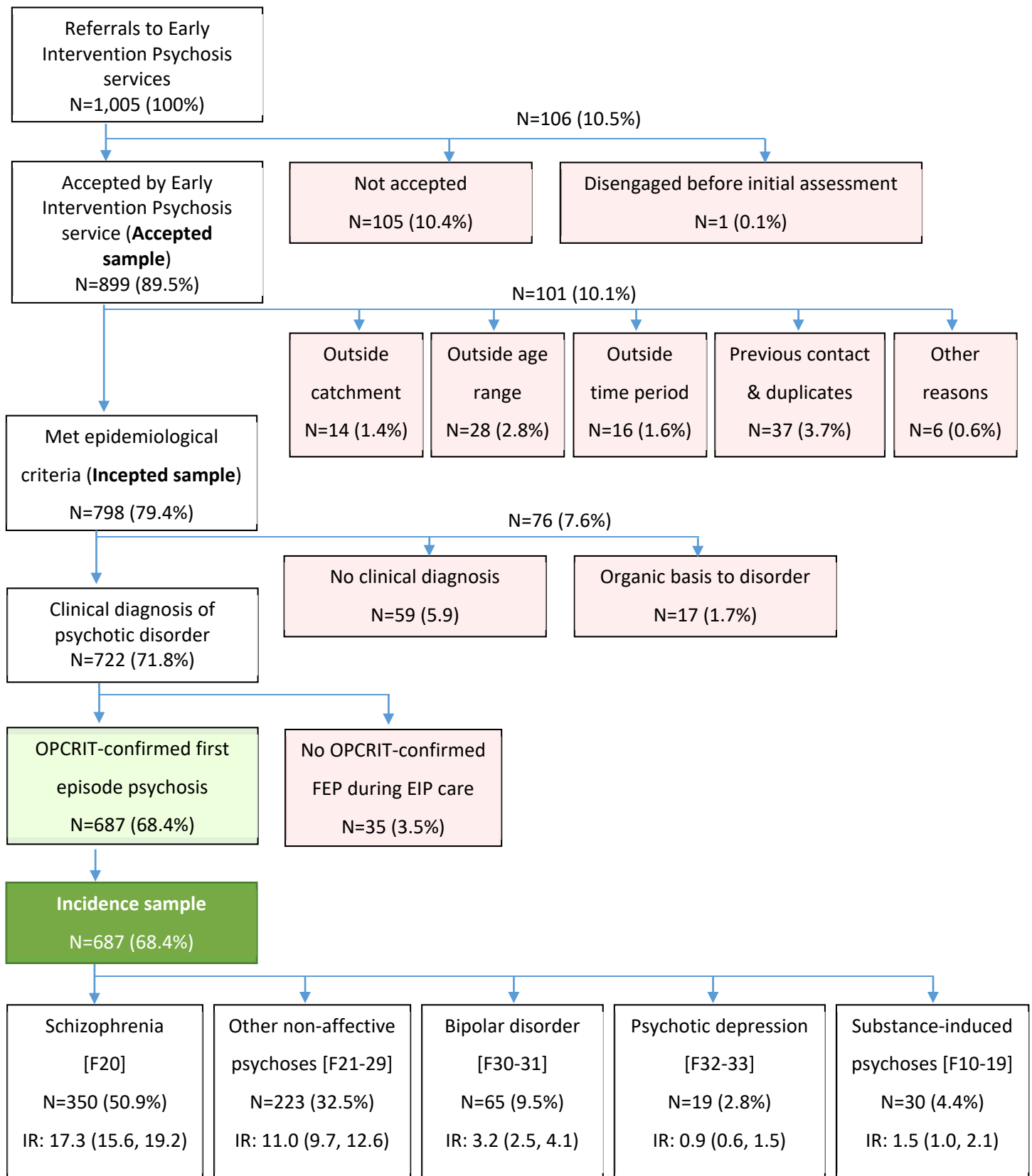
<sup>‡</sup>Analyses based on N=659 cases. Excluding N=28 cases of no fixed abode

Adjustment 1 is based on the full sample (N=687), mutually adjusted for all variables listed

Adjustment 2 is based on the restricted sample N=659. IRR are mutually adjusted for all variables listed.

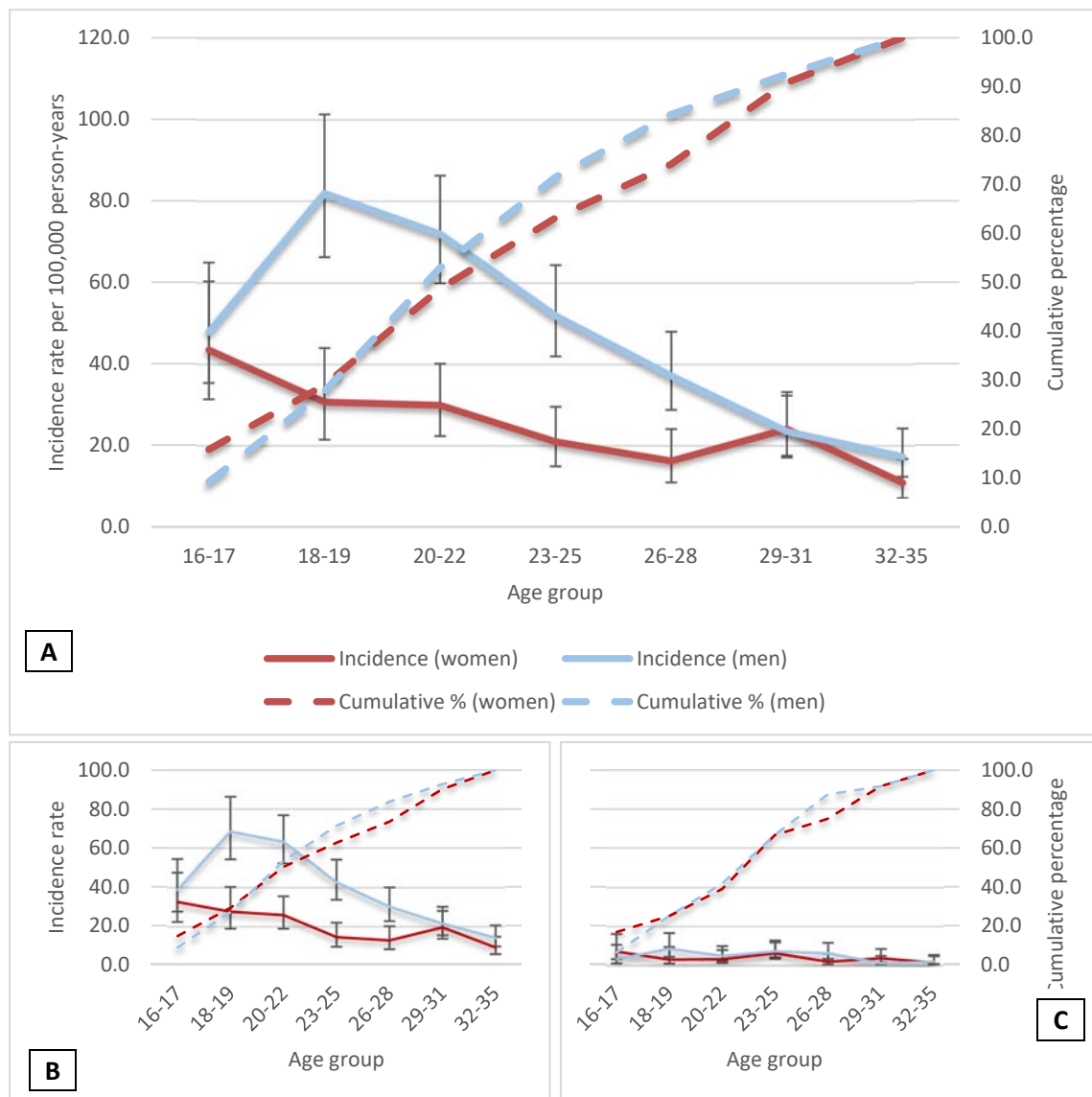


**Figure 1: Flow diagram of referrals to Early Intervention in Psychosis services**



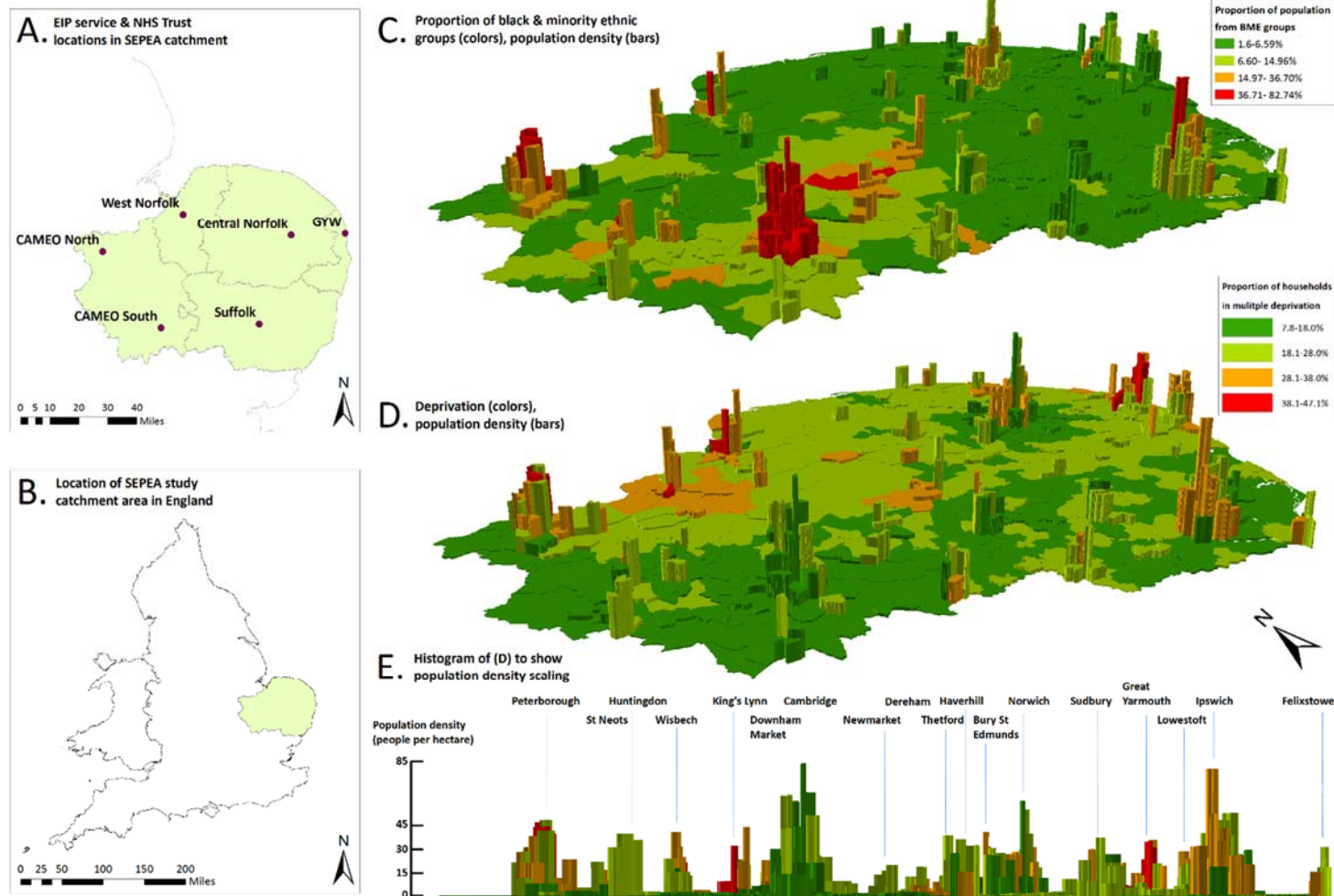
**Legend:** IR: Crude incidence rate per 100,000 person-years with 95% confidence intervals.

**Figure 2: Age-sex specific incidence rates of selected psychotic disorders with 95% confidence intervals and cumulative percentage of cases presenting to Early Intervention Psychosis services**



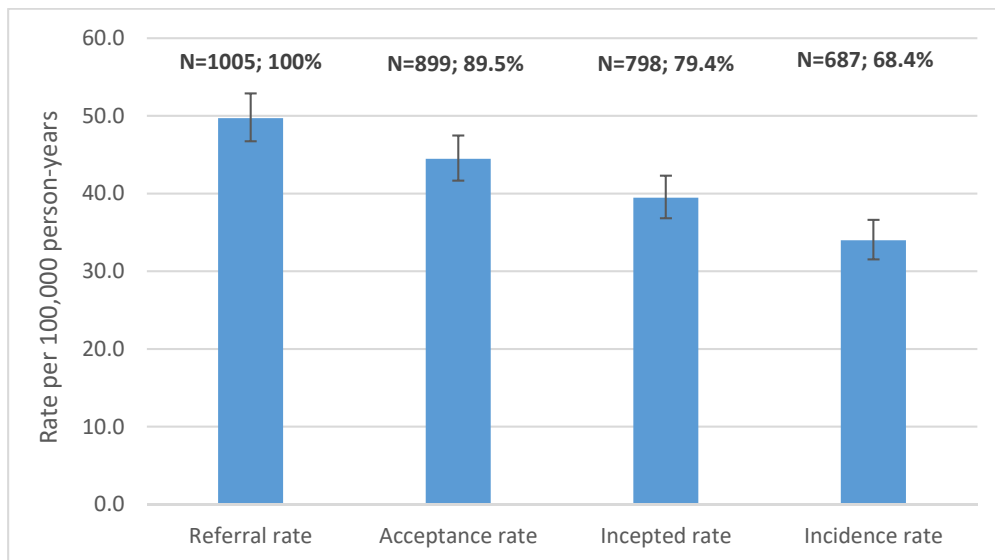
**Legend:** Crude incidence per 100,000 person-years and cumulative proportion of participants presenting to Early Intervention Psychosis services, by age and sex, with 95% confidence intervals (error bars) for (A) all clinically-relevant psychotic disorders, (B) non-affective psychotic disorders and (C) affective psychotic disorders. Likelihood ratio test [LRT] p-values for an age-sex interaction in Poisson regression models were (A)  $LRT-\chi^2$  on 6df=21.1:  $p<0.01$ , (B)  $LRT-\chi^2$  on 6df=15.4:  $p=0.02$  and (C)  $LRT-\chi^2$  on 6df=9.5:  $p=0.15$ . All graphs are plotted on the same scale to show relative differences in crude incidence between disorders.

## Supplemental Figure 1: Location, Early Intervention Psychosis service provision and selected catchment area characteristics



**Legend:** **A.** Location of six Early Intervention Psychosis services in the SEPEA catchment area. GYW: Great Yarmouth & Waveney. CAMEO is the Early Intervention Psychosis provider in Cambridge & Peterborough. **B.** Location in England. **C.** Proportion of black & minority ethnic groups (colors) and population density (bars) in 530 small area neighborhoods. Categorized in centiles relative to the proportion of ethnic minority groups in 7,689 English neighborhoods (i.e. up to median: 1.6-6.59%; 51<sup>st</sup>-75<sup>th</sup> centile: 6.60-14.96%; 76<sup>th</sup>-90<sup>th</sup> centile: 14.97-36.70%; 91<sup>st</sup> centile+: 36.71-82.7%). **D.** Proportion of households in multiple deprivation (colors), classified on 4-category interval scale used in analyses, and population density (bars). **E.** Histogram of (D) showing population density scale and notable towns & cities in catchment. Colors correspond to multiple deprivation. Data from 2011 Census of Great Britain. See also Supplemental Table 1.

**Supplemental Figure 2: Rate of contact in Early Intervention Psychosis services by contact type**



**Legend**

*Referral rate*: Number of referrals per 100,000 person-years

*Acceptance rate*: Number of referrals accepted by Early Intervention Psychosis services, per 100,000 person-years

*Incepted rate*: Number of accepted referrals who met epidemiological criteria, per 100,000 years

*Incidence rate*: Number of the incepted sample who received an OPCRIT-confirmed diagnosis for first episode psychosis, per 100,000 person years

**Supplementary Table 1: Neighborhood-level characteristics of the SEPEA study catchment – description, summary and representativeness**

Environmental variable	Description	Catchment (N=530)		Rest of England (N=7,159)		Median difference <sup>^</sup>		
		Median	IQR	Median	IQR	Diff.	95%CI	p-value
<b>Population density</b>	People per square mile	588	(209-4,653)	3,646	(573-8,976)	-3,583	(-4,347, -2,818)	<0.01
<b>Ethnicity</b>	% of population from black and minority ethnic groups	5.5	(3.5-11.1)	6.7	(4.0-15.7)	-1.2	(-1.8, -0.5)	0.01
<b>Multiple deprivation</b>	% of households in 2 or more of the domains below:	20.6	(16.7-25.7)	21.4	(16.3-28.3)	-0.7	(-1.8, 0.3)	0.14
<i>Employment domain</i>	% of households with at least one adult member reported as long-term sick or unemployed, not in full time study	N/A		N/A				-
<i>Education domain</i>	% of households without any member with at least “Level 2” education (≥5 GCSEs or equivalent) or in full-time study	N/A		N/A				-
<i>Health &amp; disability domain</i>	% of households with at least one member’s self-rated health as “bad” or “very bad”, or with a limiting long-term health problem	N/A		N/A				-
<i>Living environment domain</i>	% of households with at least one of the following: (i) in overcrowding <sup>†</sup> ; (ii) living in a shared dwelling <sup>‡</sup> ; (iii) without central heating	N/A		N/A				-

IQR – Interquartile range; GCSE – General Certificate for Secondary Education, mandatory for children in 10<sup>th</sup> and 11<sup>th</sup> years of education. N/A: Domain-specific deprivation data not published by the Office for National Statistics.

<sup>^</sup>Obtained from quantile regression

<sup>†</sup>ONS definition of overcrowding based on number of rooms and people per household, weighted for age and relationship status.

<sup>‡</sup>A unit of accommodation shared by two or more households.

**Legend:** Neighborhood-level variation in population density, ethnicity and deprivation varied across the 530 neighborhoods in the SEPEA region. The SEPEA region was, however, substantially more rural than the rest of England ( $p < 0.01$ ). Median differences in neighborhood-level ethnic composition (-1.2%; 95%CI: -1.8, -.05;  $p = 0.01$ ) and multiple deprivation (-0.7%; 95%CI: -1.8, 0.3;  $p = 0.14$ ) between the SEPEA region and the rest of England were small, but only met statistical significance for the former. 2011 Census data were obtained from: Table QS119EW (deprivation); Table PHP01 (population density), and; Table KS201EW (ethnicity); see [www.nomisweb.co.uk](http://www.nomisweb.co.uk).

**Supplementary Table 2: Multivariable Poisson analysis of non-affective and affective psychotic disorders by major sociodemographic characteristics**

Variable	Non-affective psychoses				Affective psychoses			
	N	%	IRR <sup>†</sup>	95%CI	N	%	IRR <sup>†</sup>	95%CI
<b>Total cases</b>	571	(100.0)	-		84	(100.0)	-	
<b>Sex</b>								
Women	185	(32.3)	Ref		36	(42.9)	Ref	
Men	388	(67.7)	1.97	(1.65, 2.35) <sup>‡</sup>	48	(57.1)	1.27	(0.82, 1.96)
<b>Age group</b>								
16-24	368	(64.2)	Ref		51	(60.7)	Ref	
25-29	118	(20.6)	0.64	(0.52, 0.81) <sup>‡</sup>	24	(28.6)	0.72	(0.43, 1.22)
30-35	87	(15.2)	0.45	(0.35, 0.58) <sup>‡</sup>	9	(10.7)	0.24	(0.11, 0.51) <sup>‡</sup>
<b>Ethnicity</b>								
White British	434	(75.7)	Ref		53	(64.3)	Ref	
Black & minority ethnic groups	139	(24.3)	1.41	(1.15, 1.71) <sup>‡</sup>	30	(36.7)	2.30	(1.44, 3.68) <sup>‡</sup>
<b>Participant socioeconomic status</b>								
Professional & managerial	58	(10.1)	Ref		12	(14.3)	Ref	
Intermediate occupation	63	(11.0)	1.53	(1.07, 2.19) <sup>‡</sup>	13	(15.5)	1.55	(0.70, 3.42)
Routine & manual	232	(40.5)	2.41	(1.80, 3.24) <sup>‡</sup>	31	(36.9)	1.47	(0.74, 2.92)
Long-term unemployed, students & unclassifiable	220	(38.4)	2.37	(1.73, 3.24) <sup>‡</sup>	28	(33.3)	1.17	(0.56, 2.44)
<b>Early intervention psychosis service</b>								
N. Cambridgeshire	71	(12.4)	Ref		18	(21.4)	Ref	
S. Cambridgeshire	130	(22.7)	1.29	(0.96, 1.73)	29	(34.5)	1.19	(0.65, 2.16)
West Norfolk	28	(4.9)	1.10	(0.71, 1.70)	5	(6.0)	0.85	(0.31, 2.31)
Central Norfolk	129	(22.5)	1.14	(0.85, 1.53)	13	(15.5)	0.51	(0.25, 1.04)
Great Yarmouth & Waveney	63	(11.0)	1.68	(1.19, 2.37) <sup>‡</sup>	14	(16.8)	1.73	(0.85, 3.53)
Suffolk	152	(26.5)	1.37	(1.03, 1.82) <sup>‡</sup>	5	(6.0)	0.19	(0.07, 0.51) <sup>‡</sup>

IRR: incidence rate ratio

<sup>†</sup>Adjusted for all other variables listed in table

<sup>‡</sup>p<0.05

**Supplementary Table 3: Neighborhood level variation in the incidence of non-affective and affective psychotic disorders**

Variable	Non-affective psychoses*				Affective psychoses^			
	N	%	IRR <sup>†</sup>	95%CI	N	%	IRR <sup>†</sup>	95%CI
<b>Total cases</b>	548	(100.0)	-		83	(100.0)		-
<b>Neighborhood population density (People per square mile)</b>								
48-587 (Below median)	110	(20.1)	Ref		19	(22.9)	Ref	
588-4,653 (50-75 <sup>th</sup> percentile)	154	(28.1)	1.31	(1.01, 1.70) <sup>‡</sup>	20	(24.1)	0.77	(0.39, 1.53)
4,654-11,099 (76-95 <sup>th</sup> percentile)	185	(33.8)	1.20	(0.92, 1.57)	24	(28.9)	0.99	(0.49, 2.01)
11,100-21,970 (96-100 <sup>th</sup> percentile)	99	(18.1)	1.30	(0.95, 1.77)	20	(24.1)	1.59	(0.74, 3.44)
<b>Neighborhood multiple deprivation (% households)</b>								
7.8-18.0%	129	(23.5)	Ref		28	(33.7)	Ref	
18.1-28.0%	243	(44.3)	1.47	(1.15, 1.89) <sup>‡</sup>	33	(39.8)	0.81	(0.43, 1.51)
28.1-38.0%	132	(24.1)	1.46	(1.07, 2.00) <sup>‡</sup>	17	(20.5)	0.67	(0.28, 1.58)
38.1-47.1%	44	(8.0)	2.74	(1.71, 4.39) <sup>‡</sup>	5	(6.0)	0.44	(0.12, 1.57)
<b>Early Intervention Psychosis service</b>								
North Cambridgeshire	70	(12.8)	Ref		18	(21.7)	Ref	
South Cambridgeshire	121	(22.1)	1.68	(1.19, 2.38) <sup>‡</sup>	28	(33.7)	1.00	(0.48, 2.11)
West Norfolk	27	(4.9)	1.12	(0.70, 1.79)	5	(6.0)	1.00	(0.34, 2.94)
Central Norfolk	126	(23.0)	1.28	(0.93, 1.76)	13	(15.7)	0.50	(0.23, 1.09)
Great Yarmouth & Waveney	61	(11.1)	1.41	(0.97, 2.05)	14	(16.9)	2.10	(0.94, 4.71)
Suffolk	143	(26.1)	1.58	(1.15, 2.17) <sup>‡</sup>	5	(6.0)	0.18	(0.06, 0.50) <sup>‡</sup>

IRR: incidence rate ratio; EIP: Early Intervention Psychosis

<sup>†</sup>Adjusted for all other variables listed in table and age group (three-category), sex, ethnicity and participant SES, as described

<sup>‡</sup>p<0.05

\*25 FEP participants of no fixed abode was excluded from analysis

^One FEP participant of no fixed abode was excluded from these analysis