



**A population-level prediction tool for the incidence of first episode psychosis: translational epidemiology based on cross-sectional data**

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3 **A population-level prediction tool for the incidence of first episode psychosis: translational**  
4 **epidemiology based on cross-sectional data**  
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47 **Access to online data:** Part of the development of this manuscript includes the visualisation of prediction data in  
48 map and tabular format on a website created for this project: [www.psymaptic.org](http://www.psymaptic.org). We have password-protected  
49 relevant prediction data on these pages so only editors and peer reviewers can access this data until the peer  
50 review process is complete. We invite you to access these pages by visiting [www.psymaptic.org](http://www.psymaptic.org) and navigating to  
51 "*prediction>for peer reviewers*" on the top menu bar. From here, you can access the data as *prediction maps*,  
52 *national summary tables* or *downloadable data*. Please enter the password **pr2012** when prompted.  
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## Abstract

*Objectives:* Mental health commissioners require precise information on local populations needs; these vary enormously according to social and demographic factors. We sought to develop a realistically complex population-based prediction tool for first episode psychosis [FEP] based on recent precise estimates of epidemiological risk.

*Design & participants:* Data from over 1000 FEP participants from two cross-sectional epidemiological studies were fitted to several different negative binomial regression models to estimate risk coefficients across combinations of different sociodemographic and socioenvironmental factors. We applied these coefficients to the population at-risk of a third, socioeconomically different region to predict the expected caseload over a 2.5 year period, where observed rates had been concurrently ascertained.

*Main outcome measures:* We compared observed counts with predicted counts (with 95% prediction intervals) at regional, EIS and local authority district [LAD] levels in East Anglia to establish the predictive validity of each model.

*Setting:* Empirical data from London, Nottingham and Bristol predicting counts in the population at-risk in the East Anglia region of the England.

*Results:* A model with age, sex, ethnicity and population density performed most strongly, predicting 508 FEP participants in EIS in East Anglia (95% PI: 459, 559) compared with 528 FEP participants observed over the same period. This model predicted correctly in 5 of 6 EIS (83.3%) and 19 of 21 LAD (90.5%). All models performed better than the current gold standard for early intervention in psychosis service commissioning in England (210 cases; 95% PI: 183-239).

*Conclusions:* We have developed a prediction tool for the incidence of psychotic disorder in England and Wales, and made this available as a free online tool ([www.psymaptic.org](http://www.psymaptic.org)) to provide mental healthcare commissioners with accurate forecasts based on a robust epidemiology and anticipated local population need. Our approach could potentially be applied to several other settings and disorders.

## Background

Commissioners of health and social care require precise information on the health needs of their local populations.<sup>1</sup> Recent policy promotes the importance of mental health care alongside physical health, recognising the intimate relationship between the two.<sup>2</sup> Many people with severe mental health disorders have dire physical health<sup>2</sup>; they suffer an average of 15-20 life-years lost, with premature deaths predominately attributable to cardiovascular disease.

Mental health disorders alone represent the leading disease burden in the UK (22.8%).<sup>3</sup> They contribute substantially to healthcare expenditure and societal costs even before physical ill health is taken into account. The Centre for Mental Health estimated total costs of mental health to British health services and society at £105 billion in 2009/10,<sup>4</sup> a figure expected to double over the next 20 years.<sup>2</sup> These are serious challenges compounded by a paucity of information on which to commission appropriate services. Early intervention in psychosis services [EIS] offer a useful example of failure to arm commissioners with adequate information to map services to local need. EIS are a major evidence-based innovation, systematically commissioned throughout England and Wales over the past decade.<sup>5</sup> When EIS intervention is sustained there is evidence that people with psychosis achieve better functional and social outcomes.<sup>6,7</sup> Such services are also highly cost-effective.<sup>4,8,9</sup> However, EIS were originally commissioned on an anticipated rate of 15 new cases of any psychotic disorder per 100,000 people per year in the Department of Health's Mental Health Policy Implementation Guide [MH-PIG],<sup>5</sup> a figure at least three times lower than reported thereafter.<sup>10-12</sup> The error came from confusing schizophrenia, a particular constellation of psychotic symptoms with chronicity built into its definition, with all psychotic disorders requiring care. This was compounded by the fact that recent evidence concerning the rich epidemiological profile of first episode psychosis [FEP]<sup>13</sup> was not translated into commissioning guidance.

We describe the development and validation of a population-level prediction tool capable of accurately estimating expected incidence of psychiatric disorder in a given population, underpinned by well-characterised epidemiological models. Applied to FEP as proof-of-concept, we show it is possible to precisely predict expected incidence in a given population, where the observed count of cases was within the prediction intervals forecast by our models. We applied our most precise prediction model to the population of England and Wales to provide health commissioners with a translational epidemiological prediction tool to underpin information-based service planning.

## Methods

Our prediction models were based on epidemiological data from the Aetiology and Ethnicity in Schizophrenia and Other Psychoses [ÆSOP] and the East London First Episode Psychoses [ELFEP] studies,<sup>14 15</sup> two recent, methodologically-similar FEP studies. We fitted various count-based regression models with sociodemographic and socioenvironmental factors, well-established in the literature to be associated with the incidence of psychotic disorder.<sup>16 17</sup> We first established the relative *internal validity* of each model by estimating internal model fit diagnostics to assess how well each model fitted the empirical data (henceforth referred to as the *prediction sample*). We next sought to estimate the *external validity* of each model by applying model-based parameter coefficients to the population structure of a deliberately different region of England, East Anglia (referred to as the *validation sample*). This out-of-sample prediction technique allowed us to obtain the expected incidence of disorder in this region forecast by each model, which we compared with observed rates simultaneously ascertained in this region via the ongoing Social Epidemiology of Psychoses in East Anglia [SEPEA] study.<sup>12</sup> We performed various model fit diagnostics to identify which, if any, model demonstrated utilisable predictive capability.

### Empirical data underlying prediction models (*prediction sample*)

#### *Case ascertainment (numerator)*

The designs of the ÆSOP and ELFEP studies have been described in detail elsewhere,<sup>14 15</sup> with features relevant to the present paper summarised here. Case ascertainment took place over two years in ELFEP (Newham: 1996-8; Tower Hamlets & Hackney: 1998-2000) and the Southeast London and Nottingham centres of the ÆSOP study (1997-9), and over the first 9 months of 1997 in Bristol (ÆSOP). All service bases were screened regularly for potential new contacts aged 16-64 years (18-64 in ELFEP) resident within these catchment areas. Leakage studies were conducted to identify participants missed by this initial screen, but meeting inclusion criteria for FEP.<sup>14 15</sup> All participants who received an ICD-10 F10-39 diagnosis for psychotic disorder following assessment via the Schedules for Clinical Assessment in Neuropsychiatry were included in the incident sample, except those with an organic medical basis to their disorder or profound learning difficulty. Data on age-at-contact, sex and ethnicity were collected on included participants. We geocoded participants' residential postcode at first contact to their corresponding local authority district [LAD] to allow us to model possible neighbourhood effects

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3 associated with the incidence of psychotic disorder, such as population density or socioeconomic  
4 deprivation.  
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#### 8 *Population at-risk*

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10 We estimated the population at-risk from which participants originated using the 2001 Census of Great  
11 Britain, adjusted for study duration, and stratified by age group (16-17, 18-19, then 5-year age bands),  
12 sex and ethnicity. Ethnicity was based on self-ascription according to one of ten categories derived from  
13 the census: white British, non-British white, black Caribbean, black African, Indian, Pakistani,  
14 Bangladeshi, mixed white & black Caribbean, other mixed ethnic backgrounds and all other ethnicities.  
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#### 20 *Socioenvironmental variable estimation*

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22 We estimated LAD -level deprivation using the 2004 Index of Multiple Deprivation [IMD] in England,  
23 which estimated domains of deprivation using measures predominantly collected close to the time of  
24 our case ascertainment periods (see Box 1).<sup>18</sup> We z-standardised English LAD IMD scores to have a mean  
25 of zero and standard deviation of one, and extracted IMD z-scores for the 14 LADs in the ÆSOP and  
26 ELFEP studies. To inspect whether any particular deprivation domain was a better predictor of psychosis  
27 incidence than IMD, we also considered LAD-level income deprivation, employment deprivation and the  
28 extent of deprivation in our models (). We also estimated population density, by dividing LAD usual  
29 resident population by its area (in hectares), using ArcGIS 9.3 software.  
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38 <Box 1 about here>  
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#### 41 **Observed data for external validation of prediction models (*validation sample*)**

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43 The observed numerator (participant) and denominator (population at-risk) data for our *validation*  
44 *sample* was obtained from the SEPEA study, an ongoing study of the incidence of psychotic disorders  
45 incepted over three years (2009-12) through one of six EIS covering 20 LAD and a subsection of one LAD  
46 (the town of Royston, Hertfordshire) in Norfolk (three EIS: West, Central and Great Yarmouth &  
47 Waveney), Suffolk (one EIS) and Cambridgeshire, Royston & Peterborough (CAMEO North and South  
48 EIS).<sup>12</sup>  
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#### 54 *Case ascertainment*

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3 To establish the incepted incidence of first episode psychosis as seen through EIS, entry criteria for the  
4 SEPEA study were:  
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- 9 • Referral to an EIS in East Anglia for suspected first episode of psychosis
- 10 • Aged 16-35 years old at first referral to EIS (17-35 years in CAMEO services)
- 11 • Resident within the catchment area at first referral
- 12 • First referral during case ascertainment period (2009-12)
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17 At six months after referral, or discharge from the service, whichever was sooner, we asked the clinician  
18 responsible for the care of the participant to provide an ICD-10 F10-39 psychiatric diagnosis using all  
19 information available. We excluded participants without a clinical FEP diagnosis, or participants  
20 presenting with an organic basis to disorder or profound learning disability. For remaining participants,  
21 basic sociodemographic and postcode information was recorded and classified in the same way as in the  
22 *prediction sample*. We included participants presenting to EIS during the first 2.5 years of the ongoing  
23 SEPEA study.  
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#### 29 30 31 *Population at-risk*

32 We estimated the population at-risk of East Anglia using the latest (2009) mid-year census estimates  
33 published by the Office for National Statistics [ONS] at LAD-level, by age group, sex and ethnicity.<sup>19</sup>  
34 These estimates used the 2001 census base, adjusted for immigration, births and deaths each year. It  
35 was not possible to obtain 2009 mid-year estimates for Royston, because data were only published at  
36 the LAD-level, not by town. Here, we thus used denominator data from the 2001 census data, published  
37 for Royston in order to estimate the population at-risk. We do not believe this would have substantially  
38 invalidated our results as this town represented 0.6% of the overall population at-risk (n=9,555) in the  
39 SEPEA study. Denominator data were multiplied by 2.5 to account for person-years of exposure in the  
40 *validation sample*.  
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#### 49 50 *Socioenvironmental variable estimation*

51 For each LAD in the SEPEA study we obtained corresponding socioenvironmental variables to those  
52 included in our *prediction sample*, using updated data collected as close to the SEPEA study case  
53 ascertainment period as possible. Population density was estimated using 2009 mid-term population  
54 estimates. Our measures of deprivation were derived from the IMD 2010,<sup>20</sup> which was estimated in an  
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3 analogous way to 2004 data, but collected from data sources obtained immediately prior to the SEPEA  
4 study.  
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## 8 **Statistical techniques**

### 9 *Dataset generation*

10 We constructed a dataset for the regression analysis of count data by pooling numerator and  
11 denominator data from the ÆSOP & ELFEP studies (the *prediction sample*). Data were stratified by age  
12 group, sex, ethnicity and LAD, such that each stratum represented the total count of cases in a unique  
13 sociodemographic group for a given LAD, with a corresponding estimate of the population at-risk,  
14 treated as an offset in our models. Our socioenvironmental measures (population density, deprivation)  
15 were adjoined to the dataset for each LAD.  
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24 Population at-risk data from the *validation sample* were stratified in the same way and retained in a  
25 separate database. Count of cases (which we wished to predict into, given the model) were entered as  
26 missing.  
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### 31 *Prediction models*

32 We used the *prediction sample* data to fit negative binomial regression models to obtain parameter  
33 coefficients of incidence for the sociodemographic and socioenvironmental factors included in each  
34 model. We considered the internal and external predictive capabilities of six models, all of which  
35 contained age group, sex, an age-sex interaction term and ethnicity. Model 1 contained no further  
36 covariates. Model 2 also included IMD. We replaced IMD with either income, employment or the extent  
37 of deprivation, respectively, in models 3-5. Model 6 included population density. Initial exploration of  
38 the *prediction sample* data indicated the presence of possible over-dispersion (variance ( $\delta^2=1.37$ )  
39 exceeded mean ( $\mu=0.4$ ) count of cases) so negative binomial regression was preferred to Poisson  
40 regression since it explicitly models any over-dispersion with an extra dispersion parameter.  
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### 50 *Internal model cross-validation & prediction*

51 We assessed internal model validity in three ways. First we used Akaike's Information Criterion [AIC] to  
52 assess the respective overall fit of each model to the data. Second, we conducted K-fold cross validation  
53 to assess each model's internal validity to predict cases within the *prediction sample*. This method  
54 randomly allocated strata in the *prediction sample* into *K* subsets. Each model was then re-estimated on  
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3  $K-1$  subsets (the *training data*) to predict expected counts of cases in the  $K^{\text{th}}$  subset (the *test data*). This  
4 was repeated over  $K$  trials, such that each stratum in the dataset appeared exactly once as the *test data*.  
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6 At the end of this process, we derived Lin's concordance correlation coefficient [CCC] and 95%  
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8 confidence intervals [95%CI] to estimate the correlation between predicted and observed counts of  
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10 cases across all strata in the *prediction sample*. Finally, we estimated the root mean squared error  
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12 [RMSE] to determine the average error between fitted and observed values from each model, where  
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14 lower RMSE scores indicated smaller prediction error. The RMSE is derived as

$$RMSE = \sqrt{\frac{\sum_{i=1}^n (y_i - \hat{y}_i)^2}{n}}$$

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23 where  $y_i$  and  $\hat{y}_i$  are the observed and predicted count of cases in the  $i^{\text{th}}$  stratum, respectively, and  $n$  is  
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25 the number of strata.

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28 We repeated  $K$ -fold cross-validation  $h$  times, generating  $K$  new random divisions of the data each time.  
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30 We retained model fit diagnostics across  $Kh$  iterations, and reported the mean of Lin's CCC and RMSE to  
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32 provide summary cross-validation statistics for each model. We specified  $K=10$  and  $h=20$ , as  
33  
34 recommended for cross-validation to obtain precise model fit diagnostics.<sup>21</sup>

### 35 36 37 *External model prediction & validation*

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39 We retained parameter coefficients from each model (using the full *prediction sample* data) and applied  
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41 these to the corresponding population at-risk in the *validation sample* dataset. This gave out-of-sample  
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43 prediction estimates for the expected count of cases in each stratum of the *validation sample*, given the  
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45 model. We summed expected counts across relevant strata to estimate the (i) total predicted count of  
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47 cases in the SEPEA region, (ii) predicted counts in each EIS, and (iii) predicted counts by LAD. These  
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49 counts were further stratified by broad age group (16-35, 36-64 and 16-64 years). Because census  
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51 (denominator) data was unavailable for 35 year olds alone (needed to estimate their contribution to  
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53 predicted counts in the age range for EIS, 16-35 years) we assumed the risk coefficient was the same  
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55 across all ages within the 35-39 year old age group. We apportioned predicted counts on a 1:4 ratio (35  
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57 years: 36-39 years) to their respective broad age groups.  
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3 To determine how well the MH-PIG<sup>5</sup> figure of 15 new cases per 100,000 people per year for EIS  
4 performed as a predictive tool, we also estimated the predicted count of cases in the *validation sample*  
5 under this scenario, which we termed “Model 7”.  
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10 We derived prediction intervals [95% PIs] for all summary predictions from first principles for each  
11 negative binomial regression model, since their derivation is not straightforward, nor routinely  
12 implemented by statistical software. We developed a bootstrap-like approach to obtain prediction  
13 intervals from each model by simulating 1000 model-based realisations of the quantities we wished to  
14 predict, where we took the parameters to be the maximum likelihood estimates. We obtained the lower  
15 and upper bounds of the prediction intervals as the corresponding quantiles of the simulated  
16 realisations (see Appendix for full details).  
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24 To assess each model’s external predictive capabilities, we derived five markers of predictive accuracy.  
25 We compared the number of times the observed count of cases in the SEPEA study fell within the  
26 prediction intervals estimated from each model for (i) the SEPEA region, (ii) at EIS level, and (iii) at LAD  
27 level. We also derived EIS- and LAD-level RMSE scores to estimate prediction error from each model in  
28 our *validation sample*. We ranked model performance (1: best, 7: worst) on these five measures, and  
29 estimated an overall mean rank to determine the overall predictive validity of each model.  
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36 Observational data on first episode psychosis in our *validation sample* were not available for the age  
37 range 36-64 years, so external validation was restricted to the 16-35 year old group. For completeness,  
38 however, we also reported overall predicted count of cases for this age group from each model.  
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#### 43 *Extrapolation to the United Kingdom*

44 Guided by our validation procedures, we identified which model had the greatest overall predictive  
45 validity, and proposed this as a candidate for FEP incidence prediction in England and Wales. We  
46 repeated out-of-sample prediction on the sociodemographic and socioenvironmental population  
47 characteristics of each LAD in England and Wales to obtain national and LAD-level predictions.  
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50 Denominator data was obtained from the ONS 2009 mid-term estimates and stratified as previously  
51 described. Overall counts were derived for three broad age groups (16-35, 36-64 and 65-74 years), and  
52 for each of these, by sex and ethnicity. 95% PIs were estimated as before. We visualised this data on  
53 maps and in tables to provide healthcare planners and commissioners with an easy-to-use tool to  
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3 forecast the expected incidence of psychosis in England and Wales. We have made this available as a  
4 free, open-use prediction tool, known as PsyMaptic (version 0.3) (Psychiatric Mapping Translating  
5 Innovations into Care; [www.psymaptic.org](http://www.psymaptic.org)).  
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### 10 *Software*

11 All negative binomial regression models, out-of-sample prediction and estimation of 95% PI were  
12 conducted in R (version 2.15.1). Internal cross-validation and model-fit diagnostics were conducted in  
13 Stata (version 11). Prediction maps for England and Wales were created using StatPlanet Plus (version  
14 3.0) visualisation software.<sup>22</sup>  
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## 20 **Results**

### 21 **Prediction sample**

22 Our prediction models contained data on 1,037 persons with a first episode psychosis in the ÆSOP  
23 (n=553; 53.3%) and ELFEP (n=484; 46.7%) studies, ascertained from over 2.4m person-years at-risk.  
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Twelve participants were excluded from the original ÆSOP sample because they were of no fixed abode  
and could not be geocoded to an LAD.<sup>14</sup>

The population at-risk in the *prediction sample* came from LAD with higher median levels of multiple and  
employment deprivation, extent of deprivation and population density than the population at-risk in the  
*validation sample*, though there were no statistically significant differences in median income  
deprivation between the two samples (Supplemental Table 1).

<[Supplemental Table 1 about here](#)>

Parameter coefficients obtained from the full prediction sample following negative binomial regression  
are shown in Table 1. As previously reported from these data,<sup>15 23</sup> incidence rates were generally raised  
in ethnic minority groups compared with the white British population. Models 2-6 included a measure of  
LAD deprivation (Models 2-5) or population density (Model 6), which were all associated with a  
significant increase in the incidence of psychotic disorder, after control for individual-level confounders.  
Each of these models produced a lower AIC score, indicating better fit, than a model fitted solely with  
individual-level covariates (Model 1). Internal cross-validation suggested all models achieved good CCC

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3 agreement between predicted and observed cases, with low RMSE values (Table 1). Models 2-5  
4 performed marginally better than Model 6 on these cross-validation diagnostics.  
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8 <Table 1 about here>  
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## 10 11 **Validation sample**

### 12 *Observed participants*

13 We identified 572 participants over the first 30 months of the SEPEA study, aged 16-35 years old, who  
14 met acceptance criteria for EIS in East Anglia. We excluded 44 participants (8.0%) who did not meet  
15 clinical criteria for ICD-10 psychotic disorder. This left an incidence sample of 528 participants from  
16 nearly 1.4m person-years at risk (37.8 per 100,000 person-years; 95%CI: 34.7, 41.2). A further 2.3m  
17 person-years at-risk accrued in the same region for people aged 36-64 years over this period. Median  
18 levels of multiple, income and employment deprivation in the region did not differ significantly from the  
19 remainder of England, although median population density and extent of deprivation in East Anglia were  
20 lower than elsewhere in England (Supplemental Table 1).  
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29 <Table 2 about here>  
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### 34 *External model prediction & validation*

35 The overall observed count of cases, aged 16-35 years, in the *validation sample* (n=528) fell within 95%  
36 prediction intervals in only two of seven tested models (Models 4 and 6, Table 2). Of these, the observed  
37 count was closest to the point estimate for Model 6 (508.5; 95% PI: 449.0, 559.0), fitted with age group,  
38 sex, their interaction, ethnic group and LAD population density. The observed count of cases also fell  
39 within prediction intervals from this model in five of six EIS in the study region, and 19 of 21 LADs, the  
40 most of any model (Table 3). Overall, Model 6 was ranked highest across all external model fit  
41 diagnostics (Table 3). All models outperformed the Department of Health's uniform figure of 15 cases  
42 per 100,000 people per year (Model 7), which consistently underestimated the expected count of cases  
43 observed in the *validation sample* (overall prediction: 210.5 cases; 95% PI: 183.0, 239.0).  
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52 We also reported predicted cases aged 36-64 years old from our models (Table 3), although we could  
53 not test these in our external *validation sample*. Model 6 predicted an additional 262.9 cases aged 36-64  
54 years over a 2.5 year period in East Anglia (95% PI: 233.0, 297.0).  
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3 <Table 3 about here>  
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### 7 *Extrapolation to England and Wales*

8 We selected Model 6 to predict the expected count and incidence of first episode psychosis per annum  
9 in each LAD in England and Wales, and visualised this data in maps and tables freely available at  
10 [www.psymaptic.org](http://www.psymaptic.org). Many maps can be visualised (for example, Supplemental Figure 1), including  
11 overall predicted incidence counts and rates for each broad age group at LAD level, by sex and ethnic  
12 group, as well as a variety of population and socioenvironmental data. According to our model, the  
13 annual number of new FEP cases in England and Wales would be 8745 (95% PI: 8558, 8933), of which  
14 our model predicted 67.9% (N=5939; 95% PI: 5785, 6102) would be seen through EIS. Only 176 (95% PI:  
15 151, 203) cases aged 16-64 years were forecast in Wales per annum. Assuming our prediction model is  
16 accurate, it indicated that a median of 63.4% of new service users seen by EIS as predicted by our model  
17 would not have been anticipated under the current gold standard for commissioning EIS (model 7),  
18 although this varied between LAD (10<sup>th</sup>-90<sup>th</sup> percentile: 51.3% - 67.6%; Supplemental Figure 2).  
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29 <Supplemental Figures 2 & 3 about here>  
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## 33 **Discussion**

### 34 **Principal findings**

35 We have developed and tested several epidemiological prediction models to forecast FEP incidence in  
36 England and Wales, having taken into account regional differences in the sociodemographic and  
37 socioenvironmental profile of different populations. Inspection of our data suggested that a model fitted  
38 with age group, sex, their interaction, ethnic group and LAD-level population density provided the  
39 greatest external predictive validity when compared with the observed caseload ascertained through EIS  
40 in our *validation sample*. This model also had good internal validity across the entire age range (16-64  
41 years). All prediction models performed significantly better than the Department of Health's current  
42 gold standard for EIS commissioning,<sup>5</sup> based on a low uniform anticipated incidence rate.  
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### 52 **Limitations & future development**

53 We estimated prediction intervals from first principles [DJ] since their derivation is an area of statistical  
54 development.<sup>24</sup> We used a bootstrap-like methodology to produce 95% PI accounting for natural  
55 variation in the *validation sample*, but ignoring parameter uncertainty in the coefficients included in  
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3 prediction models, which we assumed to be the true coefficients of risk in the population. Our approach  
4 therefore naturally led to slightly artificially narrow 95% PIs. Ideally, prediction intervals should take into  
5 account both these sources of variation, although we note that parameter uncertainty is usually small  
6 compared to the natural variation of the quantities of interest. Furthermore, ignoring this uncertainty  
7 was not necessarily undesirable for the purpose of model validation and the precise prediction of  
8 expected counts because we wished to apply stringent criterion. Here, the addition of more empirical  
9 data in the *prediction sample* would not lead to narrower PIs, though would tend to move the point  
10 estimate of risk for each coefficient closer to the true value in the population. We do not believe we  
11 have mis-estimated point estimates of risk across major sociodemographic groups, since our results  
12 accord with the wider English and International literature.<sup>16 17 25</sup> We sought independent confirmation  
13 that our development of 95% PI were correct (personal communication with Prof Ian White, MRC  
14 Biostatistics Unit). We recommend that all prediction point estimates from our PsyMaptic model are  
15 considered with their 95% PIs, which provide information about the natural variance in expected rates in  
16 the population.  
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29 We could not externally validate prediction models for people aged 36-64 years because comparable  
30 observed incidence data was not available in our *validation sample*. We have no reason to believe our  
31 predictions will be invalid for this group, however, since the empirical data which underpinned our  
32 models was ascertained from the same two large, well-conducted studies of first episode psychosis in  
33 England as data for the younger age group,<sup>14 23 26</sup> and published findings from these studies are  
34 consistent with the wider epidemiological literature for psychosis from England and internationally.<sup>16 25</sup>  
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27 It will be important to ascertain the predictive capability of our model(s) in this age range, and we will  
seek to identify suitable samples to do so in future versions of PsyMaptic.

All prediction models had reasonable internal validity, although our proposed model performed slightly  
worse (most noticeably for AIC) than models which included deprivation (i.e. models 2-4) instead of  
population density. Our decision to use model 6 as our proposed candidate for the prediction tool was,  
however, supported by the fact that it produced the most accurate external forecasts of any model,  
despite considerable socioenvironmental differences between regions in our *prediction* and *validation*  
samples. We were unable to predict the expected incidence of psychotic disorder in geographical areas  
smaller than LADs, such as electoral wards (N~6000), or to other parts of the UK, because appropriate  
denominator data was not published as mid-term census estimates. The 2011 census will provide small

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3 area and national data for the whole of the UK and will be released by ONS in mid-2013. This will allow  
4 us to update our tool to the latest population estimates for the UK, and refine our PsyMaptic tool at a  
5 smaller geographical level for fine-grained healthcare commissioning. Small area prediction models will  
6 require a multilevel approach, not attempted here, because obtaining predictions from multilevel  
7 random effects models is not straightforward and requires active statistical development.  
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13 We believe case ascertainment in our *validation sample* led to a reliable estimate of the incidence of  
14 psychotic disorder for people aged 16-35 years old. EIS were the only mental health service for people  
15 aged 14-35 years experiencing a first episode of psychosis in East Anglia, minimising the potential for  
16 under-ascertainment in the population at-risk when derived from careful epidemiological design.<sup>12</sup> We  
17 are confident that our *validation sample* also contained few false positive cases for any clinically-  
18 relevant psychoses, since participants were excluded who failed to meet acceptance criteria for EIS or  
19 who did not receive a clinical diagnosis of psychotic disorder during the first six months from initial  
20 referral. Future versions of PsyMaptic will include forecasts for specific psychotic disorders as  
21 standardised research-based diagnoses (using OPCRIT<sup>28</sup>) are currently being collected in the ongoing  
22 SEPEA study.  
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### 32 **Meaning of the findings**

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34 If commissioners are to meet the Department of Health's vision to orientate health services around local  
35 need,<sup>12 5</sup> differences in demand for EIS and other mental and physical health services will need to be  
36 taken into account to allocate finite resources where they are most needed. The PsyMaptic prediction  
37 model provides proof-of-concept that when robust empirical epidemiological data is combined with  
38 accurate population at-risk estimates this can be realised. As such, our modelling approach could have  
39 utility in many other settings and for many disorders. Our translational approach demonstrated good  
40 internal and external validity to predict the expected incidence of first episode psychosis, particularly  
41 through EIS, where 76% and 63% of all male and female adult-onset FEP cases, respectively, will  
42 typically present.<sup>14</sup> Since their inception in 2002, EIS in England and Wales have reported higher  
43 caseloads than they were originally envisioned to manage in the MH-PIG.<sup>5</sup> Empirical epidemiological  
44 data from such services supports this<sup>10-12</sup>; with incepted rates at least three times greater than expected  
45 based on a uniform rate of 15 per 100,000 people per year.<sup>5</sup> While the MH-PIG acknowledged that  
46 "...[a]n understanding of local epidemiology is needed as the size of population covered will depend on a  
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3 number of different factors” (p.55),<sup>5</sup> no further elaboration on how to achieve this was provided for  
4 commissioners. We believe PsyMaptic provides a possible exemplar to overcome this challenge.  
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9 Our models are not the first to be used to forecast mental illness needs in England and Wales,<sup>29</sup> though  
10 we believe this is the first attempt to forecast incidence rather than prevalence in the community. We  
11 recommend that our prediction methodology is used in conjunction with the wide range of public health  
12 observatory data available.<sup>30</sup> To this end, PsyMaptic has been included with other indicators in the Joint  
13 Commissioning Panel for Mental Health’s forthcoming guidance for commissioning of public mental  
14 health services.<sup>31</sup>  
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21 We are not the first to express concerns over the suitability of the MH-PIG for EIS implementation.<sup>32 33</sup>  
22 The epidemiological literature conducted before and after its publication does not support adoption of  
23 such a low rate of first episode psychosis as a realistic basis for psychosis service planning for young  
24 people,<sup>16 25 34-39</sup> when incidence rates are at their highest. Our heat maps (see Supplemental Figure 2 and  
25  
26 online) illuminate the magnitude of the discrepancy between MH-PIG forecasts and those from our  
27 prediction model in different regions of England and Wales; our data suggest the MH-PIG  
28 underestimated anticipated EIS caseload per annum by almost 50% anywhere in England and Wales.  
29 This figure exceeded 80% in some urban areas. Given the significant downstream economic savings  
30 associated with spending on EIS,<sup>8</sup> PsyMaptic can also be used to highlight regions where with sufficient  
31 EIS investment the greatest economic gains could be realised in terms of mental healthcare expenditure  
32 (assuming sustained intervention also leads to improved social and clinical benefit for patients<sup>6 7</sup>). We  
33 note that our heat maps broadly correlate with advocacy expressed for EIS by healthcare professionals  
34 in England and Wales.<sup>40</sup> Though by no means universal, proponents of EIS tend to be located in major  
35 conurbations – such as London,<sup>41</sup> Birmingham<sup>42</sup> or Manchester<sup>7 43</sup> – where demand for EIS will be  
36 highest, while those more critical of such services tend to work in more rural communities,<sup>33 40</sup> where  
37 but a handful of young people would be expected to come to the attention of EIS each year.  
38 Underestimating need by 50% may not produce major difficulties in a region where only two cases per  
39 year present to services, but will have great impact on service care and delivery in an EIS seeing 250 new  
40 cases per year.  
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**Box 1: Description of included socioenvironmental variables<sup>1 2</sup>**

Variable	Classification & description
Multiple deprivation	Weighted data from routine national sources across 7 domains: income, employment, education, health, barriers to housing & services, living environment, crime. Continuous, z-standardised scores for analysis.
Extent of deprivation	Proportion of LAD population living in 20% most deprived SOA in England (%)
Income deprivation	Proportion of all people in LAD classified as income deprived (%)
Employment deprivation	Proportion of adults of working age in LAD classified as employment deprived (%)
Population density	Population density at LAD level (people per hectare).

IMD: Index of Multiple Deprivation; LAD: Local authority district; SOA: super output area; IQR: inter-quartile range

<sup>1</sup>*Prediction sample* sources: Population density – 2001 census estimates; Deprivation variables: 2004 Indices of Deprivation, predominantly collected from data sources close to ÆSOP & ELFEP case ascertainment periods (i.e. 1997-2000)

<sup>2</sup>*Validation sample* sources: Population density – 2009 mid-year census estimates; Deprivation variables: 2010 Indices of Deprivation, predominantly collected from data sources just prior to SEPEA case ascertainment period (2008)

Table 1: Prediction models, covariates and fit: all clinically relevant psychoses (F10-39)

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Variable	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)
Age group*sex interaction <sup>1</sup>	p=0.07	p=0.06	p=0.06	p=0.06	p=0.06	p=0.06
Ethnicity						
White British	1	1	1	1	1	1
Non-British white	2.0 (1.5, 2.5)	1.7 (1.4, 2.2)	1.7 (1.3, 2.2)	1.7 (1.3, 2.2)	1.8 (1.4, 2.3)	1.7 (1.3, 2.2)
Black Caribbean	6.0 (4.9, 7.3)	5.3 (4.3, 6.5)	5.2 (4.3, 6.4)	5.2 (4.3, 6.4)	5.4 (4.5, 6.6)	5.1 (4.2, 6.3)
Black African	4.1 (3.3, 5.1)	3.6 (2.9, 4.5)	3.5 (2.8, 4.4)	3.5 (2.8, 4.4)	3.7 (3.0, 4.6)	3.5 (2.8, 4.3)
Indian	1.7 (1.2, 2.5)	1.5 (1.1, 2.2)	1.5 (1.0, 2.2)	1.5 (1.0, 2.1)	1.6 (1.1, 2.3)	1.6 (1.1, 2.2)
Pakistani	1.8 (1.2, 2.5)	1.6 (1.0, 2.5)	1.6 (1.0, 2.4)	1.6 (1.0, 2.4)	1.6 (1.1, 2.5)	1.8 (1.3, 2.7)
Bangladeshi	2.1 (1.5, 2.8)	1.7 (1.2, 2.3)	1.7 (1.2, 2.3)	1.6 (1.2, 2.2)	1.8 (1.3, 2.5)	1.8 (1.4, 2.4)
Mixed white & black Caribbean	4.3 (2.8, 6.7)	3.9 (2.5, 6.0)	3.9 (2.5, 6.0)	3.9 (2.5, 6.0)	4.0 (2.6, 6.1)	3.9 (2.5, 6.1)
Mixed, other	1.3 (0.8, 2.3)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)
Other	2.2 (1.6, 3.0)	1.9 (1.4, 2.7)	1.9 (1.4, 2.6)	1.9 (1.4, 2.6)	2.0 (1.4, 2.7)	1.9 (1.4, 2.7)
Socioenvironmental variables						
IMD (z-score)	-	1.184 (1.101, 1.274)	-	-	-	-
Extent of deprivation (%)	-	-	1.008 (1.004, 1.011)	-	-	-
Income deprivation (%)	-	-	-	1.025 (1.015, 1.035)	-	-
Employment deprivation (%)	-	-	-	-	1.062 (1.032, 1.093)	-
Population density (pph)	-	-	-	-	-	1.005 (1.003, 1.007)
Internal model fit diagnostics						
AIC <sup>2</sup>	2571.8	2552.4	2551.3	2549.6	2556.4	2556.3
Lin's CCC (95%CI) <sup>3</sup>	0.75 (0.74, 0.77)	0.77 (0.75, 0.78)	0.77 (0.75, 0.79)	0.77 (0.75, 0.78)	0.77 (0.75, 0.78)	0.76 (0.74, 0.77)
RMSE (s.d.) <sup>4</sup>	0.75 (0.11)	0.74 (0.11)	0.74 (0.10)	0.74 (0.10)	0.74 (0.11)	0.76 (0.13)

<sup>1</sup>All models fitted with age group by sex interaction given *a priori* evidence for effect modification.<sup>14 44</sup> Likelihood ratio test p-values reported between models with and without an interaction term fitted between age group and sex. Specific IRR not been reported for clarity, but available on request

<sup>2</sup>AIC: Akaike's Information Criterion – lower scores denote improved model fit

<sup>3</sup>CCC: Lin's correlation concordance coefficient. Higher scores indicate greater correlation between observed & predicted count of cases in the *prediction sample*. Mean CCC and 95%CI reported following *h*=20 trials during cross-validation.

<sup>4</sup>RMSE: Root mean squared error. Lower scores indicate lower prediction error. Mean RMSE and standard deviation (s.d.) reported following *h*=20 repeats of *k*-fold cross-validation, where *k*=10.

Table 2: Observed versus predicted cases in SEPEA study for all clinically relevant psychoses, 16-35 years<sup>1</sup>

EIS	Observed	Model 1	Model 2	Model 3	Model 4
		Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)
<b>Overall total, 16-35 years</b>	<b>528</b>	<b>641.2 (586.0, 696.1)</b>	<b>468.5 (422.0, 518.0)</b>	<b>474.7 (429.0, 522.0)</b>	<b>487.5 (441.0, 535.0)</b>
Cameo North	55	84.7 (66.0, 106.0)	68.5 (52.0, 87.0)	67.8 (51.0, 86.0)	70.2 (53.0, 90.0)
Cameo South	137	163.6 (135.0, 192.0)	105.5 (84.0, 129.0)	111.7 (89.0, 134.0)	110.9 (90.0, 132.0)
West Norfolk	25	29.2 (18.0, 41.0)	23.0 (13.0, 35.0)	22.0 (12.0, 32.0)	23.4 (14.0, 34.0)
Central Norfolk	121	162.6 (136.0, 191.0)	122.6 (99.0, 148.0)	123.0 (100.0, 149.0)	128.3 (104.0, 152.0)
Great Yarmouth & Waveney	60	49.1 (34.0, 65.0)	41.6 (28.0, 55.0)	39.9 (27.0, 53.0)	42.9 (30.0, 57.0)
Suffolk	130	151.9 (126.0, 178.0)	107.4 (85.0, 128.0)	110.3 (88.0, 133.0)	111.7 (90.0, 136.0)
Overall total, 36-64 years	-	332.2 (292.0, 373.0)	244.0 (213.0, 276.0)	248.6 (216.0, 280.0)	256.3 (228.0, 291.0)
EIS	Observed	Model 5	Model 6	Model 7	
		Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)	
<b>Overall total, 16-35 years</b>	<b>528</b>	<b>477.1 (428.0, 523.0)</b>	<b>508.5 (459.0, 559.0)</b>	<b>210.5 (183.0, 239.0)</b>	
Cameo North	55	69.1 (52.0, 88.0)	64.5 (48.0, 82.0)	27.1 (17.0, 38.0)	
Cameo South	137	100.7 (79.0, 123.0)	131.1 (108.0, 157.0)	49.7 (36.0, 64.0)	
West Norfolk	25	24.7 (16.0, 35.0)	22.3 (13.0, 33.0)	10.5 (5.0, 17.0)	
Central Norfolk	121	128.2 (105.0, 153.0)	132.5 (108.0, 157.0)	55.2 (41.0, 70.0)	
Great Yarmouth & Waveney	60	47.7 (35.0, 63.0)	38.0 (26.0, 51.0)	17.4 (10.0, 26.0)	
Suffolk	130	106.6 (86.0, 128.0)	120.0 (96.0, 143.0)	50.6 (37.0, 65.0)	
Overall total, 36-64 years	-	249.7 (221.0, 284.0)	262.9 (233.0, 297.0)	345.7 (310.0, 383.0)	

<sup>1</sup>Numbers in green denote where observed count fell within 95% prediction interval [95% PI] for people aged 16-35 years. Observed data for people aged 36-64 years in the *validation sample* was not available.

Model 1: Age group, sex, their interaction and ethnicity

Model 2: Model 1 + IMD

Model 3: Model 1 + extent of deprivation

Model 4: Model 1 + income deprivation

Model 5: Model 1 + employment deprivation

Model 6: Model 1 + population density

Model 7: Department of Health uniform figure for EIS of 15 new cases per 100,000 people per year.

**Table 3: External model validation diagnostics<sup>1</sup>**

Model	Overall correct prediction? [rank]	EIS (N=6)		LAD (N=21)		Mean ranking [rank of mean ranking]
		Number correct [rank]	RMSE [rank]	Number correct [rank]	RMSE [rank]	
Model 1	No [3]	4 [2]	25.6 [6]	18 [2]	8.13 [6]	3.8 [4]
Model 2	No [3]	3 [6]	18.4 [4]	17 [5]	6.87 [4]	4.4 [6]
Model 3	No [3]	4 [2]	16.4 [3]	18 [2]	6.51 [3]	2.6 [3]
Model 4	Yes [1]	4 [2]	16.3 [2]	18 [2]	6.40 [2]	1.8 [2]
Model 5	No [3]	4 [2]	19.4 [5]	16 [6]	7.11 [5]	4.2 [5]
Model 6	Yes [1]	5 [1]	11.9 [1]	19 [1]	5.93 [1]	1.0 [1]
Model 7	No [3]	0 [7]	59.4 [7]	5 [7]	18.32 [7]	6.2 [7]

<sup>1</sup>For each diagnostic, models are placed in rank order [1=best model, 7=worst model] with ties given the same ranking. The mean ranking and rank provide an estimate of the overall performance of various models.

RMSE: Root mean squared error (lower scores indicate lower error); EIS: Early Intervention in Psychosis Service; LAD: Local Authority District

**Article Summary****Article Focus**

- Commissioners require precise information on the health needs of their local populations to effectively plan health services
- A failure to arm mental health commissioners with precise epidemiological data led to an underestimate of actual activity in early intervention in psychosis services [EIS]
- We sought to develop a prediction tool for the incidence of first episode psychosis [FEP], by applying precise estimates of epidemiological risk in various sociodemographic groups to the structure of the population at-risk in a second region, where the observed incidence had been concurrently ascertained

**Key Messages**

- A model of psychosis incidence which included age, sex, ethnicity and population density yielded precise FEP predictions in our second region, out-performing the Department of Health in England's current gold standard for EIS commissioning.
- We have translated this model into a freely available prediction tool ([www.psymaptic.org](http://www.psymaptic.org)) to facilitate evidence-based healthcare commissioning
- Our tool could be extended to many international settings and other disorders to inform healthcare commissioning, when epidemiological risk can be well-characterised and the structure of the underlying population at-risk is known

**Strengths and limitations**

- Our modelling approach used robust epidemiological data from two large studies of first episode psychosis in England to provide estimates of incidence in a third study region, producing accurate forecasts
- Due to data availability it was not possible to validate our prediction tool in settings outside of England and Wales, or for specific psychotic disorders. As data become available we will extend the capability of our prediction tool.



Supplemental Table 1: Socioenvironmental variables at local authority district [LAD] level considered in epidemiological prediction models

Variable		England <sup>1</sup>	Prediction sample <sup>2</sup>	Validation sample <sup>1</sup>	Mann-Whitney test <sup>3</sup> : Z; p-value	
					Prediction vs. Validation	Validation vs. England
Number of LAD	-	326	14	20 (+1 partial)	-	-
Multiple deprivation (z-standardised)	Median (IQR): Min/Max:	<u>0 (1)</u> <sup>4</sup> -1.7 / 2.9	1.0 (-0.5, 2.4) -1.1 / 2.9	-0.7 (-1.0, 0.3) -1.4 / 1.0	2.4; p=0.02	1.5; p=0.12
Extent of deprivation (%)	Median (IQR): Min/Max:	9.0 (1.3, 23.9) 0.0 / 83.6	28.0 (4.0, 63.0) 0.0 / 83.0	1.4 (-.4, 12.8) 0.0 / 29.7	2.4; p=0.02	2.2; p=0.03
Income deprivation (%)	Median (IQR): Min/Max:	11.7 (8.6, 16.1) 3.9 / 32.8	15.5 (8.2, 24.7) 5.9 / 34.4	9.0 (8.2, 14.9) 6.0 / 19.1	1.5; p=0.14	1.3; p=0.19
Employment deprivation (%)	Median (IQR): Min/Max:	8.0 (5.8, 10.8) 2.1 / 18.8	11.6 (6.1, 14.1) 6.1 / 14.1	6.4 (5.4, 10.1) 3.9 / 13.9	2.5; p=0.01	1.4; p=0.17
Population density (people per hectare)	Median (IQR): Min/Max:	5.1 (1.8, 17.4) 0.2 / 137.1	19.4 (9.3, 81.9) 2.6 / 106.4	1.5 (1.2, 3.1) 0.9 / 30.0	3.7; p<0.001	3.4; p=0.001

IQR: inter-quartile range; LAD: Local Authority District

<sup>1</sup>Sources: Population density – 2009 mid-year census estimates; Deprivation variables: 2010 Indices of Deprivation, predominantly collected from data sources just prior to SEPEA case ascertainment period (2008)

<sup>2</sup>Sources: Population density – 2001 census estimates; Deprivation variables: 2004 Indices of Deprivation, predominantly collected from data sources close to A&SOP & ELFEP case ascertainment periods (i.e. 1997-2000).

<sup>3</sup>Mann-Whitney test performs test that the median LAD socioenvironmental scores for the prediction & validation data come from the same population distribution; p<0.05 indicates evidence that the median scores are significantly different

<sup>4</sup>For England we displayed the mean and s.d. of the z-score of deprivation (as shown, underlined), instead of the median and IQR.

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3 **Appendix (supplementary): Development of 95% prediction intervals for negative binomial regression**  
4 **models**  
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8  
9 To obtain 95% prediction intervals from each model, we took all parameter estimates from the fitted  
10 negative binomial regression, including the over-dispersion parameter  $\theta$ , as the true values when  
11 constructing prediction intervals. We then used a Monte Carlo procedure, where we simulated  
12 realisations using the Gamma-Poisson representation of the negative binomial distribution. For each  
13 iteration, we first simulated the random components of the linear predictors from  $\text{Gamma}(\theta, \theta)$ , which  
14 were multiplied by the point predictions (or equivalently  $e^{\upsilon}$ , where  $\upsilon$  is the non-random component of  
15 the linear predictor) to give the Poisson rates for the counts that comprised the predictions. We then  
16 simulated Poisson counts using these rates and summed them to provide one realisation of the quantity  
17 we wished to predict. By repeating this process many ( $n=1000$ ) times the distribution of the quantity to  
18 be predicted was obtained, from which 95% prediction intervals were obtained using the 2.5% and  
19 97.5% quantiles.  
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## Data sharing statement

Extra data is available at our prediction website, PsyMaptic: [www.psymaptic.org](http://www.psymaptic.org). We have made a large array of prediction data freely available to interested users, who can visualise prediction data in maps and tables for a range of psychotic disorder predictions by major sociodemographic subgroup and by LAD. Future versions of PsyMaptic will release data for other regions and at other geographical levels. Users can also download LAD-specific and national summaries of prediction data from our models in tabular form. Finally, additional explanatory material about how to use the data and the PsyMaptic website is also available at [www.psymaptic.org](http://www.psymaptic.org). Bespoke data not provided freely on our website may be requested from the authors at the cost of data extraction. The empirical data underlying the prediction models (ÆSOP and ELFEP) or the validation sample (SEPEA) is not freely available as the studies are ongoing, but papers detailing the main findings from these studies have previously been published elsewhere.

## Competing interests statement

All authors have completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare that (i) JBK has support from the Wellcome Trust for the submitted work (grant number WT085540) and PBJ has support from the NIHR (grant RP-PG-0606-1335); (ii) DJ, JP, FW, DF, JC, RMM have no relationships with any company that might have an interest in the submitted work in the previous 3 years; (iii) their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and (iv) no author holds non-financial interests that may be relevant to the submitted work.

### Role of funders

The funders were not involved in the design, collection, analysis, interpretation of the data, writing the report or the decision to submit the article for publication. All authors were independent from the funders in contributing to this work.

### Ethical approval

Ethical approval to conduct the original AESOP and East London First Episode Psychosis studies was granted from local research ethics committees in their respective centres prior to the original date of onset of the study. We were granted ethical approval to conduct the work related to the present manuscript, including use of data from the SEPEA study, from the Cambridgeshire 3 REC (09/H0306/39).

### Guarantorship

JBK takes full responsibility for the work and conduct of the study, had access to the data, and controlled the decision to publish.

### Contributorship

JBK was responsible for concept, design, analysis, data extrapolation, interpretation of the data, drafting the report and developing the content for the websites [www.psymaptic.org](http://www.psymaptic.org), [www.psymaptic.com](http://www.psymaptic.com) and [www.psymaptic.co.uk](http://www.psymaptic.co.uk). JBK was also the chief investigator of the SEPEA study, where the *validation sample* data was obtained. He gave final approval of this version of the manuscript to be published.

DJ was responsible for developing and initially implementing the statistical approach with regard to prediction intervals from count-based regression. He also contributed to drafting and editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

JP is principal collaborator on the SEPEA study in the CAMEO early intervention in psychosis services. He also contributed to editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

DF is co-principal collaborator on the SEPEA study in the Norfolk and Suffolk Foundation Trust. He also contributed to editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

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2  
3 FW is co-principal collaborator on the SEPEA study in the Norfolk and Suffolk Foundation Trust. He also  
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5 manuscript to be published.  
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7

8  
9 JC is chief investigator of the ELFEP study and provided part of the empirical dataset underlying the  
10 prediction model for use in this project. He also contributed to editing the final version of this  
11 manuscript. He gave final approval of this version of the manuscript to be published.  
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14 RMM is co-chief investigator of the ÆSOP study and provided part of the empirical dataset underlying  
15 the prediction model for use in this project. He also contributed to editing the final version of this  
16 manuscript. He gave final approval of this version of the manuscript to be published.  
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19  
20 PBJ is co-chief investigator of the ÆSOP study and provided part of the empirical dataset underlying the  
21 prediction model for use in this project. He contributed to the development of the prediction  
22 methodology and edited the final version of this manuscript. He gave final approval of this version of the  
23 manuscript to be published.  
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### 29 30 **Licences and granting of rights**

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### 41 42 **STROBE statement**

43 Our STROBE statement is provided as a supplementary file.  
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## Supplemental Figure 1: Screenshot of web-based PsyMaptic prediction tool

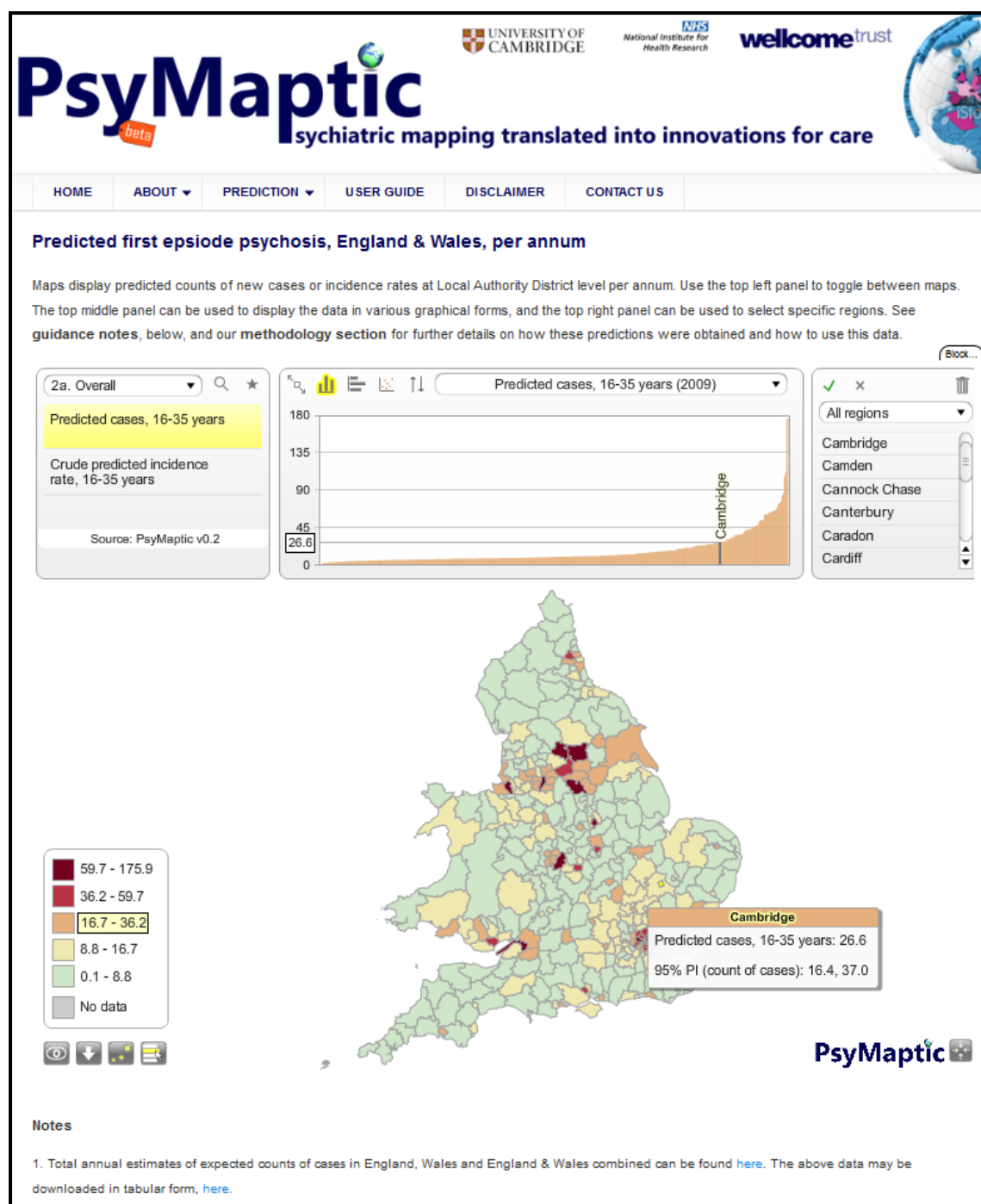


Figure legend: Screenshot shows the PsyMaptic prediction tool made freely available at [www.psymaptic.org](http://www.psymaptic.org). This example shows a prediction map of the annual expected count of new cases of psychotic disorder for people aged 16-35 years across 376 Local Authority Districts [LAD] in England & Wales from our candidate prediction model (Model 6). Each prediction is presented with corresponding 95% prediction intervals. Count data are categorised into the following percentiles: green: 0-50% of LAD; yellow: 50.1-75%; orange: 75.1-90%; red: 90.1-95%; dark red: 95.1-100%. Our PsyMaptic prediction maps are provided with additional graphical utility (histograms, scatterplots, region selection) and are freely available at [www.psymaptic.org](http://www.psymaptic.org)

Supplemental Figure 2: Proportional difference in expected counts of incident FEP cases per year, 16-35 years, between our prediction model and the Department of Health's uniform rate upon which EIS commissioning was based in England & Wales

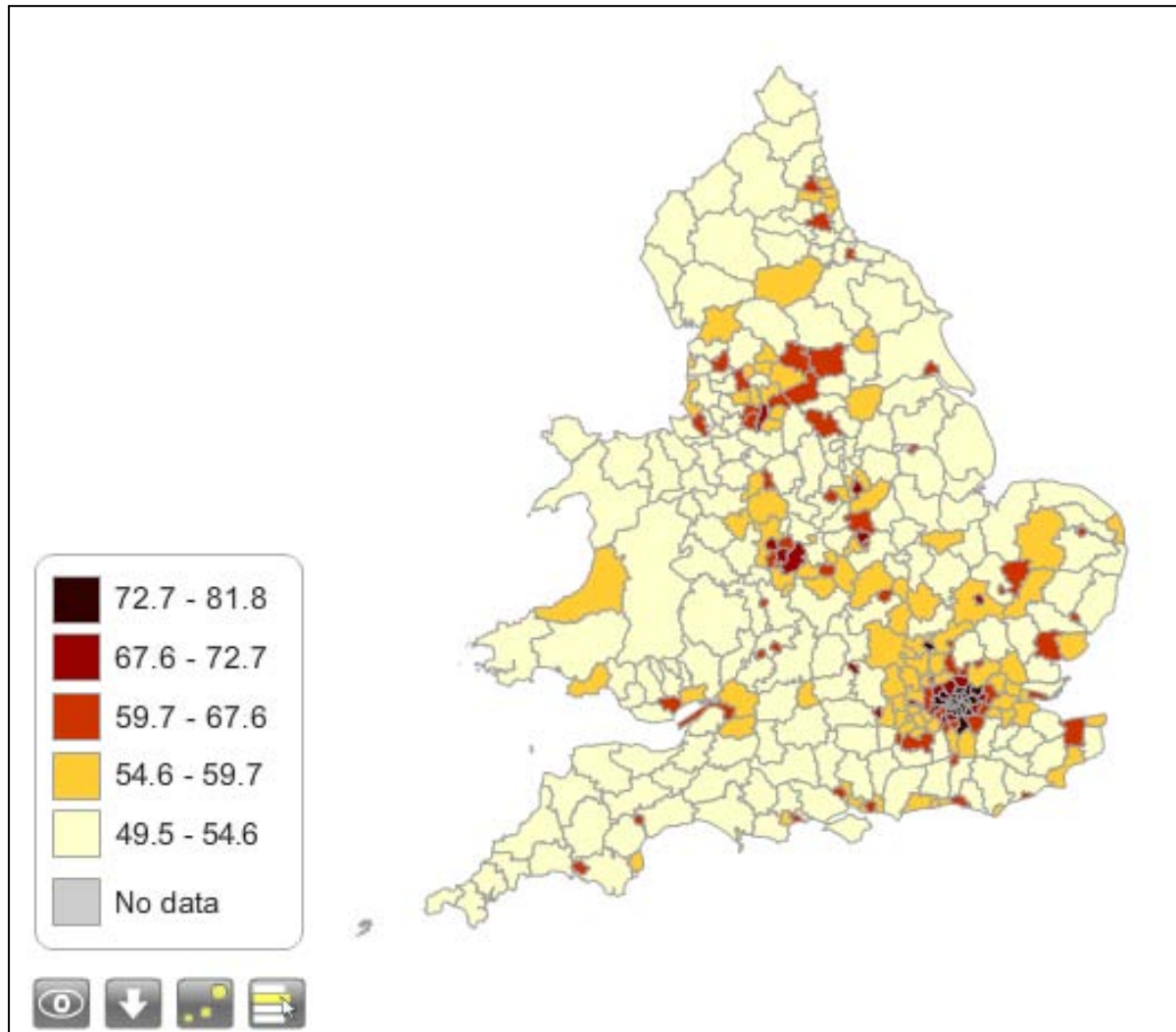


Figure legend: Annual difference in predicted counts of psychotic disorder between our proposed prediction model (Model 6) and the Department of Health's uniform rate of 15 new cases per 100,000 people per year, upon which EIS were based, expressed as a proportion. It can be interpreted as the proportion of expected cases, aged 16-35 years old, from our models which the Department of Health's uniform rate would not have predicted to have occurred in each LAD. See [www.psymaptic.org](http://www.psymaptic.org) for interactive maps.



**A population-level prediction tool for the incidence of first episode psychosis: translational epidemiology based on cross-sectional data**

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3 **A population-level prediction tool for the incidence of first episode psychosis: translational**  
4 **epidemiology based on cross-sectional data**  
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10 **For submission to BMJ Open**  
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42 Word count: 5,478  
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48 **Access to online data:** Part of the development of this manuscript includes the visualisation of prediction data in  
49 map and tabular format on a website created for this project: [www.psymaptic.org](http://www.psymaptic.org). We have password-protected  
50 relevant prediction data on these pages so only editors and peer reviewers can access this data until the peer  
51 review process is complete. We invite you to access these pages by visiting [www.psymaptic.org](http://www.psymaptic.org) and navigating to  
52 "*prediction>for peer reviewers*" on the top menu bar. From here, you can access the data as *prediction maps*,  
53 *national summary tables* or *downloadable data*. Please enter the password **pr2012** when prompted.  
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## Abstract

*Objectives:* Specialist early intervention services [EIS] for people aged 14-35 years with first episodes of psychosis [FEP] have been commissioned throughout England since 2001. A single estimate of population need was used everywhere, but true incidence varies enormously according to sociodemographic factors. We sought to develop a realistically-complex, population-based prediction tool for FEP, based on precise estimates of epidemiological risk.

*Design & participants:* Data from 1037 participants in two cross-sectional population-based FEP studies were fitted to several negative binomial regression models to estimate risk coefficients across combinations of different sociodemographic and socioenvironmental factors. We applied these coefficients to the population at-risk of a third, socioeconomically different region to predict expected caseload over 2.5 years, where observed rates of ICD-10 F10-39 FEP had been concurrently ascertained via EIS.

*Setting:* Empirical data from London, Nottingham and Bristol predicted counts in the population at-risk in the East Anglia region of England.

*Main outcome measures:* Observed counts compared with predicted counts (with 95% prediction intervals) at regional, EIS and local authority district [LAD] levels in East Anglia to establish predictive validity of each model.

*Results:* A model with age, sex, ethnicity and population density performed most strongly, predicting 508 FEP participants in EIS in East Anglia (95%PI: 459, 559), compared with 528 observed participants. This model predicted correctly in 5/6 EIS and 19/21 LAD. All models performed better than the current gold standard for EIS commissioning in England (716 cases; 95%PI: 664-769).

*Conclusions:* We have developed a prediction tool for incidence of psychotic disorders in England and Wales, made freely available online ([www.psymaptic.org](http://www.psymaptic.org)) to provide healthcare commissioners with accurate forecasts of FEP based on robust epidemiology and anticipated local population need. Initial assessment of some people who do not require subsequent EIS care means additional service resources, not addressed here, will be required.

## Background

Commissioners of health and social care require precise information on the health needs of their local populations<sup>1</sup>, especially if parity of mental and physical health is to be realised.<sup>2</sup> Mental health disorders alone represent the leading disease burden in the UK (22.8%).<sup>3</sup> They contribute substantially to healthcare expenditure and societal costs even before physical ill health is taken into account. The Centre for Mental Health estimated total costs of mental health to British health services and society at £105 billion in 2009/10,<sup>4</sup> a figure expected to double over the next 20 years.<sup>2</sup> These are serious challenges compounded by a paucity of information on which to commission appropriate services. Early intervention in psychosis services [EIS] for people aged 14-35 years with a first episode of psychosis [FEP] offer a useful example of failure to map services to local need.

EIS are a major evidence-based innovation, systematically commissioned throughout England and Wales over the past decade.<sup>5</sup> When EIS intervention is sustained there is evidence that people with psychosis achieve better functional and social outcomes.<sup>6-7</sup> Such services are also highly cost-effective.<sup>4 8-9</sup> However, EIS were originally commissioned on an anticipated rate of 150 new cases of any psychotic disorder per 1,000,000 of the total population per year in the Department of Health's Mental Health Policy Implementation Guide [MH-PIG].<sup>5</sup> In 2001 in England and Wales, 29.3% of the population were aged 14-35 years old, meaning that the MH-PIG commissioned incidence rate was approximately 51 cases per 100,000 person-years in the age range covered by EIS. Following their deployment, anecdotal reports began to emerge from EIS in different regions to suggest that a uniform figure for commissioning was simultaneously under-<sup>10</sup> and over-estimating<sup>11</sup> actual observed need in urban and rural populations, respectively. Recent epidemiological evidence of FEP incidence in rural communities in England has suggested that rates are somewhat lower than the uniform figure upon which services were commissioned,<sup>12-13</sup> confirming previous calls that a "one-size-fits-all" prescription for EIS implementation is unlikely to lead to the efficient allocation of finite mental health resources.<sup>14-15</sup>

Using rich epidemiological data on variation in the incidence of first episode psychosis according to major sociodemographic risk factors,<sup>16-19</sup> we describe the development and validation of a population-level prediction tool capable of accurately estimating the expected incidence of psychiatric disorder, based on the sociodemographic structure of the population in a given region. Applied to FEP as proof-of-concept, we show it is possible to closely predict expected incidence in a given population, where the observed count of cases was within the prediction intervals forecast by our models. We applied our

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3 most precise prediction model to the population of England and Wales to provide health commissioners  
4 with a translational epidemiological prediction tool to underpin information-based service planning.  
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## 8 **Methods**

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10 Our prediction models were based on epidemiological data from the Aetiology and Ethnicity in  
11 Schizophrenia and Other Psychoses [ÆSOP] and the East London First Episode Psychoses [ELFEP]  
12 studies,<sup>18,20</sup> two methodologically-similar population-based FEP studies. We fitted various count-based  
13 regression models with different combinations of sociodemographic and socioenvironmental factors,  
14 well-established in the literature to be associated with the incidence of psychotic disorder.<sup>21-22</sup> We first  
15 established the *relative internal validity* of each model by estimating internal model fit diagnostics to  
16 assess how well each model fitted the empirical data (henceforth, the *prediction sample*). We next  
17 sought to estimate the *external validity* of each model by applying model-based parameter coefficients  
18 to the population structure of a purposefully different region of England, East Anglia (henceforth, the  
19 *validation sample*). This out-of-sample prediction technique allowed us to obtain the expected incidence  
20 of disorder in this region forecast by each model, which we compared with observed rates  
21 simultaneously ascertained in this region via the ongoing Social Epidemiology of Psychoses in East Anglia  
22 [SEPEA] study.<sup>13</sup> We performed various model fit diagnostics to identify which, if any, model  
23 demonstrated utilisable predictive capability.  
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### 37 **Empirical data underlying prediction models (*prediction sample*)**

#### 38 *Case ascertainment (numerator)*

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40 The designs of the ÆSOP and ELFEP studies have been described in detail elsewhere,<sup>18,20</sup> with features  
41 relevant to the present paper summarised here. Case ascertainment took place over two years in ELFEP  
42 (Newham: 1996-8; Tower Hamlets & Hackney: 1998-2000) and the Southeast London and Nottingham  
43 centres of the ÆSOP study (1997-9), and over the first 9 months of 1997 in Bristol (ÆSOP). All service  
44 bases were screened regularly for potential new contacts aged 16-64 years (18-64 in ELFEP) resident  
45 within these catchment areas. Leakage studies were conducted to identify participants missed by this  
46 initial screen, but meeting inclusion criteria for FEP.<sup>18,20</sup> All participants who received an ICD-10 F10-39  
47 diagnosis for psychotic disorder following assessment via the Schedules for Clinical Assessment in  
48 Neuropsychiatry were included in the incident sample, except those with an organic medical basis to  
49 their disorder or profound learning difficulty. Data on age-at-contact, sex and ethnicity were collected  
50 on included participants. We geocoded participants' residential postcode at first contact to their  
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3 corresponding local authority district [LAD] to allow us to model possible neighbourhood effects  
4 associated with the incidence of psychotic disorder, such as population density or socioeconomic  
5 deprivation.  
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#### 10 *Population at-risk*

11 We estimated the population at-risk using the 2001 Census of Great Britain, adjusted for study duration,  
12 and stratified by age group (16-17, 18-19, then 5-year age bands), sex and ethnicity. Ethnicity was based  
13 on self-ascription according to one of ten categories derived from the census: white British, non-British  
14 white, black Caribbean, black African, Indian, Pakistani, Bangladeshi, mixed white & black Caribbean,  
15 other mixed ethnic backgrounds and all other ethnicities.  
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#### 22 *Socioenvironmental variable estimation*

23 We estimated LAD -level deprivation using the 2004 Index of Multiple Deprivation [IMD] in England,  
24 which estimated domains of deprivation using measures predominantly collected close to the time of  
25 our case ascertainment periods (see Box 1).<sup>23</sup> We z-standardised English LAD IMD scores to have a mean  
26 of zero and standard deviation of one, and extracted IMD z-scores for the 14 LADs in the ÆSOP and  
27 ELFEP studies. To inspect whether any particular deprivation domain was a better predictor of psychosis  
28 incidence than IMD, we also considered LAD-level income deprivation, employment deprivation and the  
29 extent of deprivation in our models (Box 1). We estimated population density by dividing LAD usual  
30 resident population by its area (in hectares), using ArcGIS 9.3 software.  
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40 <[Box 1 about here](#)>

#### 41 42 43 **Observed data for external validation of prediction models (*validation sample*)**

44 Observed participants and population at-risk data for our *validation sample* was obtained from the  
45 SEPEA study, an ongoing study of the incidence of psychotic disorders incepted over three years (2009-  
46 12) through one of six EIS covering 20 LAD and a subsection of one LAD (the town of Royston,  
47 Hertfordshire) in Norfolk (three EIS: West, Central and Great Yarmouth & Waveney), Suffolk (one EIS)  
48 and Cambridgeshire, Royston & Peterborough (CAMEO North and South EIS).<sup>13</sup>  
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#### 55 *Case ascertainment*

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3 To establish the incepted incidence of first episode psychosis as seen through EIS, entry criteria for the  
4 SEPEA study were:  
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- 8 • Referral to an EIS in East Anglia for suspected first episode of psychosis
  - 9 • Aged 16-35 years old at first referral to EIS (17-35 years in CAMEO services)
  - 10 • Resident within the catchment area at first referral
  - 11 • First referral during case ascertainment period (2009-12)
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17 At six months after EIS acceptance, or discharge from the service, whichever was sooner, we asked the  
18 clinician responsible for care to provide an ICD-10 F10-39 psychiatric diagnosis using all information  
19 available. We excluded participants without a clinical FEP diagnosis, or participants presenting with an  
20 organic basis to their disorder or profound learning disability. For remaining participants, basic  
21 sociodemographic and postcode information was recorded and classified in the same way as in the  
22 *prediction sample*. We included participants presenting to EIS during the first 2.5 years of the ongoing  
23 SEPEA study.  
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### 30 31 *Population at-risk*

32 We estimated the population at-risk of East Anglia using 2009 mid-year census estimates published by  
33 the Office for National Statistics [ONS] at LAD-level, by age group, sex and ethnicity.<sup>24</sup> These estimates  
34 used the 2001 census base, adjusted for immigration, births and deaths each year. It was not possible to  
35 obtain 2009 mid-year estimates for the town of Royston, because data were only published at LAD level.  
36 Here, we thus used denominator data from the 2001 census data, in order to estimate the population  
37 at-risk in Royston. We do not believe this would have substantially invalidated our results as this town  
38 represented 0.6% of the overall population at-risk (n=9,555) in the SEPEA study. Denominator data were  
39 multiplied by 2.5 to account for person-years of exposure in the *validation sample*.  
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### 48 *Socioenvironmental variable estimation*

49 For each LAD in the SEPEA study we obtained corresponding socioenvironmental variables to those  
50 included in our *prediction sample*, using updated data collected as close to the SEPEA case  
51 ascertainment period as possible. Population density was estimated using 2009 mid-term population  
52 estimates. Our measures of deprivation were derived from the IMD 2010,<sup>25</sup> which was estimated in an  
53 analogous way to 2004 data, but collected from sources obtained immediately prior to the SEPEA study.  
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## Statistical techniques

### *Dataset generation*

We constructed a dataset for the regression analysis of count data by pooling data from the ÆSOP & ELFEP studies (the *prediction sample*). Data were stratified by age group, sex, ethnicity and LAD, such that each stratum represented the total count of FEP cases in a unique sociodemographic group for a given LAD, with a corresponding estimate of the population at-risk, treated as an offset in our models. Our socioenvironmental measures (population density, deprivation) were adjoined to the dataset for each LAD.

Population at-risk data from the *validation sample* were stratified in the same way and retained in a separate database. The count of cases was entered as a variable with missing values, which we could predict into, given the model coefficients and population at-risk.

### *Prediction models*

We used the *prediction sample* data to fit negative binomial regression models to obtain parameter coefficients of incidence for the sociodemographic and socioenvironmental factors included in each model. We considered the internal and external predictive capabilities of six models, all of which contained age group, sex, an age-sex interaction term and ethnicity. Model 1 contained no further covariates. Model 2 also included IMD. We replaced IMD with either income, employment or the extent of deprivation, respectively, in models 3-5. Model 6 included population density. Initial exploration of the *prediction sample* data indicated the presence of possible over-dispersion (variance ( $\delta^2=1.37$ ) exceeded mean ( $\mu=0.4$ ) count of cases) so negative binomial regression was preferred to Poisson regression since it explicitly models any over-dispersion with an extra dispersion parameter.

### *Internal model cross-validation & prediction*

We assessed internal model validity in three ways. First we used Akaike's Information Criterion [AIC] to assess the respective overall fit of each model to the data. Second, we conducted K-fold cross validation to assess each model's internal validity to predict cases within the *prediction sample*. This method randomly allocated strata in the *prediction sample* into  $K$  subsets. Each model was then re-estimated on  $K-1$  subsets (the *training data*) to predict expected counts of cases in the  $K^{\text{th}}$  subset (the *test data*). This was repeated over  $K$  trials, such that each stratum in the dataset appeared exactly once as the *test data*.

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At the end of this process, we derived Lin's concordance correlation coefficient [CCC] and 95% confidence intervals [95%CI] to estimate the correlation between predicted and observed counts of cases across all strata in the *prediction sample*. Finally, we estimated the root mean squared error [RMSE] to determine the average error between fitted and observed values from each model, where lower RMSE scores indicated smaller prediction error. The RMSE is derived as

$$RMSE = \sqrt{\frac{\sum_{i=1}^n (y_i - \hat{y}_i)^2}{n}}$$

where  $y_i$  and  $\hat{y}_i$  are the observed and predicted count of cases in the  $i^{\text{th}}$  stratum, respectively, and  $n$  is the number of strata.

We repeated K-fold cross-validation  $h$  times, generating  $K$  new random divisions of the data each time. We retained model fit diagnostics across  $Kh$  iterations, and reported the mean of Lin's CCC and RMSE to provide summary cross-validation statistics for each model. We specified  $K=10$  and  $h=20$ , as recommended for cross-validation to obtain precise model fit diagnostics.<sup>26</sup>

#### *External model prediction & validation*

We retained parameter coefficients from each model (using the full *prediction sample* data) and applied these to the corresponding population at-risk in the *validation sample* dataset. This gave out-of-sample prediction estimates for the expected count of cases in each stratum of the *validation sample*, given the model. We summed expected counts across relevant strata to estimate the (i) total predicted count of cases in the SEPEA region, (ii) predicted counts in each EIS, and (iii) predicted counts by LAD. These counts were further stratified by broad age group (16-35, 36-64 and 16-64 years). Because census (denominator) data was unavailable for 35 year olds alone (needed to estimate their contribution to predicted counts in the age range for EIS, 16-35 years) we assumed the risk coefficient was the same across all ages within the 35-39 year old age group. We apportioned predicted counts on a 1:4 ratio (35 years: 36-39 years) to their respective broad age groups.

To determine how well the MH-PIG<sup>5</sup> figure of 51 new cases per 100,000 people per year for EIS performed as a predictive tool, we also estimated the predicted count of cases in the *validation sample* under this scenario, which we termed "Model 7".



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5 We derived prediction intervals [95% PIs] for all summary predictions from first principles for each  
6 negative binomial regression model, since their derivation is not straightforward, nor routinely  
7 implemented by statistical software. Prediction intervals are similar to confidence intervals, but account  
8 for standard errors introduced in both the *prediction* and *validation* samples. We developed a  
9 bootstrap-like approach to obtain prediction intervals from each model by simulating 1000 model-based  
10 realisations of the quantities we wished to predict, where we took the parameters to be the maximum  
11 likelihood estimates. We obtained the lower and upper bounds of the prediction intervals as the  
12 corresponding quantiles of the simulated realisations (see Appendix for full details).  
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21 To assess each model's external predictive capabilities, we considered five markers of predictive  
22 accuracy. We compared the number of times the observed count of cases in the SEPEA study fell within  
23 the prediction intervals estimated from each model for (i) the SEPEA region, (ii) at EIS level, and (iii) at  
24 LAD level. We also derived EIS- and LAD-level RMSE scores to estimate prediction error from each model  
25 in our *validation sample*. We ranked model performance (1: best, 7: worst) on these five measures, and  
26 estimated an overall mean rank to determine the overall predictive validity of each model.  
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33 Observational data on first episode psychosis in our *validation sample* were not available for the age  
34 range 36-64 years, so external validation was restricted to the 16-35 year old group. For completeness,  
35 however, we also reported overall predicted count of cases for this age group from each model.  
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#### 39 *Extrapolation to the United Kingdom*

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41 Guided by our validation procedures, we identified which model had the greatest overall predictive  
42 validity, and proposed this as a candidate for FEP incidence prediction in England and Wales. We  
43 repeated out-of-sample prediction on the sociodemographic and socioenvironmental population  
44 characteristics of each LAD in England and Wales to obtain national and LAD-level predictions.  
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48 Denominator data was obtained from the ONS 2009 mid-term estimates and stratified as previously  
49 described. Overall counts were derived for three broad age groups (16-35, 36-64 and 16-64 years), and  
50 for each of these, by sex and ethnicity. 95% PIs were estimated as before. We visualised this data on  
51 maps and in tables to provide healthcare planners and commissioners with an easy-to-use tool to  
52 forecast the expected incidence of psychosis in England and Wales. We have made this available as a  
53 free, open-use prediction tool, known as PsyMaptic (version 0.4) (Psychiatric Mapping Translating  
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Innovations into Care; [www.psymaptic.org](http://www.psymaptic.org)). Counts of cases predicted by our model were compared with those obtained under the Department of Health's uniform rate in each LAD. We expressed these comparisons as ratios with 95% CIs derived using the same method as for standardised morbidity ratios [SMR]. This approach was conservative because here we substituted the usual numerator in an SMR, the observed, O, for a predicted count. Unlike an observed count, no sampling variation is present for the predicted count, only uncertainty due to the model from which the prediction was estimated. Since variance in the prediction is therefore much smaller than the variance normally present for the numerator (O) this led to conservative estimates of 95% CI. Ratios in LAD where 95% CI did not span unity could therefore be interpreted as regions where there was strong evidence that the predictions from our model differed significantly from those predicted by the Department of Health's uniform rate.

### Software

All negative binomial regression models, out-of-sample prediction and estimation of 95% PI were conducted in R (version 2.15.1). Internal cross-validation and model-fit diagnostics were conducted in Stata (version 11). Prediction maps for England and Wales were created using StatPlanet Plus (version 3.0) visualisation software.<sup>27</sup>

## Results

### Prediction sample

Our prediction models contained data on 1,037 persons with a first episode psychosis in the ÆSOP (n=553; 53.3%) and ELFEP (n=484; 46.7%) studies, ascertained from over 2.4m person-years at-risk. Twelve participants were excluded from the original ÆSOP sample because they were of no fixed abode and could not be geocoded to an LAD.<sup>18</sup>

The population at-risk in the *prediction sample* came from LAD with higher median levels of multiple and employment deprivation, extent of deprivation and population density than the population at-risk in the *validation sample*, though there were no statistically significant differences in median income deprivation between the two samples (Supplemental Table 1).

[<Supplemental Table 1 about here>](#)

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Parameter coefficients obtained from the full prediction sample following negative binomial regression are shown in Table 1. As previously reported from these data,<sup>20 28</sup> incidence rates were generally raised in ethnic minority groups compared with the white British population. Models 2-6 included a measure of LAD deprivation (Models 2-5) or population density (Model 6), which were all significantly associated with increased incidence of psychotic disorder, after control for individual-level confounders. Each of these models produced a lower AIC score than a model fitted solely with individual-level covariates (Model 1), indicating better internal fit. Internal cross-validation suggested all models achieved good CCC agreement between predicted and observed cases, with low RMSE values (Table 1).

<Table 1 about here>

### Validation sample

#### *Observed participants*

We identified 572 participants over the first 30 months of the SEPEA study, aged 16-35 years old, who met acceptance criteria for EIS in East Anglia. We excluded 44 participants (8.0%) who did not meet clinical criteria for ICD-10 psychotic disorder. This left an incidence sample of 528 participants from nearly 1.4m person-years at risk (37.8 per 100,000 person-years; 95%CI: 34.7, 41.2). A further 2.3m person-years at-risk accrued in the same region for people aged 36-64 years over this period. Median levels of multiple, income and employment deprivation in the region did not differ significantly from the remainder of England, although median population density and extent of deprivation in East Anglia were lower than elsewhere in England (Supplemental Table 1).

<Table 2 about here>

#### *External model prediction & validation*

The overall observed count of cases, aged 16-35 years, in the *validation sample* (n=528) fell within 95% prediction intervals in only two of seven tested models (Models 4 and 6, Table 2). Of these, the observed count was closest to the point estimate for Model 6 (508.5; 95% PI: 449.0, 559.0), fitted with age group, sex, their interaction, ethnic group and LAD population density. The observed count of cases also fell within prediction intervals from this model in five of six EIS in the study region, and 19 of 21 LADs, the most of any model (Table 3). This model had the lowest error scores at EIS (RMSE=11.9) and LAD (RMSE=5.9) levels of any model. Overall, Model 6 was ranked highest across all external model fit

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diagnostics (Table 3). All models outperformed the Department of Health’s uniform figure of 51 cases per 100,000 people per year (Model 7), which generally overestimated cases in the *validation sample* (overall prediction: 715.7 cases; 95% PI: 664.0, 769.0).

We also reported predicted cases aged 36-64 years old from our models (Table 3), although we could not test these in the *validation sample*. Model 6 predicted an additional 262.9 cases aged 36-64 years over a 2.5 year period in East Anglia (95% PI: 233.0, 297.0).

<Table 3 about here>

### *Extrapolation to England and Wales*

We predicted the expected count and incidence of first episode psychosis per annum in each LAD in England and Wales based on Model 6, and visualised this data in maps and tables freely available at [www.psymaptic.org](http://www.psymaptic.org). Many maps can be visualised (for example, Supplemental Figure 1), including overall predicted incidence counts and rates for each broad age group at LAD level, by sex and ethnic group, as well as a variety of population and socioenvironmental data. According to our model, the annual number of new FEP cases in England and Wales would be 8745 (95% PI: 8558, 8933), of which our model predicted 67.9% (N=5939; 95% PI: 5785, 6102) would be seen through EIS. Only 176 (95% PI: 151, 203) cases aged 16-64 years were forecast in Wales per annum. Assuming our prediction model is accurate, it indicated that the Department of Health’s current uniform rate of 51 per 100,000 person-years was higher than the predicted point estimates for rates forecast by our PsyMaptic model in 351 LAD (93%) in England and Wales, but was lower than predicted by our model in Birmingham and several London boroughs (Supplemental Figure 2, left hand map). Under a conservative approach, these differences achieved statistical significance in parts of London (where the Department of Health’s model underestimated need as predicted by PsyMaptic), and in some more rural parts of England and Wales (where the Department of Health’s model over-estimated need) (Supplemental Figure 2, right hand map).

<Supplemental Figures 1 & 2 about here>

## **Discussion**

### **Principal findings**

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3 We have developed and tested several epidemiological prediction models to forecast FEP incidence in  
4 England and Wales, having taken into account regional differences in the sociodemographic and  
5 socioenvironmental profile of different populations. Inspection of our data suggested that a model fitted  
6 with age group, sex, their interaction, ethnic group and LAD-level population density provided the  
7 greatest external predictive validity when compared with the observed FEP caseload ascertained  
8 through EIS in our *validation sample*. This model also had good internal validity across the entire age  
9 range (16-64 years). All models performed significantly better in predicting the incidence of clinically  
10 relevant first episode psychosis than the Department of Health's current gold standard for EIS  
11 commissioning,<sup>5</sup> based on a uniform incidence rate. Our data suggested the figure used to commission  
12 EIS over-estimated the likely true incidence rates of FEP in rural areas and under-estimated them in  
13 urban settings, although we acknowledge that commissioning decisions will need to be based on several  
14 additional factors, including the level of pre-clinical or non-psychotic psychopathology requiring  
15 assessment at initial referral to EIS, and variation in service organisation, remit and delivery.  
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### 27 **Limitations & future development**

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29 Our prediction models were based on epidemiological data obtained from large, robust population-  
30 based FEP studies for people aged 16-64 years.<sup>18-19</sup> Our best-fitting model had good internal validity over  
31 this age range, and good external validity over the age range 16-35 years. While this covered the  
32 majority of adult onset psychosis cases seen in mental health services, including EIS, we recognise that  
33 some EIS teams incept people from 14 years old. We were unable to extrapolate our models to this age  
34 range, given the current absence of incidence data for this group in England. Data from Scandinavia  
35 suggest that the incidence of such "early onset" psychoses is absolutely low,<sup>29</sup> although the rate may  
36 have been increasing in the last few decades, probably as a result of movement towards earlier  
37 detection. We were also unable to externally validate prediction models for people aged 36-64 years,  
38 because comparable observed incidence data was not available in our *validation sample*. We have no  
39 reason to believe our predictions will be invalid for this group, however, since the empirical data which  
40 underpinned our models was ascertained from the same two large, well-conducted studies as for data  
41 on the younger age group.<sup>18-19 28</sup> Furthermore, published findings from these studies are consistent with  
42 the wider epidemiological literature for psychosis in England and internationally.<sup>17 21 30</sup> It will be  
43 important to validate the predictive capability of our model(s) in this age range, and we will seek to  
44 identify suitable samples to do so in future versions of PsyMaptic.  
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3 All prediction models had reasonable internal validity, although our proposed model performed slightly  
4 worse (most noticeably for AIC) than models which included deprivation (i.e. models 2-4) instead of  
5 population density. Our decision to use model 6 as our proposed candidate for the prediction tool was  
6 supported by the fact that it produced the most accurate external forecasts of any model, despite  
7 considerable socioenvironmental differences between regions in our *prediction* and *validation* samples.  
8 We were unable to predict the expected incidence of psychotic disorder in geographical areas smaller  
9 than LADs, such as electoral wards (N~6000), or to other parts of the UK, because appropriate  
10 denominator data was not published as mid-term census estimates. The 2011 census will provide small  
11 area and national data for the whole of the UK, scheduled for release by ONS in mid-2013. This will allow  
12 us to update our tool to the latest population estimates for the UK, and refine our PsyMaptic tool at a  
13 smaller geographical level for fine-grained healthcare commissioning. We will then be able to develop  
14 models to explore cross-level interactions, such as the association between individual ethnicity and  
15 neighbourhood-level ethnic density. Small area prediction models will require a multilevel approach, not  
16 attempted here, because obtaining predictions from multilevel random effects models is not  
17 straightforward and requires active statistical development.  
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31 We believe case ascertainment in our *validation sample* led to a reliable estimate of the incidence of  
32 psychotic disorder for people aged 16-35 years old. EIS were the only mental health service for people  
33 aged 14-35 years experiencing a first episode of psychosis in East Anglia, minimising the potential for  
34 under-ascertainment in the population at-risk when derived from careful epidemiological design.<sup>13</sup> We  
35 are confident that our *validation sample* also contained few false positive cases for any clinically-  
36 relevant psychoses, since participants were excluded who failed to meet acceptance criteria for EIS or  
37 who did not receive a clinical diagnosis of psychotic disorder during the first six months from initial  
38 referral. It is important to recognise that while our prediction models are based on diagnosed clinically  
39 relevant psychotic disorders, service commissioning will also need to account for additional pre-clinical  
40 or non-psychotic psychiatric morbidity presenting to EIS, particularly in services which operate early  
41 detection models or implement “watch-and-wait” briefs. The SEPEA data used to validate our models do  
42 not predict (1) the number of “false positive” subjects who may require psychiatric triage and  
43 assessment even though they are not accepted by EIS, or (2) the number of “true positive” subjects  
44 accepted by services, but who did not meet epidemiological criteria for inclusion in the *validation*  
45 *sample* of the SEPEA study (those living outside the catchment area at first contact, or those transferred  
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3 from other services); these people will consume varying degrees of service resources which needs to be  
4 considered in service planning.  
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8 We also note that pathways to care may affect the level of incidence observed in EIS, since many filters  
9 are likely to operate before subjects come to the attention of EIS. These will include local level service  
10 organisation and the relationship between Community Mental Health Teams [CMHTs], Child and  
11 Adolescent Mental Health [CAMHs] and EIS. Furthermore, acceptance criteria for entry to EIS vary,  
12 which will have a downstream effect on the number of new cases of clinically relevant psychoses  
13 received in each team. Future versions of PsyMaptic will include forecasts for specific psychotic  
14 disorders, as standardised research-based diagnoses (using OPCRIT<sup>31</sup>) are currently being collected in  
15 the ongoing SEPEA study in order to provide more detailed forecasts. Acceptance rates to EIS may also  
16 be influenced by local community awareness of such services. While our prediction models  
17 outperformed the current gold standard for EIS commissioning in England when restricted to clinically  
18 relevant caseloads, we recommend that our models are best interpreted as forecasts of the expected  
19 burden of first episode psychosis in given populations, and not the expected burden which will  
20 necessarily be seen through EIS given these issues.  
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32 We estimated prediction intervals from first principles [DJ] since there derivation is an area of statistical  
33 development.<sup>32</sup> We used a bootstrap-like methodology to produce 95% PI accounting for natural  
34 variation in the *validation sample*, but ignoring parameter uncertainty in the coefficients included in  
35 prediction models, which we assumed to be the true coefficients of risk in the population. Our approach  
36 therefore naturally led to slightly artificially narrow 95% PIs. This was not necessarily undesirable for the  
37 purpose of model validation and the precise prediction of expected counts because we wished to apply  
38 stringent criteria. Ideally, prediction intervals should take into account both these sources of variation,  
39 although we note that parameter uncertainty is usually small compared to the natural variation of the  
40 quantities of interest. The addition of more empirical data in the *prediction sample* would not lead to  
41 narrower PIs, though would tend to move the point estimate of risk for each coefficient closer to the  
42 true value in the population. We do not believe we have mis-estimated point estimates of risk across  
43 major sociodemographic groups, since our results accord with the wider literature.<sup>17 21-22</sup> We sought  
44 independent confirmation that our development of 95% PI were correct (personal communication with  
45 Prof Ian White, MRC Biostatistics Unit). We recommend that all prediction point estimates from our  
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PsyMaptic model are considered with their 95% PIs, which provide information about the natural variance in expected rates in the population.

### Meaning of the findings

If commissioners are to meet the Department of Health's vision to orientate health services around local need,<sup>1-2 5</sup> differences in demand for EIS and other mental and physical health services will need to be taken into account to allocate finite resources where they are most needed. The PsyMaptic prediction model provides proof-of-concept that when robust empirical epidemiological data is combined with accurate population at-risk estimates this can be realised. As such, our modelling approach could have utility in many other settings and for many disorders. Our translational approach demonstrated good internal and external validity to predict the expected incidence of first episode psychosis, particularly through EIS, where 76% and 63% of all male and female adult-onset FEP cases, respectively, will typically present.<sup>18</sup> Since their inception in 2002, EIS in England and Wales have reported both lower<sup>11</sup> and higher<sup>10</sup> caseloads than they were originally envisioned to manage,<sup>5</sup> with shortfalls or excesses in anticipated demand for services aligned to the degree of urbanisation in the underlying catchment area. Others have noted that EIS provision in rural areas may be difficult to implement effectively,<sup>14-15</sup> and while the MH-PIG acknowledged that "...[a]n understanding of local epidemiology is needed as the size of population covered will depend on a number of different factors" (p.55),<sup>5</sup> no further elaboration on how to achieve this was provided. We believe PsyMaptic provides a possible tool to overcome this challenge, improving the description and prediction of local population need beyond the MH-PIG and including individual- and neighbourhood-level indicators of local need.<sup>17</sup> From an aetiological perspective, we acknowledge that variables such as ethnicity or population density are likely to be markers for a suite of more complex, interactive social, genetic and environmental determinants of psychosis.<sup>33</sup>

Our models are not the first to be used to forecast mental illness needs in England and Wales,<sup>34</sup> though we believe this is the first attempt to forecast incidence rather than prevalence in the community. We recommend that our prediction methodology is used in conjunction with the wide range of public health observatory data available,<sup>35</sup> as well as the caveats presented above. PsyMaptic has been included with other indicators in the Joint Commissioning Panel for Mental Health's forthcoming guidance for commissioning of public mental health services.<sup>36</sup> Ongoing monitoring and audit of EIS will be vital to ensure services meet the fidelity criteria upon which they were originally commissioned,<sup>11 37</sup> including



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3 ensuring that service capacity matches local need as closely as possible. As part of this process, we will  
4 need to externally validate our models in a wider range of settings, refining them based on empirical  
5 observation.  
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10 We note that advocacy expressed for EIS by healthcare professionals in England and Wales broadly  
11 correlates with demand for services as predicted by PsyMaptic.<sup>38</sup> Though by no means universal,  
12 proponents of EIS tend to be located in major conurbations – such as London,<sup>39</sup> Birmingham<sup>40</sup> or  
13 Manchester<sup>7,41</sup> – where demand for EIS will be highest, while those who suggest EIS resources could be  
14 used more effectively elsewhere tend to work in more rural communities,<sup>15,38</sup> where but a handful of  
15 young people would be expected to come to the attention of EIS each year. It is possible that both sides  
16 are correct and that more resources are required to help with the tide of psychotic illness in inner cities.  
17 Resources might be used more effectively in other ways, elsewhere, so long as the needs of the small  
18 number of young people who suffer a FEP each year are met; a dedicated specialist EIS may not be the  
19 most effective approach when anticipated demand will be very low.  
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29 Given the significant downstream economic savings associated with spending on EIS as estimated in an  
30 urban setting,<sup>8</sup> PsyMaptic could be used to highlight regions where sufficient investment to appropriate  
31 mental health services would lead to greatest economic gains in terms of mental healthcare expenditure  
32 (assuming sustained intervention also leads to improved social and clinical benefit for patients<sup>6-7</sup>).  
33 PsyMaptic can also be used to highlight regional variation in demand according to age, sex and ethnic  
34 group, allowing service planners to tailor provision around the socio-cultural characteristics of their local  
35 populations. Our prediction tool for first episode psychosis, which translates robust empirical  
36 epidemiological data on psychosis risk to the population structure of different regions, offers a  
37 methodology for improving the allocation of finite mental health resources based around local need.  
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**Box 1: Description of included socioenvironmental variables <sup>1 2</sup>**

Variable	Classification & description
Multiple deprivation	Weighted data from routine national sources across 7 domains: income, employment, education, health, barriers to housing & services, living environment, crime. Continuous, z-standardised scores for analysis.
Extent of deprivation	Proportion of LAD population living in 20% most deprived SOA in England (%)
Income deprivation	Proportion of all people in LAD classified as income deprived (%)
Employment deprivation	Proportion of adults of working age in LAD classified as employment deprived (%)
Population density	Population density at LAD level (people per hectare).

IMD: Index of Multiple Deprivation; LAD: Local authority district; SOA: super output area; IQR: inter-quartile range

<sup>1</sup>*Prediction sample* sources: Population density – 2001 census estimates; Deprivation variables: 2004 Indices of Deprivation, predominantly collected from data sources close to A&SOP & ELFEP case ascertainment periods (i.e. 1997-2000)

<sup>2</sup>*Validation sample* sources: Population density – 2009 mid-year census estimates; Deprivation variables: 2010 Indices of Deprivation, predominantly collected from data sources just prior to SEPEA case ascertainment period (2008)

Table 1: Prediction models, covariates and fit: all clinically relevant psychoses (F10-39)

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Variable	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)
Age group*sex interaction <sup>1</sup>	p=0.07	p=0.06	p=0.06	p=0.06	p=0.06	p=0.06
Ethnicity						
White British	1	1	1	1	1	1
Non-British white	2.0 (1.5, 2.5)	1.7 (1.4, 2.2)	1.7 (1.3, 2.2)	1.7 (1.3, 2.2)	1.8 (1.4, 2.3)	1.7 (1.3, 2.2)
Black Caribbean	6.0 (4.9, 7.3)	5.3 (4.3, 6.5)	5.2 (4.3, 6.4)	5.2 (4.3, 6.4)	5.4 (4.5, 6.6)	5.1 (4.2, 6.3)
Black African	4.1 (3.3, 5.1)	3.6 (2.9, 4.5)	3.5 (2.8, 4.4)	3.5 (2.8, 4.4)	3.7 (3.0, 4.6)	3.5 (2.8, 4.3)
Indian	1.7 (1.2, 2.5)	1.5 (1.1, 2.2)	1.5 (1.0, 2.2)	1.5 (1.0, 2.1)	1.6 (1.1, 2.3)	1.6 (1.1, 2.2)
Pakistani	1.8 (1.2, 2.5)	1.6 (1.0, 2.5)	1.6 (1.0, 2.4)	1.6 (1.0, 2.4)	1.6 (1.1, 2.5)	1.8 (1.3, 2.7)
Bangladeshi	2.1 (1.5, 2.8)	1.7 (1.2, 2.3)	1.7 (1.2, 2.3)	1.6 (1.2, 2.2)	1.8 (1.3, 2.5)	1.8 (1.4, 2.4)
Mixed white & black Caribbean	4.3 (2.8, 6.7)	3.9 (2.5, 6.0)	3.9 (2.5, 6.0)	3.9 (2.5, 6.0)	4.0 (2.6, 6.1)	3.9 (2.5, 6.1)
Mixed, other	1.3 (0.8, 2.3)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)
Other	2.2 (1.6, 3.0)	1.9 (1.4, 2.7)	1.9 (1.4, 2.6)	1.9 (1.4, 2.6)	2.0 (1.4, 2.7)	1.9 (1.4, 2.7)
Socioenvironmental variables						
IMD (z-score)	-	1.184 (1.101, 1.274)	-	-	-	-
Extent of deprivation (%)	-	-	1.008 (1.004, 1.011)	-	-	-
Income deprivation (%)	-	-	-	1.025 (1.015, 1.035)	-	-
Employment deprivation (%)	-	-	-	-	1.062 (1.032, 1.093)	-
Population density (pph)	-	-	-	-	-	1.005 (1.003, 1.007)
Internal model fit diagnostics						
AIC <sup>2</sup>	2571.8	2552.4	2551.3	2549.6	2556.4	2556.3
Mean Lin's CCC (95%CI) <sup>3</sup>	0.75 (0.74, 0.77)	0.77 (0.75, 0.78)	0.77 (0.75, 0.79)	0.77 (0.75, 0.78)	0.77 (0.75, 0.78)	0.76 (0.74, 0.77)
Mean RMSE (s.d.) <sup>4</sup>	0.75 (0.11)	0.74 (0.11)	0.74 (0.10)	0.74 (0.10)	0.74 (0.11)	0.76 (0.13)

<sup>1</sup>All models fitted with age group by sex interaction given *a priori* evidence for effect modification.<sup>18 42</sup> Likelihood ratio test p-values reported between models with and without an interaction term fitted between age group and sex. Specific IRR not been reported for clarity, but available on request

<sup>2</sup>AIC: Akaike's Information Criterion – lower scores denote improved model fit

<sup>3</sup>CCC: Lin's correlation concordance coefficient. Higher scores indicate greater correlation between observed & predicted count of cases in the *prediction sample*. Mean CCC and 95%CI reported following *h*=20 trials during cross-validation.

<sup>4</sup>RMSE: Root mean squared error. Lower scores indicate lower prediction error. Mean RMSE and standard deviation (s.d.) reported following *h*=20 repeats of *k*-fold cross-validation, where *k*=10.

Table 2: Observed versus predicted cases in SEPEA study for all clinically relevant psychoses, 16-35 years <sup>1</sup>					
EIS	Observed	Model 1	Model 2	Model 3	Model 4
		Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)
<b>Overall total, 16-35 years</b>	<b>528</b>	<b>641.2 (586.0, 696.1)</b>	<b>468.5 (422.0, 518.0)</b>	<b>474.7 (429.0, 522.0)</b>	<b>487.5 (441.0, 535.0)</b>
Cameo North	55	84.7 (66.0, 106.0)	68.5 (52.0, 87.0)	67.8 (51.0, 86.0)	70.2 (53.0, 90.0)
Cameo South	137	163.6 (135.0, 192.0)	105.5 (84.0, 129.0)	111.7 (89.0, 134.0)	110.9 (90.0, 132.0)
West Norfolk	25	29.2 (18.0, 41.0)	23.0 (13.0, 35.0)	22.0 (12.0, 32.0)	23.4 (14.0, 34.0)
Central Norfolk	121	162.6 (136.0, 191.0)	122.6 (99.0, 148.0)	123.0 (100.0, 149.0)	128.3 (104.0, 152.0)
Great Yarmouth & Waveney	60	49.1 (34.0, 65.0)	41.6 (28.0, 55.0)	39.9 (27.0, 53.0)	42.9 (30.0, 57.0)
Suffolk	130	151.9 (126.0, 178.0)	107.4 (85.0, 128.0)	110.3 (88.0, 133.0)	111.7 (90.0, 136.0)
Overall total, 36-64 years	-	332.2 (292.0, 373.0)	244.0 (213.0, 276.0)	248.6 (216.0, 280.0)	256.3 (228.0, 291.0)
EIS	Observed	Model 5	Model 6	Model 7	
		Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)	
<b>Overall total, 16-35 years</b>	<b>528</b>	<b>477.1 (428.0, 523.0)</b>	<b>508.5 (459.0, 559.0)</b>	<b>715.6 (664.0, 769.0)</b>	
Cameo North	55	69.1 (52.0, 88.0)	64.5 (48.0, 82.0)	92.1 (74.0, 111.0)	
Cameo South	137	100.7 (79.0, 123.0)	131.1 (108.0, 157.0)	169.0 (144.0, 195.0)	
West Norfolk	25	24.7 (16.0, 35.0)	22.3 (13.0, 33.0)	35.8 (25.0, 48.0)	
Central Norfolk	121	128.2 (105.0, 153.0)	132.5 (108.0, 157.0)	187.7 (161.0, 215.0)	
Great Yarmouth & Waveney	60	47.7 (35.0, 63.0)	38.0 (26.0, 51.0)	59.1 (44.0, 74.0)	
Suffolk	130	106.6 (86.0, 128.0)	120.0 (96.0, 143.0)	172.1 (147.0, 198.0)	
Overall total, 36-64 years	-	249.7 (221.0, 284.0)	262.9 (233.0, 297.0)	1175.4 (1109.0, 1243.0)	

<sup>1</sup>Numbers in green denote where observed count fell within 95% prediction interval [95% PI] for people aged 16-35 years. Observed data for people aged 36-64 years in the *validation sample* was not available.

Model 1: Age group, sex, their interaction and ethnicity

Model 2: Model 1 + IMD

Model 3: Model 1 + extent of deprivation

Model 4: Model 1 + income deprivation

Model 5: Model 1 + employment deprivation

Model 6: Model 1 + population density

Model 7: Department of Health uniform figure for EIS of 15 new cases per 100,000 people per year.

Table 3: External model validation diagnostics<sup>1</sup>

Model	Overall correct prediction? [rank]	EIS (N=6)		LAD (N=21)		Mean ranking [rank of mean ranking]
		Number correct [rank]	RMSE [rank]	Number correct [rank]	RMSE [rank]	
Model 1	No [3]	4 [2]	25.6 [6]	18 [2]	8.1 [6]	3.8 [4]
Model 2	No [3]	3 [6]	18.4 [4]	17 [5]	6.9 [4]	4.4 [6]
Model 3	No [3]	4 [2]	16.4 [3]	18 [2]	6.5 [3]	2.6 [3]
Model 4	Yes [1]	4 [2]	16.3 [2]	18 [2]	6.4 [2]	1.8 [2]
Model 5	No [3]	4 [2]	19.4 [5]	16 [6]	7.1 [5]	4.2 [5]
Model 6	Yes [1]	5 [1]	11.9 [1]	19 [1]	5.9 [1]	1.0 [1]
Model 7	No [3]	1 [7]	38.1 [7]	13 [7]	11.0 [7]	6.2 [7]

<sup>1</sup>For each diagnostic, models are placed in rank order [1=best model, 7=worst model] with ties given the same ranking. The mean ranking and rank provide an estimate of the overall performance of various models.

RMSE: Root mean squared error (lower scores indicate lower error); EIS: Early Intervention in Psychosis Service; LAD: Local Authority District



**Article Summary****Article Focus**

- Commissioners require precise information on the health needs of their local populations to effectively plan health services
- A failure to arm mental health commissioners with precise epidemiological data led to mis-estimation of actual activity in early intervention in psychosis services [EIS]
- We sought to develop a prediction tool for the incidence of first episode psychosis [FEP], by applying precise estimates of epidemiological risk in various sociodemographic groups to the structure of the population at-risk in a second region, where the observed incidence had been concurrently ascertained

**Key Messages**

- A model of psychosis incidence which included age, sex, ethnicity and population density yielded precise FEP predictions in our second region, out-performing the Department of Health in England's current gold standard for EIS commissioning.
- We have translated this model into a freely available prediction tool ([www.psymaptic.org](http://www.psymaptic.org)) to facilitate evidence-based healthcare commissioning of socioculturally relevant services according to local need
- Our tool could be extended to many international settings and other disorders to inform healthcare commissioning, when epidemiological risk can be well-characterised and the structure of the underlying population at-risk is known

**Strengths and limitations**

- Our modelling approach used robust epidemiological data from two large studies of first episode psychosis in England to provide estimates of incidence in a third study region, producing accurate FEP forecasts
- While our models provide estimates of the expected clinical burden of FEP in the community, services may see a broader range of psychopathology consuming resources, or incepted rates may be influenced by supply-side organisational factors
- Due to data availability it was not possible to validate our prediction tool in settings outside of England and Wales, or for specific psychotic disorders. As data become available we will extend the capability of our prediction tool.

Supplemental Table 1: Socioenvironmental variables at local authority district [LAD] level considered in epidemiological prediction models

Variable		England <sup>1</sup>	Prediction sample <sup>2</sup>	Validation sample <sup>1</sup>	Mann-Whitney test <sup>3</sup> : Z; p-value	
					Prediction vs. Validation	Validation vs. England
Number of LAD	-	326	14	20 (+1 partial)	-	-
Multiple deprivation (z-standardised)	Median (IQR): Min/Max:	<u>0 (1)</u> <sup>4</sup> -1.7 / 2.9	1.0 (-0.5, 2.4) -1.1 / 2.9	-0.7 (-1.0, 0.3) -1.4 / 1.0	2.4; p=0.02	1.5; p=0.12
Extent of deprivation (%)	Median (IQR): Min/Max:	9.0 (1.3, 23.9) 0.0 / 83.6	28.0 (4.0, 63.0) 0.0 / 83.0	1.4 (., 12.8) 0.0 / 29.7	2.4; p=0.02	2.2; p=0.03
Income deprivation (%)	Median (IQR): Min/Max:	11.7 (8.6, 16.1) 3.9 / 32.8	15.5 (8.2, 24.7) 5.9 / 34.4	9.0 (8.2, 14.9) 6.0 / 19.1	1.5; p=0.14	1.3; p=0.19
Employment deprivation (%)	Median (IQR): Min/Max:	8.0 (5.8, 10.8) 2.1 / 18.8	11.6 (6.1, 14.1) 6.1 / 14.1	6.4 (5.4, 10.1) 3.9 / 13.9	2.5; p=0.01	1.4; p=0.17
Population density (people per hectare)	Median (IQR): Min/Max:	5.1 (1.8, 17.4) 0.2 / 137.1	19.4 (9.3, 81.9) 2.6 / 106.4	1.5 (1.2, 3.1) 0.9 / 30.0	3.7; p<0.001	3.4; p=0.001

IQR: inter-quartile range; LAD: Local Authority District

<sup>1</sup>Sources: Population density – 2009 mid-year census estimates; Deprivation variables: 2010 Indices of Deprivation, predominantly collected from data sources just prior to SEPEA case ascertainment period (2008)

<sup>2</sup>Sources: Population density – 2001 census estimates; Deprivation variables: 2004 Indices of Deprivation, predominantly collected from data sources close to A&SOP & ELFEP case ascertainment periods (i.e. 1997-2000).

<sup>3</sup>Mann-Whitney test performs test that the median LAD socioenvironmental scores for the prediction & validation data come from the same population distribution; p<0.05 indicates evidence that the median scores are significantly different

<sup>4</sup>For England we displayed the mean and s.d. of the z-score of deprivation (as shown, underlined), instead of the median and IQR.

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3 **Appendix (supplementary): Development of 95% prediction intervals for negative binomial regression**  
4 **models**  
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9 To obtain 95% prediction intervals from each model, we took all parameter estimates from the fitted  
10 negative binomial regression, including the over-dispersion parameter  $\theta$ , as the true values when  
11 constructing prediction intervals. We then used a Monte Carlo procedure, where we simulated  
12 realisations using the Gamma-Poisson representation of the negative binomial distribution. For each  
13 iteration, we first simulated the random components of the linear predictors from  $\text{Gamma}(\theta, \theta)$ , which  
14 were multiplied by the point predictions (or equivalently  $e^{\upsilon}$ , where  $\upsilon$  is the non-random component of  
15 the linear predictor) to give the Poisson rates for the counts that comprised the predictions. We then  
16 simulated Poisson counts using these rates and summed them to provide one realisation of the quantity  
17 we wished to predict. By repeating this process many ( $n=1000$ ) times the distribution of the quantity to  
18 be predicted was obtained, from which 95% prediction intervals were obtained using the 2.5% and  
19 97.5% quantiles.  
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## Data sharing statement

Extra data is available at our prediction website, PsyMaptic: [www.psymaptic.org](http://www.psymaptic.org). We have made a large array of prediction data freely available to interested users, who can visualise prediction data in maps and tables for a range of psychotic disorder predictions by major sociodemographic subgroup and by LAD. Future versions of PsyMaptic will release data for other regions and at other geographical levels. Users can also download LAD-specific and national summaries of prediction data from our models in tabular form. Finally, additional explanatory material about how to use the data and the PsyMaptic website is also available at [www.psymaptic.org](http://www.psymaptic.org). Bespoke data not provided freely on our website may be requested from the authors at the cost of data extraction. The empirical data underlying the prediction models (ÆSOP and ELFEP) or the validation sample (SEPEA) is not freely available as the studies are ongoing, but papers detailing the main findings from these studies have previously been published elsewhere.

## Competing interests statement

All authors have completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare that (i) JBK has support from the Wellcome Trust for the submitted work (grant number WT085540) and PBJ has support from the NIHR (grant RP-PG-0606-1335); (ii) DJ, JP, FW, DF, JC, RMM have no relationships with any company that might have an interest in the submitted work in the previous 3 years; (iii) their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and (iv) no author holds non-financial interests that may be relevant to the submitted work.

### Role of funders

The funders were not involved in the design, collection, analysis, interpretation of the data, writing the report or the decision to submit the article for publication. All authors were independent from the funders in contributing to this work.

### Ethical approval

Ethical approval to conduct the original AESOP and East London First Episode Psychosis studies was granted from local research ethics committees in their respective centres prior to the original date of onset of the study. We were granted ethical approval to conduct the work related to the present manuscript, including use of data from the SEPEA study, from the Cambridgeshire 3 REC (09/H0306/39).

### Guarantorship

JBK takes full responsibility for the work and conduct of the study, had access to the data, and controlled the decision to publish.

### Contributorship

JBK was responsible for concept, design, analysis, data extrapolation, interpretation of the data, drafting the report and developing the content for the websites [www.psymaptic.org](http://www.psymaptic.org), [www.psymaptic.com](http://www.psymaptic.com) and [www.psymaptic.co.uk](http://www.psymaptic.co.uk). JBK was also the chief investigator of the SEPEA study, where the *validation sample* data was obtained. He gave final approval of this version of the manuscript to be published.

DJ was responsible for developing and initially implementing the statistical approach with regard to prediction intervals from count-based regression. He also contributed to drafting and editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

JP is principal collaborator on the SEPEA study in the CAMEO early intervention in psychosis services. He also contributed to editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

DF is co-principal collaborator on the SEPEA study in the Norfolk and Suffolk Foundation Trust. He also contributed to editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

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8  
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11 manuscript. He gave final approval of this version of the manuscript to be published.  
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17 manuscript. He gave final approval of this version of the manuscript to be published.  
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22 prediction model for use in this project. He contributed to the development of the prediction  
23 methodology and edited the final version of this manuscript. He gave final approval of this version of the  
24 manuscript to be published.  
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### 41 42 **STROBE statement**

43 Our STROBE statement is provided as a supplementary file.  
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3 **A population-level prediction tool for the incidence of first episode psychosis: translational**  
4 **epidemiology based on cross-sectional data**  
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10 **For submission to BMJ Open**  
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47 Word count: 5, ~~478586~~  
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50 **Access to online data:** Part of the development of this manuscript includes the visualisation of prediction data in  
51 map and tabular format on a website created for this project: [www.psymaptic.org](http://www.psymaptic.org). We have password-protected  
52 relevant prediction data on these pages so only editors and peer reviewers can access this data until the peer  
53 review process is complete. We invite you to access these pages by visiting [www.psymaptic.org](http://www.psymaptic.org) and navigating to  
54 "*prediction>for peer reviewers*" on the top menu bar. From here, you can access the data as *prediction maps*,  
55 *national summary tables* or *downloadable data*. Please enter the password **pr2012** when prompted.  
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## Abstract

*Objectives:* [Specialist early intervention services \[EIS\] for people aged 14-35 years with first episodes of psychosis \[FEP\] have been commissioned throughout England since 2001. A single estimate of population need was used everywhere, but true incidence](#) ~~Mental health commissioners require precise information on local populations needs; these vary~~ [varies](#) enormously according to ~~soci~~al and demographic factors. We sought to develop a realistically-complex, population-based prediction tool for FEP, based on precise estimates of epidemiological risk.

*Design & participants:* Data from ~~over 103700 FEP~~ participants ~~from in~~ two cross-sectional [population-based FEP epidemiological](#) studies were fitted to several ~~different~~ negative binomial regression models to estimate risk coefficients across combinations of different sociodemographic and socioenvironmental factors. We applied these coefficients to the population at-risk of a third, socioeconomically different region to predict expected caseload over ~~a~~ 2.5 years ~~s~~ period, where observed rates [of ICD-10 F10-39 FEP](#) had been concurrently ascertained [via EIS](#).

*Setting:* Empirical data from London, Nottingham and Bristol ~~predict~~ed counts in the population at-risk in the East Anglia region of England.

*Main outcome measures:* ~~We compared o~~bserved counts [compared](#) with predicted counts (with 95% prediction intervals) at regional, EIS and local authority district [LAD] levels in East Anglia to establish ~~the~~ predictive validity of each model.

*Results:* A model with age, sex, ethnicity and population density performed most strongly, predicting 508 FEP participants in EIS in East Anglia (95%PI: 459, 559), compared with 528 ~~FEP-observed~~ participants ~~observed over the same period~~. This model predicted correctly in 5/6 EIS and 19/21 LAD. All models performed better than the current gold standard for ~~EIS early intervention in psychosis service~~ commissioning in England ([210716](#) cases; 95%PI: [664183-769239](#)).

*Conclusions:* We have developed a prediction tool for ~~the~~ incidence of psychotic disorders in England and Wales, ~~and~~ made [this freely](#) available ~~as a free~~ online tool ([www.psymaptic.org](http://www.psymaptic.org)) to provide ~~mental~~ healthcare commissioners with accurate forecasts [of FEP](#) based on ~~a~~ robust epidemiology and anticipated local population need. ~~Our approach could potentially be applied to several other settings and disorders.~~ [Initial assessment of some people who do not require subsequent EIS care means additional service resources, not addressed here, will be required.](#)



## Background

Commissioners of health and social care require precise information on the health needs of their local populations,<sup>1</sup> especially if parity of mental and physical health is to be realised. Recent policy promotes the importance of mental health care alongside physical health, recognising the intimate relationship between the two.<sup>2</sup> Many people with severe mental health disorders have dire physical health<sup>2</sup>; they suffer an average of 15-20 life years lost, with premature deaths predominately attributable to cardiovascular disease.

Mental health disorders alone represent the leading disease burden in the UK (22.8%).<sup>3</sup> They contribute substantially to healthcare expenditure and societal costs even before physical ill health is taken into account. The Centre for Mental Health estimated total costs of mental health to British health services and society at £105 billion in 2009/10,<sup>4</sup> a figure expected to double over the next 20 years.<sup>2</sup> These are serious challenges compounded by a paucity of information on which to commission appropriate services. Early intervention in psychosis services [EIS] for people aged 14-35 years with a first episode of psychosis [FEP] offer a useful example of failure to arm commissioners with adequate information to map services to local need.

EIS are a major evidence-based innovation, systematically commissioned throughout England and Wales over the past decade.<sup>5</sup> When EIS intervention is sustained there is evidence that people with psychosis achieve better functional and social outcomes.<sup>6-7</sup> Such services are also highly cost-effective.<sup>4,8-9</sup>

However, EIS were originally commissioned on an anticipated rate of 150 new cases of any psychotic disorder per 1,000,000 of the total population people per year in the Department of Health's Mental Health Policy Implementation Guide [MH-PIG].<sup>5</sup> In 2001 in England and Wales, 29.3% of the population were aged 14-35 years old, meaning that the MH-PIG commissioned incidence rate was approximately 51 cases per 100,000 person-years in the age range covered by EIS. Following their deployment, anecdotal reports began to emerge from EIS in different regions to suggest that a uniform figure for commissioning was simultaneously under-<sup>10</sup> and over-estimating<sup>11</sup> actual observed need in urban and rural populations, respectively. Recent epidemiological evidence of FEP incidence in rural communities

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3 [in England has suggested that rates are somewhat lower than the uniform figure upon which services](#)  
4 [were commissioned,](#) <sup>12-13</sup> [confirming previous calls that a “one-size-fits-all” prescription for EIS](#)  
5 [implementation is unlikely to lead to the efficient allocation of finite mental health resources.](#) <sup>14-15</sup>  
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10 [Using rich epidemiological data on variation in the incidence of first episode psychosis according to](#)  
11 [major sociodemographic risk factors,](#) <sup>16-19</sup> [a figure at least three times lower than reported thereafter.](#)  
12 ~~The error came from confusing schizophrenia, a particular constellation of psychotic symptoms with~~  
13 ~~chronicity built into its definition, with all psychotic disorders requiring care. This was compounded by~~  
14 ~~the fact that recent evidence concerning the rich epidemiological profile of first episode psychosis [FEP]~~  
15 ~~was not translated into commissioning guidance.~~  
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22 ~~We~~ describe the development and validation of a population-level prediction tool capable of  
23 accurately estimating [the](#) expected incidence of psychiatric disorder, [based on the sociodemographic](#)  
24 [structure of the population in a given region in a given population, underpinned by well-characterised](#)  
25 [epidemiological models.](#) Applied to FEP as proof-of-concept, we show it is possible to [precisely-closely](#)  
26 predict expected incidence in a given population, where the observed count of cases was within the  
27 prediction intervals forecast by our models. We applied our most precise prediction model to the  
28 population of England and Wales to provide health commissioners with a translational epidemiological  
29 prediction tool to underpin information-based service planning.  
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## 38 **Methods**

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40 Our prediction models were based on epidemiological data from the Aetiology and Ethnicity in  
41 Schizophrenia and Other Psychoses [AESOP] and the East London First Episode Psychoses [ELFEP]  
42 studies, <sup>18 20</sup> two ~~recent,~~ methodologically-similar [population-based](#) FEP studies. We fitted various count-  
43 based regression models with [different combinations of](#) sociodemographic and socioenvironmental  
44 factors, well-established in the literature to be associated with the incidence of psychotic disorder. <sup>21-22</sup>  
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48 We first established the relative *internal validity* of each model by estimating internal model fit  
49 diagnostics to assess how well each model fitted the empirical data (henceforth, [referred to as](#) the  
50 *prediction sample*). We next sought to estimate the *external validity* of each model by applying model-  
51 based parameter coefficients to the population structure of a [purposefully deliberately](#) different region  
52 of England, East Anglia ([henceforth, referred to as](#) the *validation sample*). This out-of-sample prediction  
53 technique allowed us to obtain the expected incidence of disorder in this region forecast by each model,  
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3 which we compared with observed rates simultaneously ascertained in this region via the ongoing Social  
4 Epidemiology of Psychoses in East Anglia [SEPEA] study.<sup>13</sup> We performed various model fit diagnostics to  
5 identify which, if any, model demonstrated utilisable predictive capability.  
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### 10 **Empirical data underlying prediction models (*prediction sample*)**

#### 11 *Case ascertainment (numerator)*

12 The designs of the ÆSOP and ELFEP studies have been described in detail elsewhere,<sup>18 20</sup> with features  
13 relevant to the present paper summarised here. Case ascertainment took place over two years in ELFEP  
14 (Newham: 1996-8; Tower Hamlets & Hackney: 1998-2000) and the Southeast London and Nottingham  
15 centres of the ÆSOP study (1997-9), and over the first 9 months of 1997 in Bristol (ÆSOP). All service  
16 bases were screened regularly for potential new contacts aged 16-64 years (18-64 in ELFEP) resident  
17 within these catchment areas. Leakage studies were conducted to identify participants missed by this  
18 initial screen, but meeting inclusion criteria for FEP.<sup>18 20</sup> All participants who received an ICD-10 F10-39  
19 diagnosis for psychotic disorder following assessment via the Schedules for Clinical Assessment in  
20 Neuropsychiatry were included in the incident sample, except those with an organic medical basis to  
21 their disorder or profound learning difficulty. Data on age-at-contact, sex and ethnicity were collected  
22 on included participants. We geocoded participants' residential postcode at first contact to their  
23 corresponding local authority district [LAD] to allow us to model possible neighbourhood effects  
24 associated with the incidence of psychotic disorder, such as population density or socioeconomic  
25 deprivation.  
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#### 40 *Population at-risk*

41 We estimated the population at-risk ~~from which participants originated~~ using the 2001 Census of Great  
42 Britain, adjusted for study duration, and stratified by age group (16-17, 18-19, then 5-year age bands),  
43 sex and ethnicity. Ethnicity was based on self-ascription according to one of ten categories derived from  
44 the census: white British, non-British white, black Caribbean, black African, Indian, Pakistani,  
45 Bangladeshi, mixed white & black Caribbean, other mixed ethnic backgrounds and all other ethnicities.  
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#### 51 *Socioenvironmental variable estimation*

52 We estimated LAD -level deprivation using the 2004 Index of Multiple Deprivation [IMD] in England,  
53 which estimated domains of deprivation using measures predominantly collected close to the time of  
54 our case ascertainment periods (see Box 1).<sup>23</sup> We z-standardised English LAD IMD scores to have a mean  
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of zero and standard deviation of one, and extracted IMD z-scores for the 14 LADs in the AESOP and ELFEP studies. To inspect whether any particular deprivation domain was a better predictor of psychosis incidence than IMD, we also considered LAD-level income deprivation, employment deprivation and the extent of deprivation in our models (Box 1). We also estimated population density, by dividing LAD usual resident population by its area (in hectares), using ArcGIS 9.3 software.

<Box 1 about here>

### Observed data for external validation of prediction models (*validation sample*)

The observed numerator (participants) and denominator (population at-risk) data for our *validation sample* was obtained from the SEPEA study, an ongoing study of the incidence of psychotic disorders incepted over three years (2009-12) through one of six EIS covering 20 LAD and a subsection of one LAD (the town of Royston, Hertfordshire) in Norfolk (three EIS: West, Central and Great Yarmouth & Waveney), Suffolk (one EIS) and Cambridgeshire, Royston & Peterborough (CAMEO North and South EIS).<sup>13</sup>

### Case ascertainment

To establish the incepted incidence of first episode psychosis as seen through EIS, entry criteria for the SEPEA study were:

- Referral to an EIS in East Anglia for suspected first episode of psychosis
- Aged 16-35 years old at first referral to EIS (17-35 years in CAMEO services)
- Resident within the catchment area at first referral
- First referral during case ascertainment period (2009-12)

At six months after [EIS acceptance referral](#), or discharge from the service, whichever was sooner, we asked the clinician responsible for [the care of the participant](#) to provide an ICD-10 F10-39 psychiatric diagnosis using all information available. We excluded participants without a clinical FEP diagnosis, or participants presenting with an organic basis to [their](#) disorder or profound learning disability. For remaining participants, basic sociodemographic and postcode information was recorded and classified in the same way as in the *prediction sample*. We included participants presenting to EIS during the first 2.5 years of the ongoing SEPEA study.

### *Population at-risk*

We estimated the population at-risk of East Anglia using ~~the latest (2009)~~ mid-year census estimates published by the Office for National Statistics [ONS] at LAD-level, by age group, sex and ethnicity.<sup>24</sup> These estimates used the 2001 census base, adjusted for immigration, births and deaths each year. It was not possible to obtain 2009 mid-year estimates for ~~the town of~~ Royston, because data were only published at ~~the LAD-level, not by town~~. Here, we thus used denominator data from the 2001 census data, ~~published for Royston~~ in order to estimate the population at-risk ~~in Royston~~. We do not believe this would have substantially invalidated our results as this town represented 0.6% of the overall population at-risk (n=9,555) in the SEPEA study. Denominator data were multiplied by 2.5 to account for person-years of exposure in the *validation sample*.

### *Socioenvironmental variable estimation*

For each LAD in the SEPEA study we obtained corresponding socioenvironmental variables to those included in our *prediction sample*, using updated data collected as close to the SEPEA ~~study~~-case ascertainment period as possible. Population density was estimated using 2009 mid-term population estimates. Our measures of deprivation were derived from the IMD 2010,<sup>25</sup> which was estimated in an analogous way to 2004 data, but collected from ~~data~~-sources obtained immediately prior to the SEPEA study.

## **Statistical techniques**

### *Dataset generation*

We constructed a dataset for the regression analysis of count data by pooling ~~numerator and denominator~~ data from the ÆSOP & ELFEP studies (the *prediction sample*). Data were stratified by age group, sex, ethnicity and LAD, such that each stratum represented the total count of ~~FEP~~ cases in a unique sociodemographic group for a given LAD, with a corresponding estimate of the population at-risk, treated as an offset in our models. Our socioenvironmental measures (population density, deprivation) were adjoined to the dataset for each LAD.

Population at-risk data from the *validation sample* were stratified in the same way and retained in a separate database. ~~The C~~count of cases ~~was were~~ entered as ~~a variable with~~ missing ~~values~~, which we ~~could wished to~~ predict into, given the model ~~coefficients and population at-risk~~.

### Prediction models

We used the *prediction sample* data to fit negative binomial regression models to obtain parameter coefficients of incidence for the sociodemographic and socioenvironmental factors included in each model. We considered the internal and external predictive capabilities of six models, all of which contained age group, sex, an age-sex interaction term and ethnicity. Model 1 contained no further covariates. Model 2 also included IMD. We replaced IMD with either income, employment or the extent of deprivation, respectively, in models 3-5. Model 6 included population density. Initial exploration of the *prediction sample* data indicated the presence of possible over-dispersion (variance ( $\delta^2=1.37$ ) exceeded mean ( $\mu=0.4$ ) count of cases) so negative binomial regression was preferred to Poisson regression since it explicitly models any over-dispersion with an extra dispersion parameter.

### Internal model cross-validation & prediction

We assessed internal model validity in three ways. First we used Akaike's Information Criterion [AIC] to assess the respective overall fit of each model to the data. Second, we conducted K-fold cross validation to assess each model's internal validity to predict cases within the *prediction sample*. This method randomly allocated strata in the *prediction sample* into  $K$  subsets. Each model was then re-estimated on  $K-1$  subsets (the *training data*) to predict expected counts of cases in the  $K^{\text{th}}$  subset (the *test data*). This was repeated over  $K$  trials, such that each stratum in the dataset appeared exactly once as the *test data*. At the end of this process, we derived Lin's concordance correlation coefficient [CCC] and 95% confidence intervals [95%CI] to estimate the correlation between predicted and observed counts of cases across all strata in the *prediction sample*. Finally, we estimated the root mean squared error [RMSE] to determine the average error between fitted and observed values from each model, where lower RMSE scores indicated smaller prediction error. The RMSE is derived as

$$RMSE = \sqrt{\frac{\sum_{i=1}^n (y_i - \hat{y}_i)^2}{n}}$$

where  $y_i$  and  $\hat{y}_i$  are the observed and predicted count of cases in the  $i^{\text{th}}$  stratum, respectively, and  $n$  is the number of strata.

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3 We repeated K-fold cross-validation  $h$  times, generating  $K$  new random divisions of the data each time.  
4  
5 We retained model fit diagnostics across  $Kh$  iterations, and reported the mean of Lin's CCC and RMSE to  
6  
7 provide summary cross-validation statistics for each model. We specified  $K=10$  and  $h=20$ , as  
8  
9 recommended for cross-validation to obtain precise model fit diagnostics.<sup>26</sup>

#### 10 11 12 *External model prediction & validation*

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14 We retained parameter coefficients from each model (using the full *prediction sample* data) and applied  
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16 these to the corresponding population at-risk in the *validation sample* dataset. This gave out-of-sample  
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18 prediction estimates for the expected count of cases in each stratum of the *validation sample*, given the  
19  
20 model. We summed expected counts across relevant strata to estimate the (i) total predicted count of  
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22 cases in the SEPEA region, (ii) predicted counts in each EIS, and (iii) predicted counts by LAD. These  
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24 counts were further stratified by broad age group (16-35, 36-64 and 16-64 years). Because census  
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26 (denominator) data was unavailable for 35 year olds alone (needed to estimate their contribution to  
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28 predicted counts in the age range for EIS, 16-35 years) we assumed the risk coefficient was the same  
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30 across all ages within the 35-39 year old age group. We apportioned predicted counts on a 1:4 ratio (35  
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32 years: 36-39 years) to their respective broad age groups.

33  
34 | To determine how well the MH-PIG<sup>5</sup> figure of 151 new cases per 100,000 people per year for EIS  
35  
36 performed as a predictive tool, we also estimated the predicted count of cases in the *validation sample*  
37  
38 under this scenario, which we termed "Model 7".

39  
40 We derived prediction intervals [95% PIs] for all summary predictions from first principles for each  
41  
42 negative binomial regression model, since their derivation is not straightforward, nor routinely  
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44 implemented by statistical software. [Prediction intervals are similar to confidence intervals, but account](#)  
45  
46 [for standard errors introduced in both the prediction and validation samples.](#) We developed a  
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48 bootstrap-like approach to obtain prediction intervals from each model by simulating 1000 model-based  
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50 realisations of the quantities we wished to predict, where we took the parameters to be the maximum  
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52 likelihood estimates. We obtained the lower and upper bounds of the prediction intervals as the  
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54 corresponding quantiles of the simulated realisations (see Appendix for full details).

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56 | To assess each model's external predictive capabilities, we ~~derived~~ [considered](#) five markers of predictive  
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58 accuracy. We compared the number of times the observed count of cases in the SEPEA study fell within  
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3 the prediction intervals estimated from each model for (i) the SEPEA region, (ii) at EIS level, and (iii) at  
4 LAD level. We also derived EIS- and LAD-level RMSE scores to estimate prediction error from each model  
5 in our *validation sample*. We ranked model performance (1: best, 7: worst) on these five measures, and  
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7 estimated an overall mean rank to determine the overall predictive validity of each model.  
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12 Observational data on first episode psychosis in our *validation sample* were not available for the age  
13 range 36-64 years, so external validation was restricted to the 16-35 year old group. For completeness,  
14 however, we also reported overall predicted count of cases for this age group from each model.  
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### 17 18 19 *Extrapolation to the United Kingdom*

20 Guided by our validation procedures, we identified which model had the greatest overall predictive  
21 validity, and proposed this as a candidate for FEP incidence prediction in England and Wales. We  
22 repeated out-of-sample prediction on the sociodemographic and socioenvironmental population  
23 characteristics of each LAD in England and Wales to obtain national and LAD-level predictions.  
24

25 Denominator data was obtained from the ONS 2009 mid-term estimates and stratified as previously  
26 described. Overall counts were derived for three broad age groups (16-35, 36-64 and 16-64 years), and  
27 for each of these, by sex and ethnicity. 95% PIs were estimated as before. We visualised this data on  
28 maps and in tables to provide healthcare planners and commissioners with an easy-to-use tool to  
29 forecast the expected incidence of psychosis in England and Wales. We have made this available as a  
30 free, open-use prediction tool, known as PsyMaptic (version 0.43) (Psychiatric Mapping Translating  
31 Innovations into Care; [www.psymaptic.org](http://www.psymaptic.org)). Counts of cases predicted by our model were compared  
32 with those obtained under the Department of Health's uniform rate in each LAD. We expressed these  
33 comparisons as ratios with 95% CIs derived using the same method as for standardised morbidity ratios  
34 [SMR]. This approach was conservative because here we substituted the usual numerator in an SMR, the  
35 observed, O, for a predicted count. Unlike an observed count, no sampling variation is present for the  
36 predicted count, only uncertainty due to the model from which the prediction was estimated. Since  
37 variance in the prediction is therefore much smaller than the variance normally present for the  
38 numerator (O) this led to conservative estimates of 95% CI. Ratios in LAD where 95% CI did not span  
39 unity could therefore be interpreted as regions where there was strong evidence that the predictions  
40 from our model differed significantly from those predicted by the Department of Health's uniform rate.  
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### Software

All negative binomial regression models, out-of-sample prediction and estimation of 95% PI were conducted in R (version 2.15.1). Internal cross-validation and model-fit diagnostics were conducted in Stata (version 11). Prediction maps for England and Wales were created using StatPlanet Plus (version 3.0) visualisation software.<sup>27</sup>

## Results

### Prediction sample

Our prediction models contained data on 1,037 persons with a first episode psychosis in the ÆSOP (n=553; 53.3%) and ELFEP (n=484; 46.7%) studies, ascertained from over 2.4m person-years at-risk. Twelve participants were excluded from the original ÆSOP sample because they were of no fixed abode and could not be geocoded to an LAD.<sup>18</sup>

The population at-risk in the *prediction sample* came from LAD with higher median levels of multiple and employment deprivation, extent of deprivation and population density than the population at-risk in the *validation sample*, though there were no statistically significant differences in median income deprivation between the two samples (Supplemental Table 1).

[<Supplemental Table 1 about here>](#)

Parameter coefficients obtained from the full prediction sample following negative binomial regression are shown in Table 1. As previously reported from these data,<sup>20,28</sup> incidence rates were generally raised in ethnic minority groups compared with the white British population. Models 2-6 included a measure of LAD deprivation (Models 2-5) or population density (Model 6), which were all [significantly](#) associated with [a significant increase in the](#) incidence of psychotic disorder, after control for individual-level confounders. Each of these models produced a lower AIC score, [indicating better fit](#), than a model fitted solely with individual-level covariates (Model 1), [indicating better internal fit](#). Internal cross-validation suggested all models achieved good CCC agreement between predicted and observed cases, with low RMSE values (Table 1). ~~Models 2-5 performed marginally better than Model 6 on these cross-validation diagnostics.~~

[<Table 1 about here>](#)

## Validation sample

### *Observed participants*

We identified 572 participants over the first 30 months of the SEPEA study, aged 16-35 years old, who met acceptance criteria for EIS in East Anglia. We excluded 44 participants (8.0%) who did not meet clinical criteria for ICD-10 psychotic disorder. This left an incidence sample of 528 participants from nearly 1.4m person-years at risk (37.8 per 100,000 person-years; 95%CI: 34.7, 41.2). A further 2.3m person-years at-risk accrued in the same region for people aged 36-64 years over this period. Median levels of multiple, income and employment deprivation in the region did not differ significantly from the remainder of England, although median population density and extent of deprivation in East Anglia were lower than elsewhere in England (Supplemental Table 1).

[<Table 2 about here>](#)

### *External model prediction & validation*

The overall observed count of cases, aged 16-35 years, in the *validation sample* (n=528) fell within 95% prediction intervals in only two of seven tested models (Models 4 and 6, Table 2). Of these, the observed count was closest to the point estimate for Model 6 (508.5; 95% PI: 449.0, 559.0), fitted with age group, sex, their interaction, ethnic group and LAD population density. The observed count of cases also fell within prediction intervals from this model in five of six EIS in the study region, and 19 of 21 LADs, the most of any model (Table 3). [This model had the lowest error scores at EIS \(RMSE=11.9\) and LAD \(RMSE=5.9\) levels of any model.](#) Overall, Model 6 was ranked highest across all external model fit diagnostics (Table 3). All models outperformed the Department of Health's uniform figure of ~~451~~ cases per 100,000 people per year (Model 7), which ~~consistently generally over~~underestimated ~~the expected count of~~ cases ~~observed~~ in the *validation sample* (overall prediction: ~~715.72~~~~10.5~~ cases; 95% PI: ~~664183.0, 769239.0~~).

We also reported predicted cases aged 36-64 years old from our models (Table 3), although we could not test these in ~~our external the~~ *validation sample*. Model 6 predicted an additional 262.9 cases aged 36-64 years over a 2.5 year period in East Anglia (95% PI: 233.0, 297.0).

[<Table 3 about here>](#)

### Extrapolation to England and Wales

We ~~selected Model 6 to predict~~<sup>ed</sup> the expected count and incidence of first episode psychosis per annum in each LAD in England and Wales based on Model 6, and visualised this data in maps and tables freely available at [www.psymaptic.org](http://www.psymaptic.org). Many maps can be visualised (for example, Supplemental Figure 1), including overall predicted incidence counts and rates for each broad age group at LAD level, by sex and ethnic group, as well as a variety of population and socioenvironmental data. According to our model, the annual number of new FEP cases in England and Wales would be 8745 (95% PI: 8558, 8933), of which our model predicted 67.9% (N=5939; 95% PI: 5785, 6102) would be seen through EIS. Only 176 (95% PI: 151, 203) cases aged 16-64 years were forecast in Wales per annum. Assuming our prediction model is accurate, it indicated that the Department of Health's current uniform rate of 51 per 100,000 person-years was higher than the predicted point estimates for rates forecast by our PsyMaptic model in 351 LAD (93%) in England and Wales, but was lower than predicted by our model in Birmingham and several London boroughs (Supplemental Figure 2, left hand map). Under a conservative approach, these differences achieved statistical significance in parts of London (where the Department of Health's model underestimated need as predicted by PsyMaptic), and in some more rural parts of England and Wales (where the Department of Health's model over-estimated need) (Supplemental Figure 2, right hand map), a median of 63.4% of new service users seen by EIS as predicted by our model would not have been anticipated under the current gold standard for commissioning EIS (model 7), although this varied between LAD (10<sup>th</sup>-90<sup>th</sup> percentile: 51.3% - 67.6%; Supplemental Figure 2).

<Supplemental Figures [12](#) & [23](#) about here>

## Discussion

### Principal findings

We have developed and tested several epidemiological prediction models to forecast FEP incidence in England and Wales, having taken into account regional differences in the sociodemographic and socioenvironmental profile of different populations. Inspection of our data suggested that a model fitted with age group, sex, their interaction, ethnic group and LAD-level population density provided the greatest external predictive validity when compared with the observed FEP caseload ascertained through EIS in our *validation sample*. This model also had good internal validity across the entire age range (16-64 years). All ~~prediction~~ models performed significantly better in predicting the incidence of

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4 [clinically relevant first episode psychosis](#) than the Department of Health's current gold standard for EIS  
5 commissioning,<sup>5</sup> based on a ~~low~~-uniform ~~anticipated~~ incidence rate. [Our data suggested the figure used](#)  
6 [to commission EIS over-estimated the likely true incidence rates of FEP in rural areas and under-](#)  
7 [estimated them in urban settings, although we acknowledge that commissioning decisions will need to](#)  
8 [be based on several additional factors, including the level of pre-clinical or non-psychotic](#)  
9 [psychopathology requiring assessment at initial referral to EIS, and variation in service organisation,](#)  
10 [remit and delivery.](#)

### 17 **Limitations & future development**

19 [Our prediction models were based on epidemiological data obtained from large, robust population-](#)  
20 [based FEP studies for people aged 16-64 years.](#)<sup>18-19</sup> [Our best-fitting model had good internal validity over](#)  
21 [this age range, and good external validity over the age range 16-35 years. While this covered the](#)  
22 [majority of adult onset psychosis cases seen in mental health services, including EIS, we recognise that](#)  
23 [some EIS teams incept people from 14 years old. We were unable to extrapolate our models to this age](#)  
24 [range, given the current absence of incidence data for this group in England. Data from Scandinavia](#)  
25 [suggest that the incidence of such "early onset" psychoses is absolutely low,](#)<sup>29</sup> [although the rate may](#)  
26 [have been increasing in the last few decades, probably as a result of movement towards earlier](#)  
27 [detection.](#) We ~~were also unable to~~ ~~could not~~ externally validate prediction models for people aged 36-  
28 64 years, because comparable observed incidence data was not available in our *validation sample*. We  
29 have no reason to believe our predictions will be invalid for this group, however, since the empirical  
30 data which underpinned our models was ascertained from the same two large, well-conducted studies  
31 ~~of first episode psychosis in England~~ as ~~for~~ data ~~on~~ ~~for~~ the younger age group,<sup>18-19 28</sup> ~~Furthermore, and~~  
32 published findings from these studies are consistent with the wider epidemiological literature for  
33 psychosis ~~in from~~ England and internationally.<sup>17 21 30</sup> It will be important to ~~ascertain~~ ~~validate~~ the  
34 predictive capability of our model(s) in this age range, and we will seek to identify suitable samples to do  
35 so in future versions of PsyMaptic.

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50 All prediction models had reasonable internal validity, although our proposed model performed slightly  
51 worse (most noticeably for AIC) than models which included deprivation (i.e. models 2-4) instead of  
52 population density. Our decision to use model 6 as our proposed candidate for the prediction tool was,  
53 ~~however,~~ supported by the fact that it produced the most accurate external forecasts of any model,  
54 despite considerable socioenvironmental differences between regions in our *prediction* and *validation*

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3 samples. We were unable to predict the expected incidence of psychotic disorder in geographical areas  
4 smaller than LADs, such as electoral wards (N~6000), or to other parts of the UK, because appropriate  
5 denominator data was not published as mid-term census estimates. The 2011 census will provide small  
6 area and national data for the whole of the UK, [scheduled for ~~and will be~~ released](#) by ONS in mid-2013.  
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8 This will allow us to update our tool to the latest population estimates for the UK, and refine our  
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10 PsyMaptic tool at a smaller geographical level for fine-grained healthcare commissioning. [We will then](#)  
11  
12 [be able to develop models to explore cross-level interactions, such as the association between individual](#)  
13 [ethnicity and neighbourhood-level ethnic density](#). Small area prediction models will require a multilevel  
14 approach, not attempted here, because obtaining predictions from multilevel random effects models is  
15 not straightforward and requires active statistical development.  
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22 We believe case ascertainment in our *validation sample* led to a reliable estimate of the incidence of  
23 psychotic disorder for people aged 16-35 years old. EIS were the only mental health service for people  
24 aged 14-35 years experiencing a first episode of psychosis in East Anglia, minimising the potential for  
25 under-ascertainment in the population at-risk when derived from careful epidemiological design.<sup>13</sup> We  
26 are confident that our *validation sample* also contained few false positive cases for any clinically-  
27 relevant psychoses, since participants were excluded who failed to meet acceptance criteria for EIS or  
28 who did not receive a clinical diagnosis of psychotic disorder during the first six months from initial  
29 referral. [It is important to recognise that while our prediction models are based on diagnosed clinically](#)  
30 [relevant psychotic disorders, service commissioning will also need to account for additional pre-clinical](#)  
31 [or non-psychotic psychiatric morbidity presenting to EIS, particularly in services which operate early](#)  
32 [detection models or implement “watch-and-wait” briefs. The SEPEA data used to validate our models do](#)  
33 [not predict \(1\) the number of “false positive” subjects who may require psychiatric triage and](#)  
34 [assessment even though they are not accepted by EIS, or \(2\) the number of “true positive” subjects](#)  
35 [accepted by services, but who did not meet epidemiological criteria for inclusion in the validation](#)  
36 [sample of the SEPEA study \(those living outside the catchment area at first contact, or those transferred](#)  
37 [from other services\); these people will consume varying degrees of service resources which needs to be](#)  
38 [considered in service planning.](#)  
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53 [We also note that pathways to care may affect the level of incidence observed in EIS, since many filters](#)  
54 [are likely to operate before subjects come to the attention of EIS. These will include local level service](#)  
55 [organisation and the relationship between Community Mental Health Teams \[CMHTs\], Child and](#)  
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3 [Adolescent Mental Health \[CAMHs\] and EIS. Furthermore, acceptance criteria for entry to EIS vary,](#)  
4 [which will have a downstream effect on the number of new cases of clinically relevant psychoses](#)  
5 [received in each team.](#) -Future versions of PsyMaptic will include forecasts for specific psychotic  
6 disorders, as standardised research-based diagnoses (using OPCRIT<sup>31</sup>) are currently being collected in  
7 the ongoing SEPEA study [in order to provide more detailed forecasts.](#) [Acceptance rates to EIS may also](#)  
8 [be influenced by local community awareness of such services.](#) [While our prediction models](#)  
9 [outperformed the current gold standard for EIS commissioning in England when restricted to clinically](#)  
10 [relevant caseloads, we recommend that our models are best interpreted as forecasts of the expected](#)  
11 [burden of first episode psychosis in given populations, and not the expected burden which will](#)  
12 [necessarily be seen through EIS given these issues.](#)  
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22 We estimated prediction intervals from first principles [DJ] since their derivation is an area of statistical  
23 development.<sup>32</sup> We used a bootstrap-like methodology to produce 95% PI accounting for natural  
24 variation in the *validation sample*, but ignoring parameter uncertainty in the coefficients included in  
25 prediction models, which we assumed to be the true coefficients of risk in the population. Our approach  
26 therefore naturally led to slightly artificially narrow 95% PIs. [This was not necessarily undesirable for the](#)  
27 [purpose of model validation and the precise prediction of expected counts because we wished to apply](#)  
28 [stringent criteria.](#) Ideally, prediction intervals should take into account both these sources of variation,  
29 although we note that parameter uncertainty is usually small compared to the natural variation of the  
30 quantities of interest. ~~[Furthermore, ignoring this uncertainty was not necessarily undesirable for the](#)~~  
31 ~~[purpose of model validation and the precise prediction of expected counts because we wished to apply](#)~~  
32 ~~[stringent criterion.](#)~~ Here, ~~the~~ addition of more empirical data in the *prediction sample* would not lead  
33 to narrower PIs, though would tend to move the point estimate of risk for each coefficient closer to the  
34 true value in the population. We do not believe we have mis-estimated point estimates of risk across  
35 major sociodemographic groups, since our results accord with the wider [English and International](#)  
36 literature.<sup>17 21-22</sup> We sought independent confirmation that our development of 95% PI were correct  
37 (personal communication with Prof Ian White, MRC Biostatistics Unit). We recommend that all  
38 prediction point estimates from our PsyMaptic model are considered with their 95% PIs, which provide  
39 information about the natural variance in expected rates in the population.  
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### 55 **Meaning of the findings**

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3 If commissioners are to meet the Department of Health's vision to orientate health services around local  
4 need,<sup>1-2,5</sup> differences in demand for EIS and other mental and physical health services will need to be  
5 taken into account to allocate finite resources where they are most needed. The PsyMaptic prediction  
6 model provides proof-of-concept that when robust empirical epidemiological data is combined with  
7 accurate population at-risk estimates this can be realised. As such, our modelling approach could have  
8 utility in many other settings and for many disorders. Our translational approach demonstrated good  
9 internal and external validity to predict the expected incidence of first episode psychosis, particularly  
10 through EIS, where 76% and 63% of all male and female adult-onset FEP cases, respectively, will typically  
11 present.<sup>18</sup> Since their inception in 2002, EIS in England and Wales have reported [both lower<sup>11</sup> and](#)  
12 [higher<sup>10</sup> caseloads than they were originally envisioned to manage in the MH-PIG,<sup>5</sup> with shortfalls or](#)  
13 [excesses in anticipated demand for services aligned to the degree of urbanisation in the underlying](#)  
14 [catchment area. Others have noted that EIS provision in rural areas may be difficult to implement](#)  
15 [effectively.<sup>14-15</sup> Empirical epidemiological data from such services supports this; with incepted rates at](#)  
16 [least three times greater than expected based on a uniform rate of 15 per 100,000 people per year.](#)  
17 [and](#) while the MH-PIG acknowledged that "...[a]n understanding of local epidemiology is needed as  
18 the size of population covered will depend on a number of different factors" (p.55),<sup>5</sup> no further  
19 elaboration on how to achieve this was provided [for commissioners](#). We believe PsyMaptic provides a  
20 possible [exemplar tool](#) to overcome this challenge, [improving the description and prediction of local](#)  
21 [population need beyond the MH-PIG and including individual- and neighbourhood-level indicators of](#)  
22 [local need.<sup>17</sup> From an aetiological perspective, we acknowledge that variables such as ethnicity or](#)  
23 [population density are likely to be markers for a suite of more complex, interactive social, genetic and](#)  
24 [environmental determinants of psychosis.<sup>33</sup>](#)

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43 Our models are not the first to be used to forecast mental illness needs in England and Wales,<sup>34</sup> though  
44 we believe this is the first attempt to forecast incidence rather than prevalence in the community. We  
45 recommend that our prediction methodology is used in conjunction with the wide range of public health  
46 observatory data available,<sup>35</sup> [as well as the caveats presented above. To this end,](#) PsyMaptic has been  
47 included with other indicators in the Joint Commissioning Panel for Mental Health's forthcoming  
48 guidance for commissioning of public mental health services.<sup>36</sup> [Ongoing monitoring and audit of EIS will](#)  
49 [be vital to ensure services meet the fidelity criteria upon which they were originally commissioned,<sup>11,37</sup>](#)  
50 [including ensuring that service capacity matches local need as closely as possible. As part of this process,](#)

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we will need to externally validate our models in a wider range of settings, refining them based on empirical observation.

We note that ~~our heat maps broadly correlate with~~ advocacy expressed for EIS by healthcare professionals in England and Wales broadly correlates with demand for services as predicted by PsyMaptic.<sup>38</sup> Though by no means universal, proponents of EIS tend to be located in major conurbations – such as London,<sup>39</sup> Birmingham<sup>40</sup> or Manchester<sup>7,41</sup> – where demand for EIS will be highest, while those ~~who suggest EIS resources could be used more effectively elsewhere~~ ~~more critical of such services~~ tend to work in more rural communities,<sup>15,38</sup> where but a handful of young people would be expected to come to the attention of EIS each year. It is possible that both sides are correct and that more resources are required to help with the tide of psychotic illness in inner cities. Resources might be used more effectively in other ways, elsewhere, so long as the needs of the small number of young people who suffer a FEP each year are met; a dedicated specialist EIS may not be the most effective approach when anticipated demand will be very low.

~~We are not the first to express concerns over the suitability of the MH-PIG for EIS implementation.~~<sup>44-45</sup>  
~~The epidemiological literature conducted before and after its publication does not support adoption of such a low rate of first episode psychosis as a realistic basis for psychosis service planning for young people, when incidence rates are at their highest. Our heat maps (see Supplemental Figure 2 and online) illuminate the magnitude of the discrepancy between MH-PIG forecasts and those from our prediction model in different regions of England and Wales; our data suggest the MH-PIG underestimated anticipated EIS caseload per annum by almost 50% anywhere in England and Wales. This figure exceeded 80% in some urban areas.~~ Given the significant downstream economic savings associated with spending on EIS as estimated in an urban setting,<sup>8</sup> PsyMaptic ~~could~~ ~~an~~ ~~also~~ be used to highlight regions where ~~with~~ sufficient EIS investment to appropriate mental health services would lead to the greatest economic gains ~~could be realised~~ in terms of mental healthcare expenditure (assuming sustained intervention also leads to improved social and clinical benefit for patients<sup>6-7</sup>). If valid, PsyMaptic can also be used to highlight regional variation in demand according to age, sex and ethnic group, allowing service planners to tailor provision around the socio-cultural characteristics of their local populations.  
Our prediction tool for first episode psychosis, which translates robust empirical epidemiological data on psychosis risk to the population structure of different regions, offers a methodology for improving the allocation of finite mental health resources based around local need. Underestimating need by 50% may



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not produce major difficulties in a region where only two cases per year present to services, but will have great impact on service care and delivery in an EIS seeing 250 new cases per year.

For peer review only

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**Box 1: Description of included socioenvironmental variables <sup>1 2</sup>**

Variable	Classification & description
Multiple deprivation	Weighted data from routine national sources across 7 domains: income, employment, education, health, barriers to housing & services, living environment, crime. Continuous, z-standardised scores for analysis.
Extent of deprivation	Proportion of LAD population living in 20% most deprived SOA in England (%)
Income deprivation	Proportion of all people in LAD classified as income deprived (%)
Employment deprivation	Proportion of adults of working age in LAD classified as employment deprived (%)
Population density	Population density at LAD level (people per hectare).

IMD: Index of Multiple Deprivation; LAD: Local authority district; SOA: super output area; IQR: inter-quartile range

<sup>1</sup>*Prediction sample* sources: Population density – 2001 census estimates; Deprivation variables: 2004 Indices of Deprivation, predominantly collected from data sources close to A&SOP & ELFEP case ascertainment periods (i.e. 1997-2000)

<sup>2</sup>*Validation sample* sources: Population density – 2009 mid-year census estimates; Deprivation variables: 2010 Indices of Deprivation, predominantly collected from data sources just prior to SEPEA case ascertainment period (2008)

Table 1: Prediction models, covariates and fit: all clinically relevant psychoses (F10-39)

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Variable	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)
Age group*sex interaction <sup>1</sup>	p=0.07	p=0.06	p=0.06	p=0.06	p=0.06	p=0.06
Ethnicity						
White British	1	1	1	1	1	1
Non-British white	2.0 (1.5, 2.5)	1.7 (1.4, 2.2)	1.7 (1.3, 2.2)	1.7 (1.3, 2.2)	1.8 (1.4, 2.3)	1.7 (1.3, 2.2)
Black Caribbean	6.0 (4.9, 7.3)	5.3 (4.3, 6.5)	5.2 (4.3, 6.4)	5.2 (4.3, 6.4)	5.4 (4.5, 6.6)	5.1 (4.2, 6.3)
Black African	4.1 (3.3, 5.1)	3.6 (2.9, 4.5)	3.5 (2.8, 4.4)	3.5 (2.8, 4.4)	3.7 (3.0, 4.6)	3.5 (2.8, 4.3)
Indian	1.7 (1.2, 2.5)	1.5 (1.1, 2.2)	1.5 (1.0, 2.2)	1.5 (1.0, 2.1)	1.6 (1.1, 2.3)	1.6 (1.1, 2.2)
Pakistani	1.8 (1.2, 2.5)	1.6 (1.0, 2.5)	1.6 (1.0, 2.4)	1.6 (1.0, 2.4)	1.6 (1.1, 2.5)	1.8 (1.3, 2.7)
Bangladeshi	2.1 (1.5, 2.8)	1.7 (1.2, 2.3)	1.7 (1.2, 2.3)	1.6 (1.2, 2.2)	1.8 (1.3, 2.5)	1.8 (1.4, 2.4)
Mixed white & black Caribbean	4.3 (2.8, 6.7)	3.9 (2.5, 6.0)	3.9 (2.5, 6.0)	3.9 (2.5, 6.0)	4.0 (2.6, 6.1)	3.9 (2.5, 6.1)
Mixed, other	1.3 (0.8, 2.3)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)
Other	2.2 (1.6, 3.0)	1.9 (1.4, 2.7)	1.9 (1.4, 2.6)	1.9 (1.4, 2.6)	2.0 (1.4, 2.7)	1.9 (1.4, 2.7)
Socioenvironmental variables						
IMD (z-score)	-	1.184 (1.101, 1.274)	-	-	-	-
Extent of deprivation (%)	-	-	1.008 (1.004, 1.011)	-	-	-
Income deprivation (%)	-	-	-	1.025 (1.015, 1.035)	-	-
Employment deprivation (%)	-	-	-	-	1.062 (1.032, 1.093)	-
Population density (pph)	-	-	-	-	-	1.005 (1.003, 1.007)
Internal model fit diagnostics						
AIC <sup>2</sup>	2571.8	2552.4	2551.3	2549.6	2556.4	2556.3
Mean Lin's CCC (95%CI) <sup>3</sup>	0.75 (0.74, 0.77)	0.77 (0.75, 0.78)	0.77 (0.75, 0.79)	0.77 (0.75, 0.78)	0.77 (0.75, 0.78)	0.76 (0.74, 0.77)
Mean RMSE (s.d.) <sup>4</sup>	0.75 (0.11)	0.74 (0.11)	0.74 (0.10)	0.74 (0.10)	0.74 (0.11)	0.76 (0.13)

<sup>1</sup>All models fitted with age group by sex interaction given *a priori* evidence for effect modification.<sup>18 42</sup> Likelihood ratio test p-values reported between models with and without an interaction term fitted between age group and sex. Specific IRR not been reported for clarity, but available on request

<sup>2</sup>AIC: Akaike's Information Criterion – lower scores denote improved model fit

<sup>3</sup>CCC: Lin's correlation concordance coefficient. Higher scores indicate greater correlation between observed & predicted count of cases in the *prediction sample*. Mean CCC and 95%CI reported following *h*=20 trials during cross-validation.

<sup>4</sup>RMSE: Root mean squared error. Lower scores indicate lower prediction error. Mean RMSE and standard deviation (s.d.) reported following *h*=20 repeats of *k*-fold cross-validation, where *k*=10.

Table 2: Observed versus predicted cases in SEPEA study for all clinically relevant psychoses, 16-35 years<sup>1</sup>

EIS	Observed	Model 1	Model 2	Model 3	Model 4
		Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)
<b>Overall total, 16-35 years</b>	<b>528</b>	<b>641.2 (586.0, 696.1)</b>	<b>468.5 (422.0, 518.0)</b>	<b>474.7 (429.0, 522.0)</b>	<b>487.5 (441.0, 535.0)</b>
Cameo North	55	84.7 (66.0, 106.0)	68.5 (52.0, 87.0)	67.8 (51.0, 86.0)	70.2 (53.0, 90.0)
Cameo South	137	163.6 (135.0, 192.0)	105.5 (84.0, 129.0)	111.7 (89.0, 134.0)	110.9 (90.0, 132.0)
West Norfolk	25	29.2 (18.0, 41.0)	23.0 (13.0, 35.0)	22.0 (12.0, 32.0)	23.4 (14.0, 34.0)
Central Norfolk	121	162.6 (136.0, 191.0)	122.6 (99.0, 148.0)	123.0 (100.0, 149.0)	128.3 (104.0, 152.0)
Great Yarmouth & Waveney	60	49.1 (34.0, 65.0)	41.6 (28.0, 55.0)	39.9 (27.0, 53.0)	42.9 (30.0, 57.0)
Suffolk	130	151.9 (126.0, 178.0)	107.4 (85.0, 128.0)	110.3 (88.0, 133.0)	111.7 (90.0, 136.0)
Overall total, 36-64 years	-	332.2 (292.0, 373.0)	244.0 (213.0, 276.0)	248.6 (216.0, 280.0)	256.3 (228.0, 291.0)
EIS	Observed	Model 5	Model 6	Model 7	
		Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)	
<b>Overall total, 16-35 years</b>	<b>528</b>	<b>477.1 (428.0, 523.0)</b>	<b>508.5 (459.0, 559.0)</b>	<b>715.2 (651.0, 779.0)</b>	<b>769.2 (705.0, 833.0)</b>
Cameo North	55	69.1 (52.0, 88.0)	64.5 (48.0, 82.0)	92.7 (74.0, 111.0)	92.7 (74.0, 111.0)
Cameo South	137	100.7 (79.0, 123.0)	131.1 (108.0, 157.0)	169.0 (144.0, 195.0)	169.0 (144.0, 195.0)
West Norfolk	25	24.7 (16.0, 35.0)	22.3 (13.0, 33.0)	35.8 (25.0, 47.0)	35.8 (25.0, 47.0)
Central Norfolk	121	128.2 (105.0, 153.0)	132.5 (108.0, 157.0)	187.5 (161.0, 215.0)	187.5 (161.0, 215.0)
Great Yarmouth & Waveney	60	47.7 (35.0, 63.0)	38.0 (26.0, 51.0)	59.1 (44.0, 74.0)	59.1 (44.0, 74.0)
Suffolk	130	106.6 (86.0, 128.0)	120.0 (96.0, 143.0)	172.5 (143.0, 198.0)	172.5 (143.0, 198.0)
Overall total, 36-64 years	-	249.7 (221.0, 284.0)	262.9 (233.0, 297.0)	345.1 (310.0, 380.0)	345.1 (310.0, 380.0)

<sup>1</sup>Numbers in green denote where observed count fell within 95% prediction interval [95% PI] for people aged 16-35 years. Observed data for people aged 36-64 years in the *validation sample* was not available.

Model 1: Age group, sex, their interaction and ethnicity

Model 2: Model 1 + IMD

Model 3: Model 1 + extent of deprivation

Model 5: Model 1 + employment deprivation

Model 6: Model 1 + population density

Model 7: Department of Health uniform figure for EIS of 15 new cases per

Model 4: Model 1 + income deprivation

100,000 people per year.

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Table 3: External model validation diagnostics<sup>1</sup>

Model	Overall correct prediction? [rank]	EIS (N=6)		LAD (N=21)		Mean ranking [rank of mean ranking]
		Number correct [rank]	RMSE [rank]	Number correct [rank]	RMSE [rank]	
Model 1	No [3]	4 [2]	25.6 [6]	18 [2]	8.13 [6]	3.8 [4]
Model 2	No [3]	3 [6]	18.4 [4]	17 [5]	6.987 [4]	4.4 [6]
Model 3	No [3]	4 [2]	16.4 [3]	18 [2]	6.54 [3]	2.6 [3]
Model 4	Yes [1]	4 [2]	16.3 [2]	18 [2]	6.40 [2]	1.8 [2]
Model 5	No [3]	4 [2]	19.4 [5]	16 [6]	7.14 [5]	4.2 [5]
Model 6	Yes [1]	5 [1]	11.9 [1]	19 [1]	5.93 [1]	1.0 [1]
Model 7	No [3]	01 [7]	38.159.4 [7]	135 [7]	181.032 [7]	6.2 [7]

<sup>1</sup>For each diagnostic, models are placed in rank order [1=best model, 7=worst model] with ties given the same ranking. The mean ranking and rank provide an estimate of the overall performance of various models.

RMSE: Root mean squared error (lower scores indicate lower error); EIS: Early Intervention in Psychosis Service; LAD: Local Authority District

## Article Summary

### Article Focus

- Commissioners require precise information on the health needs of their local populations to effectively plan health services
- A failure to arm mental health commissioners with precise epidemiological data led to [mis-estimation an underestimate](#) of actual activity in early intervention in psychosis services [EIS]
- We sought to develop a prediction tool for the incidence of first episode psychosis [FEP], by applying precise estimates of epidemiological risk in various sociodemographic groups to the structure of the population at-risk in a second region, where the observed incidence had been concurrently ascertained

### Key Messages

- A model of psychosis incidence which included age, sex, ethnicity and population density yielded precise FEP predictions in our second region, out-performing the Department of Health in England's current gold standard for EIS commissioning.
- We have translated this model into a freely available prediction tool ([www.psymaptic.org](http://www.psymaptic.org)) to facilitate evidence-based healthcare commissioning [of socioculturally relevant services according to local need](#)
- Our tool could be extended to many international settings and other disorders to inform healthcare commissioning, when epidemiological risk can be well-characterised and the structure of the underlying population at-risk is known

### Strengths and limitations

- Our modelling approach used robust epidemiological data from two large studies of first episode psychosis in England to provide estimates of incidence in a third study region, producing accurate [FEP](#) forecasts
- [While our models provide estimates of the expected clinical burden of FEP in the community, services may see a broader range of psychopathology consuming resources, or incepted rates may be influenced by supply-side organisational factors](#)
- Due to data availability it was not possible to validate our prediction tool in settings outside of England and Wales, or for specific psychotic disorders. As data become available we will extend the capability of our prediction tool.

Supplemental Table 1: Socioenvironmental variables at local authority district [LAD] level considered in epidemiological prediction models

Variable		England <sup>1</sup>	Prediction sample <sup>2</sup>	Validation sample <sup>1</sup>	Mann-Whitney test <sup>3</sup> : Z; p-value	
					Prediction vs. Validation	Validation vs. England
Number of LAD	-	326	14	20 (+1 partial)	-	-
Multiple deprivation (z-standardised)	Median (IQR): Min/Max:	<u>0 (1)</u> <sup>4</sup> -1.7 / 2.9	1.0 (-0.5, 2.4) -1.1 / 2.9	-0.7 (-1.0, 0.3) -1.4 / 1.0	2.4; p=0.02	1.5; p=0.12
Extent of deprivation (%)	Median (IQR): Min/Max:	9.0 (1.3, 23.9) 0.0 / 83.6	28.0 (4.0, 63.0) 0.0 / 83.0	1.4 (., 12.8) 0.0 / 29.7	2.4; p=0.02	2.2; p=0.03
Income deprivation (%)	Median (IQR): Min/Max:	11.7 (8.6, 16.1) 3.9 / 32.8	15.5 (8.2, 24.7) 5.9 / 34.4	9.0 (8.2, 14.9) 6.0 / 19.1	1.5; p=0.14	1.3; p=0.19
Employment deprivation (%)	Median (IQR): Min/Max:	8.0 (5.8, 10.8) 2.1 / 18.8	11.6 (6.1, 14.1) 6.1 / 14.1	6.4 (5.4, 10.1) 3.9 / 13.9	2.5; p=0.01	1.4; p=0.17
Population density (people per hectare)	Median (IQR): Min/Max:	5.1 (1.8, 17.4) 0.2 / 137.1	19.4 (9.3, 81.9) 2.6 / 106.4	1.5 (1.2, 3.1) 0.9 / 30.0	3.7; p<0.001	3.4; p=0.001

IQR: inter-quartile range; LAD: Local Authority District

<sup>1</sup>Sources: Population density – 2009 mid-year census estimates; Deprivation variables: 2010 Indices of Deprivation, predominantly collected from data sources just prior to SEPEA case ascertainment period (2008)

<sup>2</sup>Sources: Population density – 2001 census estimates; Deprivation variables: 2004 Indices of Deprivation, predominantly collected from data sources close to A&SOP & ELFEP case ascertainment periods (i.e. 1997-2000).

<sup>3</sup>Mann-Whitney test performs test that the median LAD socioenvironmental scores for the prediction & validation data come from the same population distribution; p<0.05 indicates evidence that the median scores are significantly different

<sup>4</sup>For England we displayed the mean and s.d. of the z-score of deprivation (as shown, underlined), instead of the median and IQR.

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3 **Appendix (supplementary): Development of 95% prediction intervals for negative binomial regression**  
4 **models**  
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9 To obtain 95% prediction intervals from each model, we took all parameter estimates from the fitted  
10 negative binomial regression, including the over-dispersion parameter  $\theta$ , as the true values when  
11 constructing prediction intervals. We then used a Monte Carlo procedure, where we simulated  
12 realisations using the Gamma-Poisson representation of the negative binomial distribution. For each  
13 iteration, we first simulated the random components of the linear predictors from  $\text{Gamma}(\theta, \theta)$ , which  
14 were multiplied by the point predictions (or equivalently  $e^{\upsilon}$ , where  $\upsilon$  is the non-random component of  
15 the linear predictor) to give the Poisson rates for the counts that comprised the predictions. We then  
16 simulated Poisson counts using these rates and summed them to provide one realisation of the quantity  
17 we wished to predict. By repeating this process many ( $n=1000$ ) times the distribution of the quantity to  
18 be predicted was obtained, from which 95% prediction intervals were obtained using the 2.5% and  
19 97.5% quantiles.  
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## Data sharing statement

Extra data is available at our prediction website, PsyMaptic: [www.psymaptic.org](http://www.psymaptic.org). We have made a large array of prediction data freely available to interested users, who can visualise prediction data in maps and tables for a range of psychotic disorder predictions by major sociodemographic subgroup and by LAD. Future versions of PsyMaptic will release data for other regions and at other geographical levels. Users can also download LAD-specific and national summaries of prediction data from our models in tabular form. Finally, additional explanatory material about how to use the data and the PsyMaptic website is also available at [www.psymaptic.org](http://www.psymaptic.org). Bespoke data not provided freely on our website may be requested from the authors at the cost of data extraction. The empirical data underlying the prediction models (ÆSOP and ELFEP) or the validation sample (SEPEA) is not freely available as the studies are ongoing, but papers detailing the main findings from these studies have previously been published elsewhere.

## Competing interests statement

All authors have completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare that (i) JBK has support from the Wellcome Trust for the submitted work (grant number WT085540) and PBJ has support from the NIHR (grant RP-PG-0606-1335); (ii) DJ, JP, FW, DF, JC, RMM have no relationships with any company that might have an interest in the submitted work in the previous 3 years; (iii) their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and (iv) no author holds non-financial interests that may be relevant to the submitted work.

### Role of funders

The funders were not involved in the design, collection, analysis, interpretation of the data, writing the report or the decision to submit the article for publication. All authors were independent from the funders in contributing to this work.

### Ethical approval

Ethical approval to conduct the original AESOP and East London First Episode Psychosis studies was granted from local research ethics committees in their respective centres prior to the original date of onset of the study. We were granted ethical approval to conduct the work related to the present manuscript, including use of data from the SEPEA study, from the Cambridgeshire 3 REC (09/H0306/39).

### Guarantorship

JBK takes full responsibility for the work and conduct of the study, had access to the data, and controlled the decision to publish.

### Contributorship

JBK was responsible for concept, design, analysis, data extrapolation, interpretation of the data, drafting the report and developing the content for the websites [www.psymaptic.org](http://www.psymaptic.org), [www.psymaptic.com](http://www.psymaptic.com) and [www.psymaptic.co.uk](http://www.psymaptic.co.uk). JBK was also the chief investigator of the SEPEA study, where the *validation sample* data was obtained. He gave final approval of this version of the manuscript to be published.

DJ was responsible for developing and initially implementing the statistical approach with regard to prediction intervals from count-based regression. He also contributed to drafting and editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

JP is principal collaborator on the SEPEA study in the CAMEO early intervention in psychosis services. He also contributed to editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

DF is co-principal collaborator on the SEPEA study in the Norfolk and Suffolk Foundation Trust. He also contributed to editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

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3 FW is co-principal collaborator on the SEPEA study in the Norfolk and Suffolk Foundation Trust. He also  
4 contributed to editing the final version of this manuscript. He gave final approval of this version of the  
5 manuscript to be published.  
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8  
9 JC is chief investigator of the ELFEP study and provided part of the empirical dataset underlying the  
10 prediction model for use in this project. He also contributed to editing the final version of this  
11 manuscript. He gave final approval of this version of the manuscript to be published.  
12  
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14 RMM is co-chief investigator of the ÆSOP study and provided part of the empirical dataset underlying  
15 the prediction model for use in this project. He also contributed to editing the final version of this  
16 manuscript. He gave final approval of this version of the manuscript to be published.  
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20 PBJ is co-chief investigator of the ÆSOP study and provided part of the empirical dataset underlying the  
21 prediction model for use in this project. He contributed to the development of the prediction  
22 methodology and edited the final version of this manuscript. He gave final approval of this version of the  
23 manuscript to be published.  
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### 29 **Licences and granting of rights**

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### 41 **STROBE statement**

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43 Our STROBE statement is provided as a supplementary file.  
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Supplemental Figure 1: Screenshot of web-based PsyMaptic prediction tool

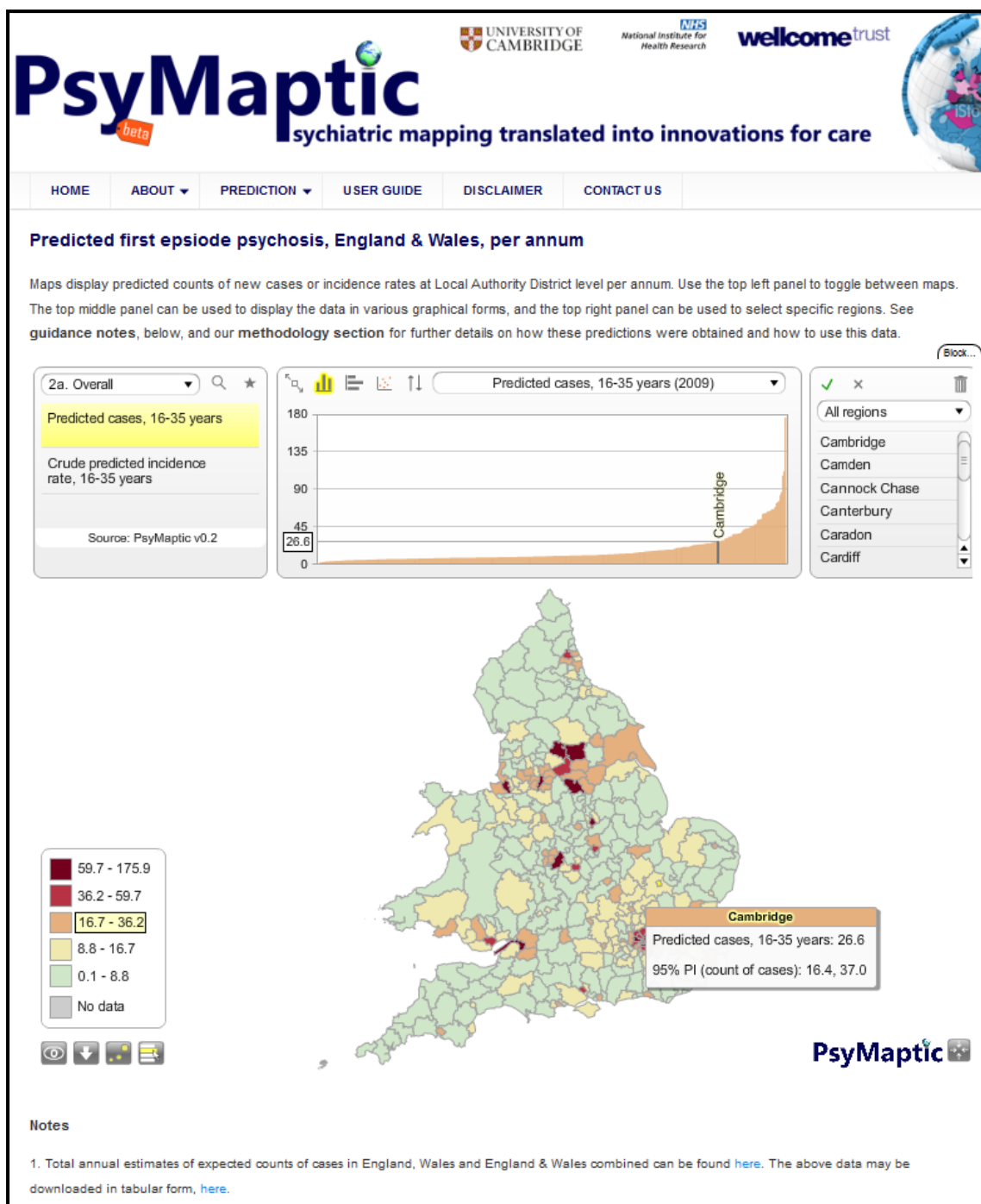


Figure legend: Screenshot shows the PsyMaptic prediction tool made freely available at [www.psymaptic.org](http://www.psymaptic.org). This example shows a prediction map of the annual expected count of new cases of psychotic disorder for people aged 16-35 years across 376 Local Authority Districts [LAD] in England & Wales from our candidate prediction model (Model 6). Each prediction is presented with corresponding 95% prediction intervals. Count data are categorised into the following percentiles: green: 0-50% of LAD; yellow: 50.1-75%; orange: 75.1-90%; red: 90.1-95%; dark red: 95.1-100%. Our PsyMaptic prediction maps are provided with additional graphical utility (histograms, scatterplots, region selection) and are freely available at [www.psymaptic.org](http://www.psymaptic.org)



Supplemental Figure 2: PsyMaptic predicted incidence rate of psychotic disorder in England and Wales, aged 16-35 years old, compared with Department of Health uniform rate for EIS commissioning

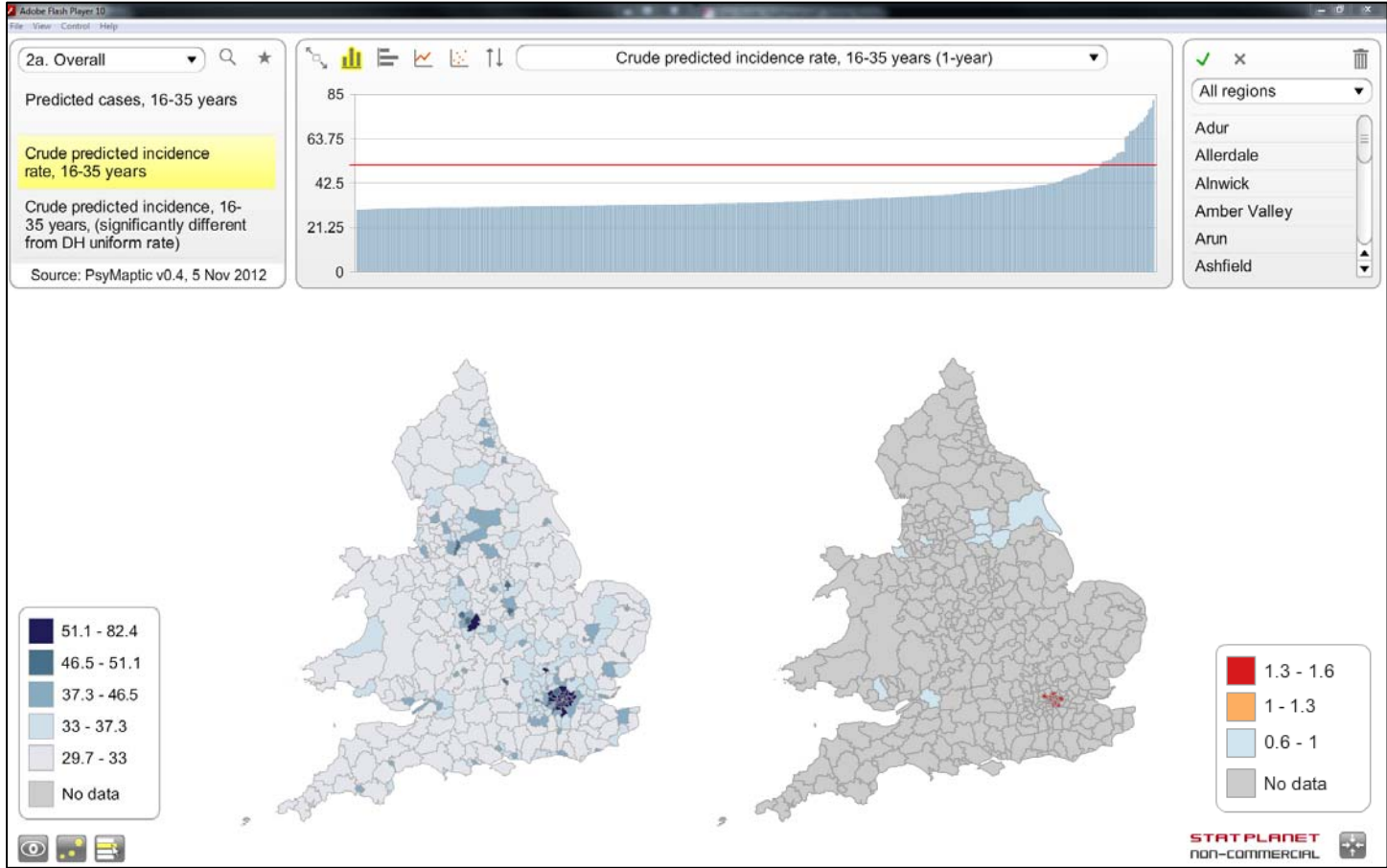


Figure legend: The graph (top) plots all LADs according to predicted incidence rates in people aged 16-35 years (per 100,000 person-years) using PsyMaptic (model 6). The red line is the uniform rate (51 cases per 100kpy), used to commission EIS. Our predicted rates fall below this in 93% of LAD in England & Wales (n=351), indicating that the Department of Health’s [DH] uniform rate may have over-estimated incidence in these regions. Predicted incidence rates are plotted geographically on the left hand map, The darkest shading indicates LAD (in London and Birmingham) where the point estimate of incidence exceeded the DH uniform rate. The right hand map plots the ratio between predicted cases from PsyMaptic & the DH uniform rate. Ratios significantly exceeding unity (in orange & red) show regions where the DH rate under-estimated incidence; ratios significantly less than unity (in blue) show regions where the DH rate over-estimated incidence. This method is conservative (see methodology).

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
<b>Title and abstract</b>	1	<p>(a) Indicate the study's design with a commonly used term in the title or the abstract</p> <p>We entitled our paper <b>A population-level prediction tool for first episode psychosis: development and validation</b>. While our paper uses cross-section data to base prediction models on, the central study design is in reference to prediction <u>modelling using epidemiological data, which we have duly referred to.</u></p> <hr/> <p>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</p> <p>Our abstract was written in the structured style required by the British Medical Journal for publication and included information on <i>background, objectives, design, setting, main outcome measures, results and conclusions.</i></p>
<b>Introduction</b>		
Background/rationale	2	<p>Explain the scientific background and rationale for the investigation being reported</p> <p>Health care planners and commissioners require accurate data on the incidence of psychotic disorder to anticipate the burdens faced by different populations in different regions. Only by using precise predictions, which take into account local need, will it be possible for health care funders and commissioners to allocate finite resources where they are most needed. There is evidence that Early Intervention in Psychosis services [EIS] were commissioned on an erroneously low uniform rate, and that commissioners were unable to satisfactorily take into local population need based on established sociodemographic and environmental risk factors for disorder. This led to misestimation of demand for EIS services in many parts of the UK. We sought to improve the information available for health care commissioners in psychosis, and particularly EIS, by developing an epidemiological prediction tool for disorder.</p>
Objectives	3	<p>State specific objectives, including any prespecified hypotheses</p> <p>To develop a population-based epidemiological prediction tool for first episode psychosis [FEP]. Our hypothesis was that our best prediction model, using informed empirical epidemiological data, should be more valid than the current gold standard for EIS planning, based on the Department of Health's Mental Health Policy Implementation Guide figure of 51 new cases per year per 100,000 people.</p>
<b>Methods</b>		
Study design	4	<p>Present key elements of study design early in the paper</p> <p>Pooled data from two large epidemiological studies of First Episode Psychosis [FEP] conducted with similar methodologies (the Aetiology and Ethnicity in Schizophrenia and Other Psychoses [AESOP] study, and the East London First Episode Psychosis [ELFEP] study) were used to generate risk coefficients from six negative binomial regression models, which tested different combinations of sociodemographic (i.e. age, sex, ethnicity) and socioenvironmental factors (deprivation, population density at local authority district [LAD] level) associated with psychosis incidence. Coefficients were applied to the population at-risk of a third, markedly different region, to predict expected FEP counts over a 2.5 year period, where the observed incidence had also been ascertained.</p>
Setting	5	<p>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</p> <p>Empirical data from the AESOP (1997-9) and ELFEP (1996-8 &amp; 1998-2000) studies</p>

in London, Nottingham and Bristol was used in regression models to estimate out-of-sample predictions for the expected count of new FEP cases in the population at-risk of East Anglia over a 2.5 year period (2009-2012), where the observed count of cases incepted through EIS has also been ascertained through a third study, the Social Epidemiology of Psychoses in East Anglia [SEPEA] study.

Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants
<p>All participants in the AESOP and ELFEP studies, aged 16-64 years old at referral, were identified using the same study design based on the principles of the World Health Organisation Ten-Country study. Any participant presenting to services in each study's defined catchment areas with a suspected first episode of psychotic disorder over the case ascertainment period were screened. Participants were included if they were diagnosed by consensus with an ICD-10 F10-39 first episode of psychotic disorder, using standardised diagnostic data from the Schedule for the Clinical Assessment of Neuropsychiatry [SCAN] presented to a panel of clinicians blind to the ethnicity of the subject. A leakage study was conducted to identify participants missed by the initial screen.</p>		
<p>Participants in the SEPEA study, aged 16-35 years old, were identified if they were referred to one of six EIS in East Anglia for the first time with a suspected first episode of psychosis in the defined catchment area of these services over a 2.5 year period. Participants were excluded if they did not meet clinical criteria for acceptance into EIS or if, at six months after referral, a clinical diagnosis of ICD-10 F10-39 psychosis had not been observed. Observational data in people aged 36-64 years old could not be obtained as this was not part of the SEPEA study objective and no routine surveillance of this group was in place.</p>		
<p>Participants from any study were excluded if they were found to have a profound learning disability or an organic basis to their psychotic episode.</p>		
<p>The denominator populations for AESOP and ELFEP were estimated from the 2001 Census of Great Britain, while the latest mid-term census estimates (2009) stratified by age, sex and ethnicity were obtained for the denominator population in the SEPEA study.</p>		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
<p>All clinically relevant psychotic disorders as per ICD-10 F10-39 psychotic disorders were included as the main outcome variable. We included age group (16-19, then 5 year age groups until 60-64 years), sex and ethnic group (ten categories based on the 2001 census 16-category variable to include: white British, non-British white, black Caribbean, black African, Indian, Pakistani, Bangladeshi, mixed white &amp; black Caribbean, other mixed ethnicities and all other ethnicities). Given evidence of effect modification of the risk of psychotic disorder over age by sex, we considered an <i>a priori</i> interaction between these variables. All individual level variables are known to be associated with the incidence of psychotic disorder and were therefore considered important predictors in our models. Additionally, for some prediction models (see</p>		

below), we also included various socioenvironmental measures at the Local Authority District [LAD] level, such as socioeconomic deprivation or population density, since there is evidence that the incidence of psychotic disorder varies by urbanicity and deprivation. Population density was measured by dividing total population size (2001 or 2009) by LAD area. The Indices of Deprivation (2004/2010) were used to include the potential effects of four domains of deprivation relevant to psychosis incidence – multiple deprivation, the extent of deprivation in the LAD (i.e. an inequality-like measure), income deprivation and employment deprivation. These domains were obtained from the 2004 and 2010 indices of deprivation for the AESOP/ELFEP and SEPEA studies, respectively, with the source data originating from national surveys and other data sources predominantly collected close to the case ascertainment periods of each study.

Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
		For numerator participants: Age was based on age at first referral for suspected psychotic disorder. Ethnicity and sex were assigned by self-ascription. Neighbourhood-level socioenvironmental factors were assigned to participants based on their residential address at first referral to services.
		For denominator (census) participants: Age was defined as age at the time of the census or mid-term census estimate. Sex and ethnicity were defined through self-ascription. LAD population density was based on the total census/mid-term population in each LAD, divided by each LAD's area (in hectares) estimated using ArcGIS software. Deprivation domains were assessed by the 2004/2010 indices of deprivation, which use a comparable methodology to assess changes in deprivation over time, integrating data from a range of nationally-collected routine data sources.
Bias	9	Describe any efforts to address potential sources of bias To minimise the risk of missing incidence participants from the AESOP and ELFEP studies leakage studies were conducted to identify all subjects with a potential FEP, not picked up by the initial screen. This was achieved by close contact with other services where FEP subjects may present, including prisons, the judicial systems, homeless shelters and so forth. In the SEPEA study, EIS provide the only service base for people experiencing FEP up to 35 years old. No leakage study was possible in SEPEA, but all services engaged in active outreach to ensure missing participants were minimised in their communities. One potential source of bias in the SEPEA study is the over-estimation of incidence rates given that EIS do not tend to diagnose participants at referral to avoid stigmatisation and to allow the full course of symptoms to emerge. We minimised the possibility of over-inclusion here by excluding all participants who did not meet clinical criteria for entry to EIS (clear evidence of psychotic symptoms, no previous referral, no previous antipsychotic treatments) and by restricting the sample only to those participants who were given a clinician-rate ICD-10 F10-39 diagnosis of psychotic disorder at first episode.

1 2 3 4 5 6 7 8 9 10	Study size	10	<p>Explain how the study size was arrived at</p> <p>Studies of incidence rates have a sample size equivalent to the ability of the study to identify all true instances of first episode psychosis in a defined catchment area and population over a given time period. Thus, the sample size for all studies here is a function of these factors. We included data from the SEPEA study for 2.5 years of the 3 year study, since it was presently ongoing at the time of these analyses. We included 14 LADs in our empirical prediction data (AESOP/ELFEP) and 21 LADs in our SEPEA study region.</p>
11 12 13 14 15 16 17 18 19 20 21 22	Quantitative variables	11	<p>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</p> <p>Variable groupings for individual level variables have been described in Section 7. For LAD-level variables, population density was entered as a continuous variable. Multiple deprivation and the extent of deprivation were entered as continuous z-standardised variables (across variation in these scores over England) to have a mean of zero and standard deviation of one. Income and employment deprivation were classified as the proportion of people in a given LAD classed as income or employment deprived.</p>
23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60	Statistical methods	12	<p>(a) Describe all statistical methods, including those used to control for confounding</p> <p>A summary of our statistical methodology is provided here. Full details are provided at <a href="http://www.psymaptic.org">www.psymaptic.org</a> or in the accompanying paper to this checklist:</p> <p>[i] Six negative binomial regression models were fitted to the empirical data (AESOP/ELFEP). Model 1 was fitted with age group, sex, their interaction and ethnic group. Models 2-5 included the variables in Model 1 plus a single LAD deprivation measure (multiple deprivation, extent of deprivation, income and employment deprivation, respectively). Model 6 included the variables in Model 1 plus LAD population density.</p> <p>[ii] Internal predictive error for the whole sample, aged 16-64 years, was estimated using repeat k-fold validation to obtain estimates of the Residual Mean Squared Error and Lin's Correlation Concordance Coefficient (correlation between model predictions and the observed count of cases in the data). For each full</p> <p>[iii] Regression coefficients from each model obtained in [i] were applied to the population structure of the population at-risk, aged 16-35 years old, in the SEPEA study to obtain out-of-sample predictions of the expected count of cases in East Anglia over 2.5 years as seen in the age range for EIS. Predicted counts for each model were obtained for the (1) overall predicted count (2) EIS-specific counts and (3) LAD-specific counts in East Anglia. For every prediction, 95% prediction intervals were estimated, using a bootstrap-like method developed from first principles to take into account prediction error in both the prediction data and the out-of-sample dataset.</p> <p>[iv] We obtained similar predictions to [iii] based on a "model" (Model 7) which fitted the Department of Health's current gold standard incidence rate for EIS commissioning (51 per 100000 per year) to the SEPEA data and obtained predictions [iii](1-3) as before.</p>

[v] The predicted counts from each model obtained in [iii] (1-3) were compared with the observed counts of cases for each grouping. We considered the number of times the observed count fell within the 95% prediction intervals from the model prediction to indicate satisfactory model fit. RMSE estimates of model fit between the predicted and observed counts at the EIS- and LAD-levels were obtained for external model validation and comparison. For each of the five diagnostics (overall fit to the observed data, number of times fitted correctly to six EIS, number of times fitted correctly to the 21 LAD, EIS-level RMSE, LAD-level RMSE) we ranked models in terms of performance (1: best, 7: worst). Ranks were averaged across these 5 diagnostics to give an overall ranking for the model which had the greatest predictive power.

[vi] Using the best model obtained in [v] we extrapolated our findings to the population structure (2009 mid-term estimates) of every LAD in England and Wales to produce a freely available prediction tool for commissioners, which forecasts (with 95% Prediction Intervals) the expected incidence of psychotic disorder in every LAD, across all major sociodemographic groups, based on empirical risk coefficients and applied to each LAD's unique population structure. This prediction data was visualised using software known as StatPlanet and uploaded to our website [www.psymaptic.org](http://www.psymaptic.org) to provide Psychiatric Mapping Translated into Innovations for Care [PsyMaptic], a free, online commissioning tool for health care planners, providers and commissioners.

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(b) Describe any methods used to examine subgroups and interactions

We used the full empirical dataset aged 16-64 years to predict the expected count of cases in our validation sample (SEPEA), where the observed caseload had been restricted to the ages 16-35 years old, consistent with the age range covered by EIS. SEPEA did not identify an incidence sample in this region for people aged 36-64 years old and so we could not externally validate our models in this age range. However internal validity of our models across the entire age range, 16-64 years old, was good, and we have no reasons to believe our empirical data in the older age range would be any less valid for prediction than at younger age ranges given it was obtained from the same two studies (AESOP/ELFEP).

Interactions between age group and sex were entered into our regression models as a multiplicative statistical interaction.

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(c) Explain how missing data were addressed

There were no missing data in this dataset

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(d) If applicable, describe analytical methods taking account of sampling strategy

N/A

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(e) Describe any sensitivity analyses

95% prediction intervals were developed for negative binomial regression prediction and reported for all predicted counts and incidence rates of FEP. These intervals give a measure of the confidence we have in our prediction estimates.

**Results**

Participants	13*	<p>(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</p> <p>1037 participants with a first episode psychosis were included in the prediction sample of an initial sample of 1049, where 12 participants were of no fixed abode at time of entry to the study. For the SEPEA study 528 cases were observed over the study period who met entry criteria for the study from an initial sample of 572. Those excluded did not meet clinical criteria for FEP.</p> <p>(b) Give reasons for non-participation at each stage</p> <p>See above</p> <p>(c) Consider use of a flow diagram</p> <p>Not necessary</p>
Descriptive data	14*	<p>(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders.</p> <p>See previously published papers on the AESOP, ELFEP and SEPEA studies as this is not directly relevant here. Of more relevance are the risk coefficients for psychosis incidence across sociodemographic and socioenvironmental groups, as reported in Table 1 of the paper accompanying to this Strobe statement includes. This table confirms the typical risk coefficients seen across these variables.</p> <p>(b) Indicate number of participants with missing data for each variable of interest</p> <p>12 participants were excluded because of no fixed abode in the AESOP. These subjects were more likely to be men, but otherwise did not differ from the remainder of the sample.</p>
Outcome data	15*	<p>Report numbers of outcome events or summary measures</p> <p>N/A – see below for full results</p>
Main results	16	<p>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included.</p> <p>A model with age, sex, ethnicity and population density performed strongest overall, predicting 508 FEP participants in EIS in East Anglia (95%PI: 459, 559) compared with an observed count of 528 over the same period. This model predicted correctly in 5 of 6 EIS (83.3%) and 19 of 21 LAD (90.5%). This model achieved the highest ranking on all external diagnostic measures of any model, and reasonable internal RMSE (0.76; s.d.: 0.13) and CCC (0.76; 95% CI: 0.74, 0.77) estimates across the entire age range. All models performed better than the current gold standard for EIS service commissioning (716 cases; 95%PI: 664-769).</p> <p>(b) Report category boundaries when continuous variables were categorized</p> <p>Age groups – see above</p> <p>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period</p> <p>Not relevant</p>
Other analyses	17	<p>Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses</p>
<b>Discussion</b>		
Key results	18	<p>Summarise key results with reference to study objectives</p>

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We have developed several epidemiological prediction models to forecast expected incidence of first episode psychosis in England and Wales, and assessed their relative internal and external validity, taking into account regional differences in the sociodemographic and socioenvironmental profile of different populations. Inspection of the data suggested that a model fitted with age group, sex, their interaction, ethnic group and LAD-level population density provided the best external predictive capabilities compared with the observed caseload ascertained through EIS in our *validation sample*. This model also had good internal validity across the entire age range considered here (16-64 years). All prediction models performed significantly better than the Department of Health's current gold standard for EIS resource allocation, based on a low uniform anticipated incidence rate.

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Limitations

19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias

Our predictions are based upon the assumed true rate of disorder in the population aged 16-64, 16-35 or 36-64 years old. This may differ from the caseloads observed by services, due to supply-side and demand-side issues. For example, services may see a broader range of referrals who are not psychotic or in the prodromal stage of disorder. Additional resources for false positive caseloads need to be considered in any commissioning decisions. Furthermore, demand for services may differ from the true underlying rate of FEP in the community if people are not aware of the relevant mental health services available to them. Services vary considerably in organisation, remit and structure and such factors may also affect the incepted (versus true) rate of disorder seen in EIS and other mental health services.

Prediction intervals for count-based regression models are not computationally-straightforward to derive. We estimated prediction intervals from first principles [DJ], using a bootstrap-like methodology to produce 95%PI accounting for uncertainty in the *validation sample*, but ignoring parameter uncertainty in the coefficients included in prediction models, which were assumed to be the true coefficients of risk in the population. This approach naturally leads to narrow 95%PIs given ignorance of parameter uncertainty, and is therefore desirable for model validation and the precise prediction of expected counts. The addition of more empirical data to the prediction model would thus not lead to narrower PIs, though might move the point estimate of risk for each coefficient closer to the true value in the population. We sought independent confirmation that our formula was correct (Prof Ian White, MRC Biostatistics Unit) and full details of our methodology are made available in the Appendix. We recommend that all prediction point estimates made available in our PsyMaptic model are considered with their 95%PIs, which provide information about the natural variance in expected rates in the population.

We could not externally validate our prediction models for people aged 36-64 years because comparable observed incidence data was not available in our *validation sample*. We have no reason to believe our predictions will be invalid for this group, however, since the empirical data which underpinned our models was ascertained from the same two large, well-conducted studies of first episode psychosis in England as the data for the younger age group, and published findings from these studies are



consistent with the wider epidemiological literature for psychosis from England and internationally. It will be important to ascertain the predictive capability of our model(s) where we could not externally validate our model, and we will seek to identify suitable samples to do so in future versions of PsyMaptic.

All prediction models had reasonable internal validity, although our proposed model had slightly poorer internal validity (most noticeably in terms of AIC) than models which included deprivation instead of population density (i.e. Models 2-4). Model 4 (including income deprivation) had marginally greater internal validity than our candidate prediction model, but performed worse during *external validation* (Table 4), which we considered more important for the development of a prediction tool. This decision was supported by the fact that despite considerable socioenvironmental differences between regions in our *prediction* and *validation samples*, our prediction model produced accurate forecasts in a markedly different population. We were unable to predict the expected incidence of psychotic disorder in geographical areas smaller than LADs, such as electoral wards (N~6000), or to other parts of the UK, because the appropriate denominator data was not published as mid-term census estimates. The 2011 census will provide small area and national data for the whole of the UK and will be released by ONS in mid-2013. This will allow us to update our tool to the latest population estimates for the UK, and refine our PsyMaptic tool at a smaller geographical level for fine-grained healthcare commissioning. Small area prediction models will require a multilevel approach, not attempted here, because obtaining predictions from multilevel random effects models is not straightforward and requires active statistical development.

We believe case ascertainment in our *validation sample* led to a reliable estimate of the incidence of psychotic disorder for people aged 16-35 years old. EIS are the only mental health service for people aged 14-35 years experiencing a first episode of psychosis, minimising the potential for under-ascertainment in the population at-risk when derived from a careful epidemiological design. We are confident that our *validation sample* also contained few false positive cases for any clinically-relevant psychoses, since participants were excluded who failed to meet acceptance criteria for EIS or who did not receive a clinical diagnosis of psychotic disorder at six months after referral. Future versions of PsyMaptic will include forecasts for specific psychotic disorders, but these are unavailable at present because standardised research-based diagnostic data (using OPCRIT) needed to obtain specific reliable diagnoses are currently being collected in the ongoing SEPEA study.

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Interpretation	20	<p>Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence</p> <p>If commissioners are to meet the Department of Health's vision to orientate health services around local need, differences in demand for EIS and other mental and physical health services will need to be taken into account to allocate finite resources where they are most needed. The PsyMaptic prediction model provides proof-of-concept that when robust empirical epidemiological data is combined with accurate population at-risk estimates this can be realised. Our translational approach demonstrated good internal and external validity to predict the expected incidence of first episode psychosis, particularly through EIS where 76% and 63% of all male and female adult-onset FEP cases, respectively, would typically present. Since their</p>
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inception in 2002, EIS in England and Wales have reported both lower and higher caseloads than they were originally typically commissioned to manage, usually depending on the urbanicity of the population. Rural communities saw much lower demand for EIS than urban services. The Mental Health-Policy Implementation Guide [MH-PIG] anticipated a uniform rate of 51 per 100,000 people per year. While the MH-PIG also acknowledged that "...[a]n understanding of local epidemiology is needed as the size of population covered will depend on a number of different factors" (p.55), no further elaboration on how to achieve this was provided for commissioners. We believe PsyMaptic provides one possible exemplar to overcome this challenge.

Generalisability	21	<p>Discuss the generalisability (external validity) of the study results</p> <p>We believe our results are generalisable to the populations of England and Wales. The empirical data we used is consistent with the wider international and national literature regarding the pattern of incidence rates across different sociodemographic and socioenvironmental subgroups. Our model had good external validity in the age range 16-35 years, and we have no reason to doubt its validity for the entire adult age range for psychosis, 16-64 years old given the reasonable internal validity demonstrated. That our prediction data was based on a very different environment (urban London, Nottingham and Bristol) but still produced valid forecasts in a markedly more diverse, rural and less deprived region overall (East Anglia), suggests our model will have good validity in England and Wales. This will make our prediction model a valuable tool for mental health service planning and commissioning, based on local need and translational epidemiology, when the prediction intervals we produce here are also taken into account. Service commissioners must also provide allowances for differing structure of services and the extra (false positive) referrals that may consume service resources but do not meet clinical criteria for FEP.</p>
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#### Other information

Funding	22	<p>Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based</p> <p>James Kirkbride was supported by a Sir Henry Wellcome Research Fellowship from the Wellcome Trust (grant number WT085540), through which the SEPEA study (<a href="http://www.sepea.org">www.sepea.org</a>) was established. Peter Jones directs the NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC) for Cambridgeshire &amp; Peterborough and is supported by NIHR grant RP-PG-0606-1335. The SEPEA study has been adopted by the Mental Health Research Network [MHRN]. The authors are grateful to the clinical services and staff participating in the SEPEA study, and the MHRN for their support. We are grateful to Professor Ian White of the MRC Biostatistics Unit (University of Cambridge) for his guidance on developing our prediction interval methodology for negative binomial regression.</p>
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\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).



**A population-level prediction tool for the incidence of first episode psychosis: translational epidemiology based on cross-sectional data**

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3 **A population-level prediction tool for the incidence of first episode psychosis: translational**  
4 **epidemiology based on cross-sectional data**  
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## Article Summary

### Article Focus

- Commissioners require precise information on the health needs of their local populations to effectively plan health services
- A failure to arm mental health commissioners with precise epidemiological data led to mis-estimation of actual activity in early intervention in psychosis services [EIS]
- We sought to develop a prediction tool for the incidence of first episode psychosis [FEP], by applying precise estimates of epidemiological risk in various sociodemographic groups to the structure of the population at-risk in a second region, where the observed incidence had been concurrently ascertained

### Key Messages

- A model of psychosis incidence which included age, sex, ethnicity and population density yielded precise FEP predictions in our second region, out-performing the Department of Health in England's current gold standard for EIS commissioning.
- While our model provides forecasts of the burden of FEP in different populations, initial assessment of some people who do not require subsequent EIS care means additional service resources, not addressed here, will be required.
- We have translated this model into a freely available prediction tool ([www.psymaptic.org](http://www.psymaptic.org)) to facilitate evidence-based healthcare commissioning of socioculturally relevant services according to local need
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### Strengths and limitations

- Our modelling approach used robust epidemiological data from two large studies of first episode psychosis in England to provide estimates of incidence in a third study region, producing accurate FEP forecasts
- While our models provide estimates of the expected clinical burden of FEP in the community, services may see a broader range of psychopathology consuming resources, or incepted rates may be influenced by supply-side organisational factors
- Due to data availability it was not possible to validate our prediction tool in settings outside of England and Wales, or for specific psychotic disorders. As data become available we will extend the capability of our prediction tool, including into other settings and disorders.

## Abstract

*Objectives:* Specialist early intervention services [EIS] for people aged 14-35 years with first episodes of psychosis [FEP] have been commissioned throughout England since 2001. A single estimate of population need was used everywhere, but true incidence varies enormously according to sociodemographic factors. We sought to develop a realistically-complex, population-based prediction tool for FEP, based on precise estimates of epidemiological risk.

*Design & participants:* Data from 1037 participants in two cross-sectional population-based FEP studies were fitted to several negative binomial regression models to estimate risk coefficients across combinations of different sociodemographic and socioenvironmental factors. We applied these coefficients to the population at-risk of a third, socioeconomically different region to predict expected caseload over 2.5 years, where observed rates of ICD-10 F10-39 FEP had been concurrently ascertained via EIS.

*Setting:* Empirical data from London, Nottingham and Bristol predicted counts in the population at-risk in the East Anglia region of England.

*Main outcome measures:* Observed counts compared with predicted counts (with 95% prediction intervals) at regional, EIS and local authority district [LAD] levels in East Anglia to establish predictive validity of each model.

*Results:* A model with age, sex, ethnicity and population density performed most strongly, predicting 508 FEP participants in EIS in East Anglia (95%PI: 459, 559), compared with 521 observed participants. This model predicted correctly in 5/6 EIS and 19/21 LAD. All models performed better than the current gold standard for EIS commissioning in England (716 cases; 95%PI: 664-769).

*Conclusions:* We have developed a prediction tool for incidence of psychotic disorders in England and Wales, made freely available online ([www.psymaptic.org](http://www.psymaptic.org)) to provide healthcare commissioners with accurate forecasts of FEP based on robust epidemiology and anticipated local population need. Initial assessment of some people who do not require subsequent EIS care means additional service resources, not addressed here, will be required.

## Background

Commissioners of health and social care require precise information on the health needs of their local populations<sup>1</sup>, especially if parity of mental and physical health is to be realised.<sup>2</sup> Mental health disorders alone represent the leading disease burden in the UK (22.8%).<sup>3</sup> They contribute substantially to healthcare expenditure and societal costs even before physical ill health is taken into account. The Centre for Mental Health estimated total costs of mental health to British health services and society at £105 billion in 2009/10,<sup>4</sup> a figure expected to double over the next 20 years.<sup>2</sup> These are serious challenges compounded by a paucity of information on which to commission appropriate services. Early intervention in psychosis services [EIS] for people aged 14-35 years with a first episode of psychosis [FEP] offer a useful example of failure to map services to local need.

EIS are a major evidence-based innovation, systematically commissioned throughout England and Wales over the past decade.<sup>5</sup> When EIS intervention is sustained there is evidence that people with psychosis achieve better functional and social outcomes.<sup>6,7</sup> Such services are also highly cost-effective.<sup>4,8,9</sup> However, EIS were originally commissioned on an anticipated rate of 150 new cases of any psychotic disorder per 1,000,000 of the total population per year in the Department of Health's Mental Health Policy Implementation Guide [MH-PIG].<sup>5</sup> In 2001 in England and Wales, 29.3% of the population were aged 14-35 years old, meaning that the MH-PIG commissioned incidence rate was approximately 51 cases per 100,000 person-years in the age range covered by EIS. Following their deployment, anecdotal reports began to emerge from EIS in different regions to suggest that a uniform figure for commissioning was simultaneously under-<sup>10</sup> and over-estimating<sup>11</sup> actual observed need in urban and rural populations, respectively. Recent epidemiological evidence of FEP incidence in rural communities in England has suggested that rates are somewhat lower than the uniform figure upon which services were commissioned,<sup>12,13</sup> confirming previous calls that a "one-size-fits-all" prescription for EIS implementation is unlikely to lead to the efficient allocation of finite mental health resources.<sup>14,15</sup>

Using rich epidemiological data on variation in the incidence of first episode psychosis according to major sociodemographic risk factors,<sup>16-19</sup> we describe the development and validation of a population-level prediction tool capable of accurately estimating the expected incidence of psychiatric disorder, based on the sociodemographic structure of the population in a given region. Applied to FEP as proof-of-concept, we show it is possible to closely predict expected incidence in a given population, where the observed count of cases was within the prediction intervals forecast by our models. We applied our

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3 most precise prediction model to the population of England and Wales to provide health commissioners  
4 with a translational epidemiological prediction tool to underpin information-based service planning.  
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## 8 9 **Methods**

10 Our prediction models were based on epidemiological data from the Aetiology and Ethnicity in  
11 Schizophrenia and Other Psychoses [ÆSOP] and the East London First Episode Psychoses [ELFEP]  
12 studies,<sup>18, 20</sup> two methodologically-similar population-based FEP studies. We fitted various count-based  
13 regression models with different combinations of sociodemographic and socioenvironmental factors,  
14 well-established in the literature to be associated with the incidence of psychotic disorder.<sup>21, 22</sup> We first  
15 established the *relative apparent validity* of each model by estimating model fit diagnostics to assess  
16 how well each model fitted the empirical data (henceforth, the *prediction sample*). We next sought to  
17 estimate the *external validity* of each model by applying model-based parameter coefficients to the  
18 population structure of a purposefully different region of England, East Anglia (henceforth, the  
19 *validation sample*). This out-of-sample prediction technique allowed us to obtain the expected incidence  
20 of disorder in this region forecast by each model, which we compared with observed rates  
21 simultaneously ascertained in this region via the ongoing Social Epidemiology of Psychoses in East Anglia  
22 [SEPEA] study.<sup>13</sup> We performed various model fit diagnostics to identify which, if any, model  
23 demonstrated utilisable predictive capability.  
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### 37 **Empirical data underlying prediction models (*prediction sample*)**

#### 38 *Case ascertainment (numerator)*

39 The designs of the ÆSOP and ELFEP studies have been described in detail elsewhere,<sup>18, 20</sup> with features  
40 relevant to the present paper summarised here. Case ascertainment took place over two years in ELFEP  
41 (Newham: 1996-8; Tower Hamlets & Hackney: 1998-2000) and the Southeast London and Nottingham  
42 centres of the ÆSOP study (1997-9), and over the first 9 months of 1997 in Bristol (ÆSOP). All service  
43 bases were screened regularly for potential new contacts aged 16-64 years (18-64 in ELFEP) resident  
44 within these catchment areas. Leakage studies were conducted to identify participants missed by this  
45 initial screen, but meeting inclusion criteria for FEP.<sup>18, 20</sup> All participants who received an ICD-10 F10-39  
46 diagnosis for psychotic disorder following assessment via the Schedules for Clinical Assessment in  
47 Neuropsychiatry were included in the incident sample, except those with an organic medical basis to  
48 their disorder or profound learning difficulty. Data on age-at-contact, sex and ethnicity were collected  
49 on included participants. We geocoded participants' residential postcode at first contact to their  
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3 corresponding local authority district [LAD] to allow us to model possible neighbourhood effects  
4 associated with the incidence of psychotic disorder, such as population density or socioeconomic  
5 deprivation.  
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### 10 *Population at-risk*

11 We estimated the population at-risk using the 2001 Census of Great Britain, adjusted for study duration,  
12 and stratified by age group (16-17, 18-19, then 5-year age bands), sex and ethnicity. Ethnicity was based  
13 on self-ascription according to one of ten categories derived from the census: white British, non-British  
14 white, black Caribbean, black African, Indian, Pakistani, Bangladeshi, mixed white & black Caribbean,  
15 other mixed ethnic backgrounds and all other ethnicities.  
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### 22 *Socioenvironmental variable estimation*

23 We estimated LAD -level deprivation using the 2004 Index of Multiple Deprivation [IMD] in England,  
24 which estimated domains of deprivation using measures predominantly collected close to the time of  
25 our case ascertainment periods (see Box 1).<sup>23</sup> We z-standardised English LAD IMD scores to have a mean  
26 of zero and standard deviation of one, and extracted IMD z-scores for the 14 LADs in the ÆSOP and  
27 ELFEP studies. To inspect whether any particular deprivation domain was a better predictor of psychosis  
28 incidence than IMD, we also considered LAD-level income deprivation, employment deprivation and the  
29 extent of deprivation in our models (Box 1). We estimated population density by dividing LAD usual  
30 resident population by its area (in hectares), using ArcGIS 9.3 software.  
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40 <[Box 1 about here](#)>  
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### 43 **Observed data for external validation of prediction models (*validation sample*)**

44 Observed participants and population at-risk data for our *validation sample* was obtained from the  
45 SEPEA study, an ongoing study of the incidence of psychotic disorders incepted over three years (2009-  
46 12) through one of six EIS covering 20 LAD and a subsection of one LAD (the town of Royston,  
47 Hertfordshire) in Norfolk (three EIS: West, Central and Great Yarmouth & Waveney), Suffolk (one EIS)  
48 and Cambridgeshire, Royston & Peterborough (CAMEO North and South EIS).<sup>13</sup>  
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### 55 *Case ascertainment*

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3 To establish the incepted incidence of first episode psychosis as seen through EIS, entry criteria for the  
4 SEPEA study were:  
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- 9 • Referral to an EIS in East Anglia for suspected first episode of psychosis
- 10 • Aged 16-35 years old at first referral to EIS (17-35 years in CAMEO services)
- 11 • Resident within the catchment area at first referral
- 12 • First referral during case ascertainment period (2009-12)
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17 At six months after EIS acceptance, or discharge from the service, whichever was sooner, we asked the  
18 clinician responsible for care to provide an ICD-10 F10-39 psychiatric diagnosis using all information  
19 available. We excluded participants without a clinical FEP diagnosis, or participants presenting with an  
20 organic basis to their disorder or profound learning disability. For remaining participants, basic  
21 sociodemographic and postcode information was recorded and classified in the same way as in the  
22 *prediction sample*. We included participants presenting to EIS during the first 2.5 years of the ongoing  
23 SEPEA study.  
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#### 29 30 31 *Population at-risk*

32 We estimated the population at-risk of East Anglia using 2009 mid-year census estimates published by  
33 the Office for National Statistics [ONS] at LAD-level, by age group, sex and ethnicity.<sup>24</sup> These estimates  
34 used the 2001 census base, adjusted for immigration, births and deaths each year. It was not possible to  
35 obtain 2009 mid-year estimates for the town of Royston, because data were only published at LAD level.  
36 Here, we thus used denominator data from the 2001 census data, in order to estimate the population  
37 at-risk in Royston. We do not believe this would have substantially invalidated our results as this town  
38 represented 0.6% of the overall population at-risk (n=9,555) in the SEPEA study. Denominator data were  
39 multiplied by 2.5 to account for person-years of exposure in the *validation sample*.  
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#### 48 *Socioenvironmental variable estimation*

49 For each LAD in the SEPEA study we obtained corresponding socioenvironmental variables to those  
50 included in our *prediction sample*, using updated data collected as close to the SEPEA case  
51 ascertainment period as possible. Population density was estimated using 2009 mid-term population  
52 estimates. Our measures of deprivation were derived from the IMD 2010,<sup>25</sup> which was estimated in an  
53 analogous way to 2004 data, but collected from sources obtained immediately prior to the SEPEA study.  
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## Statistical techniques

### *Dataset generation*

We constructed a dataset for the regression analysis of count data by pooling data from the ÆSOP & ELFEP studies (the *prediction sample*). Data were stratified by age group, sex, ethnicity and LAD, such that each stratum (N=2,536) represented the total count of FEP cases in a unique sociodemographic group for a given LAD, with a corresponding estimate of the population at-risk, treated as an offset in our models. Our socioenvironmental measures (population density, deprivation) were adjoined to the dataset for each LAD. Population at-risk data from the *validation sample* were stratified in the same way and retained in a separate database. Here, the count of cases, which we wished to predict, was entered as a vector of missing data which would be populated with predicted case estimates following prediction modelling.

### *Prediction models*

We used the *prediction sample* data to fit negative binomial regression models to obtain parameter coefficients of incidence for the sociodemographic and socioenvironmental factors included in each model. We considered the internal and external predictive capabilities of six models, all of which contained age group, sex, an age-sex interaction term and ethnicity. Model 1 contained no further covariates. Model 2 also included IMD. We replaced IMD with either income, employment or the extent of deprivation, respectively, in models 3-5. Model 6 included population density. Initial exploration of the *prediction sample* data indicated the presence of possible over-dispersion (variance ( $\delta^2=1.37$ ) exceeded mean ( $\mu=0.4$ ) count of cases) so negative binomial regression was preferred to Poisson regression since it explicitly models any over-dispersion with an extra dispersion parameter.

### *Internal model cross-validation & prediction*

We assessed apparent model validity in three ways. First we used Akaike's Information Criterion [AIC] to assess the respective overall fit of each model to the data. Second, we conducted K-fold cross-validation to assess each model's apparent validity to predict cases within the *prediction sample*. This method randomly allocated strata in the *prediction sample* into  $K$  subsets. Each model was then re-estimated on  $K-1$  subsets (the *training data*) to predict expected counts of cases in the  $K^{\text{th}}$  subset (the *test data*). This was repeated over  $K$  trials, such that each stratum in the dataset appeared exactly once as the *test data*. At the end of this process, we derived Lin's concordance correlation coefficient [CCC] and 95%

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3 confidence intervals [95%CI] to estimate the correlation between predicted and observed counts of  
4 cases across all strata in the *prediction sample*. Finally, we estimated the root mean squared error  
5 [RMSE] to determine the average error between fitted and observed values from each model, where  
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7 lower RMSE scores indicated smaller prediction error. The RMSE is derived as  
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$$RMSE = \sqrt{\frac{\sum_{i=1}^n (y_i - \hat{y}_i)^2}{n}}$$

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18 where  $y_i$  and  $\hat{y}_i$  are the observed and predicted count of cases in the  $i^{\text{th}}$  stratum, respectively, and  $n$  is  
19 the number of strata.  
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23 We repeated K-fold cross-validation  $h$  times, generating  $K$  new random divisions of the data each time.  
24 We retained model fit diagnostics across  $Kh$  iterations, and reported the mean of Lin's CCC and RMSE to  
25 provide summary cross-validation statistics for each model. We specified  $K=10$  and  $h=20$ , as  
26 recommended for cross-validation to obtain precise model fit diagnostics.<sup>26</sup>  
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### 30 31 *External model prediction & validation*

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33 We retained parameter coefficients from each model (using the full *prediction sample* data) and applied  
34 these to the corresponding population at-risk in the *validation sample* dataset. This gave out-of-sample  
35 prediction estimates for the expected count of cases in each stratum of the *validation sample*, given the  
36 model. We summed expected counts across relevant strata to estimate the (i) total predicted count of  
37 cases in the SEPEA region, (ii) predicted counts in each EIS, and (iii) predicted counts by LAD. These  
38 counts were further stratified by broad age group (16-35, 36-64 and 65-94 years). Because census  
39 (denominator) data was unavailable for 35 year olds alone (needed to estimate their contribution to  
40 predicted counts in the age range for EIS, 16-35 years) we assumed the risk coefficient was the same  
41 across all ages within the 35-39 year old age group. We apportioned predicted counts on a 1:4 ratio (35  
42 years: 36-39 years) to their respective broad age groups.  
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52 To determine how well the MH-PIG<sup>5</sup> figure of 51 new cases per 100,000 people per year for EIS  
53 performed as a predictive tool, we also estimated the predicted count of cases in the *validation sample*  
54 under this scenario, which we termed "Model 7".  
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3 We derived prediction intervals [95% PIs] for all summary predictions from first principles for each  
4 negative binomial regression model, since their derivation is not straightforward, nor routinely  
5 implemented by statistical software. Prediction intervals are similar to confidence intervals, but account  
6 for standard errors introduced in both the *prediction* and *validation* samples. We developed a  
7 bootstrap-like approach to obtain prediction intervals from each model by simulating 1000 model-based  
8 realisations of the quantities we wished to predict, where we took the parameters to be the maximum  
9 likelihood estimates. We obtained the lower and upper bounds of the prediction intervals as the  
10 corresponding quantiles of the simulated realisations (see Appendix for full details).  
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19 To assess each model's external predictive capabilities, we considered five markers of predictive  
20 accuracy. We compared the number of times the observed count of cases in the SEPEA study fell within  
21 the prediction intervals estimated from each model for (i) the SEPEA region, (ii) at EIS level, and (iii) at  
22 LAD level. We also derived EIS- and LAD-level RMSE scores to estimate prediction error from each model  
23 in our *validation sample*. We ranked model performance (1: best, 7: worst) on these five measures, and  
24 estimated an overall mean rank to determine the overall predictive validity of each model.  
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31 Observational data on first episode psychosis in our *validation sample* were not available for the age  
32 range 36-64 years, so external validation was restricted to the 16-35 year old group. For completeness,  
33 however, we also reported overall predicted count of cases for this age group from each model.  
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### 38 *Extrapolation to the United Kingdom*

39 Guided by our validation procedures, we identified which model had the greatest overall predictive  
40 validity, and proposed this as a candidate for FEP incidence prediction in England and Wales. We  
41 repeated out-of-sample prediction on the sociodemographic and socioenvironmental population  
42 characteristics of each LAD in England and Wales to obtain national and LAD-level predictions.  
43 Denominator data was obtained from the ONS 2009 mid-term estimates and stratified as previously  
44 described. Overall counts were derived for three broad age groups (16-35, 36-64 and 65-74 years), and  
45 for each of these, by sex and ethnicity. 95% PIs were estimated as before. We visualised this data on  
46 maps and in tables to provide healthcare planners and commissioners with an easy-to-use tool to  
47 forecast the expected incidence of psychosis in England and Wales. We have made this available as a  
48 free, open-use prediction tool, known as PsyMaptic (version 0.5) (Psychiatric Mapping Translating  
49 Innovations into Care; [www.psymaptic.org](http://www.psymaptic.org)). Counts of cases predicted by our model were compared  
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3 with those obtained under the Department of Health's uniform rate in each LAD. We expressed these  
4 comparisons as ratios with 95% CIs derived using the same method as for standardised morbidity ratios  
5 [SMR]. This approach was conservative because here we substituted the usual numerator in an SMR, the  
6 observed, O, for a predicted count. Unlike an observed count, no sampling variation is present for the  
7 predicted count, only uncertainty due to the model from which the prediction was estimated. Since  
8 variance in the prediction is therefore much smaller than the variance normally present for the  
9 numerator (O) this led to conservative estimates of 95% CI. Ratios in LAD where 95% CI did not span  
10 unity could therefore be interpreted as regions where there was strong evidence that the predictions  
11 from our model differed significantly from those predicted by the Department of Health's uniform rate.  
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### 20 21 *Software*

22 All negative binomial regression models, out-of-sample prediction and estimation of 95% PI were  
23 conducted in R (version 2.15.1). Cross-validation and model-fit diagnostics were conducted in Stata  
24 (version 11). Prediction maps for England and Wales were created using StatPlanet Plus (version 3.0)  
25 visualisation software.<sup>27</sup>  
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## 31 **Results**

### 32 **Prediction sample**

33 Our prediction models contained data on 1,037 persons with a first episode psychosis in the ÆSOP  
34 (n=553; 53.3%) and ELFEP (n=484; 46.7%) studies, ascertained from over 2.4m person-years at-risk.  
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Twelve participants were excluded from the original ÆSOP sample because they were of no fixed abode  
and could not be geocoded to an LAD.<sup>18</sup>

The population at-risk in the *prediction sample* came from LAD with higher median levels of multiple and  
employment deprivation, extent of deprivation and population density than the population at-risk in the  
*validation sample*, though there were no statistically significant differences in median income  
deprivation between the two samples (Supplemental Table 1).

[<Supplemental Table 1 about here>](#)

Parameter coefficients obtained from the full prediction sample following negative binomial regression  
are shown in Table 1. As previously reported from these data,<sup>20,28</sup> incidence rates were generally raised

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3 in ethnic minority groups compared with the white British population. Models 2-6 included a measure of  
4 LAD deprivation (Models 2-5) or population density (Model 6), which were all significantly associated  
5 with increased incidence of psychotic disorder, after control for individual-level confounders. Each of  
6 these models produced a lower AIC score than a model fitted solely with individual-level covariates  
7 (Model 1), indicating better fit. Cross-validation suggested all models achieved good CCC agreement  
8 between predicted and observed cases, with low RMSE values (Table 1).  
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### 18 19 **Validation sample**

#### 20 *Observed participants*

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22 We identified 572 participants over the first 30 months of the SEPEA study, aged 16-35 years old, who  
23 met acceptance criteria for EIS in East Anglia. We excluded 51 participants (8.9%) who did not meet  
24 clinical criteria for ICD-10 psychotic disorder. This left an incidence sample of 521 participants from  
25 nearly 1.4m person-years at risk (37.3 per 100,000 person-years; 95%CI: 34.2, 40.6). A further 2.3m  
26 person-years at-risk accrued in the same region for people aged 36-64 years over this period. Median  
27 levels of multiple, income and employment deprivation in the region did not differ significantly from the  
28 remainder of England, although median population density and extent of deprivation in East Anglia were  
29 lower than elsewhere in England (Supplemental Table 1).  
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#### 41 *External model prediction & validation*

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43 The overall observed count of cases, aged 16-35 years, in the *validation sample* (n=528) fell within 95%  
44 prediction intervals in four of seven models (Models 3 -6, Table 2). Of these, the observed count (N=521)  
45 was closest to the point estimate for Model 6 (508.5; 95% PI: 449.0, 559.0), fitted with age group, sex,  
46 their interaction, ethnic group and LAD population density. The observed count of cases also fell within  
47 prediction intervals from this model in five of six EIS in the study region, and 19 of 21 LADs, the most of  
48 any model (Table 3). This model had the lowest error scores at EIS (RMSE=11.5) and LAD (RMSE=6.0)  
49 levels of any model. Overall, Model 6 was ranked highest across all external model fit diagnostics (Table  
50 3). All models outperformed the Department of Health's uniform figure of 51 cases per 100,000 people  
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3 per year (Model 7), which generally overestimated cases in the *validation sample* (overall prediction:  
4 715.7 cases; 95% PI: 664.0, 769.0).  
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11 We also reported predicted cases aged 36-64 years old from our models (Table 3), although we could  
12 not test these in the *validation sample*. Model 6 predicted an additional 262.9 cases aged 36-64 years  
13 over a 2.5 year period in East Anglia (95% PI: 233.0, 297.0).  
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18 We also inspected the stratum-specific external validity of our best-fitting model (Model 6,  
19 Supplementary Table 2), which performed accurately for sex-specific predictions, but less well in age-  
20 and ethnicity-specific strata. Thus, our model tended to under-predict observed cases in people aged 16-  
21 19 years, but over-predicted cases observed in people over 25 years old. With respect to ethnicity,  
22 model predictions were consistent with observed FEP cases for people of non-British white, black  
23 African, Bangladeshi and mixed ethnicities. However, our model under-predicted observed rates in the  
24 white British group, and over-predicted rates in black Caribbean, Indian and Pakistani populations.  
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32 <Supplemental Table 2 about here>  
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### 36 *Extrapolation to England and Wales*

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38 We predicted the expected count and incidence of first episode psychosis per annum in each LAD in  
39 England and Wales based on Model 6, and visualised this data in maps and tables freely available at  
40 [www.psymaptic.org](http://www.psymaptic.org). Many maps can be visualised (for example, Supplemental Figure 1), including  
41 overall predicted incidence counts and rates for each broad age group at LAD level, and by sex. We will  
42 make PsyMaptic data available by ethnic group when we can improve the validity of future versions of  
43 these models for these strata. According to our model, the annual number of new FEP cases in England  
44 and Wales would be 8745 (95% PI: 8558, 8933), of which our model predicted 67.9% (N=5939; 95% PI:  
45 5785, 6102) would be seen through EIS. Only 176 (95% PI: 151, 203) cases aged 16-64 years were  
46 forecast in Wales per annum. Assuming our prediction model is accurate, it indicated that the  
47 Department of Health's current uniform rate of 51 per 100,000 person-years was higher than the  
48 predicted point estimates for rates forecast by our PsyMaptic model in 351 LAD (93%) in England and  
49 Wales, but was lower than predicted by our model in Birmingham and several London boroughs  
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3 (Supplemental Figure 2, left hand map). Under a conservative approach, these differences achieved  
4 statistical significance in parts of London (where the Department of Health's model underestimated  
5 need as predicted by PsyMaptic), and in some more rural parts of England and Wales (where the  
6 Department of Health's model over-estimated need) (Supplemental Figure 2, right hand map).  
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12 <[Supplemental Figures 1 & 2 about here](#)>  
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## 14 15 16 **Discussion**

### 17 18 **Principal findings**

19 We have developed and tested several epidemiological prediction models to forecast FEP incidence in  
20 England and Wales, having taken into account regional differences in the sociodemographic and  
21 socioenvironmental profile of different populations. Inspection of our data suggested that a model fitted  
22 with age group, sex, their interaction, ethnic group and LAD-level population density provided the  
23 greatest external predictive validity when compared with the observed FEP caseload ascertained  
24 through EIS in our *validation sample*. This model also had good apparent validity across the entire age  
25 range (16-64 years). All models performed significantly better in predicting the incidence of clinically  
26 relevant first episode psychosis than the Department of Health's current gold standard for EIS  
27 commissioning,<sup>5</sup> based on a uniform incidence rate. Our data suggested the figure used to commission  
28 EIS over-estimated the likely true incidence rates of FEP in rural areas, and under-estimated them in  
29 urban settings, although we acknowledge that commissioning decisions will need to be based on several  
30 additional factors, including the level of pre-clinical or non-psychotic psychopathology requiring  
31 assessment at initial referral to EIS, and variation in service organisation, remit and delivery.  
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### 43 44 **Limitations & future development**

45 Our prediction models were based on epidemiological data obtained from large, robust population-  
46 based FEP studies for people aged 16-64 years.<sup>18,19</sup> The best-fitting model, overall, had good apparent  
47 validity over this age range, and good external validity over the age range 16-35 years. While this  
48 covered the majority of adult onset psychosis cases seen in mental health services, including EIS, we  
49 recognise that some EIS teams incept people from 14 years old. We were unable to extrapolate our  
50 models to this age range, given the current absence of incidence data for this group in England. Data  
51 from Scandinavia suggest that the incidence of such "early onset" psychoses is absolutely low,<sup>29</sup>  
52 although the rate may have been increasing in the last few decades, probably as a result of movement  
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3 towards earlier detection. We were also unable to externally validate prediction models for people aged  
4 36-64 years, because comparable observed incidence data was not available in our *validation sample*.  
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6 We have no reason to believe our predictions will be invalid for this group, however, since the empirical  
7 data which underpinned our models was ascertained from the same two large, well-conducted studies  
8 as for data on the younger age group.<sup>18, 19, 28</sup> Furthermore, published findings from these studies are  
9 consistent with the wider epidemiological literature for psychosis in England and internationally.<sup>17, 21, 30</sup> It  
10 will be important to validate the predictive capability of our model(s) in this age range, and we will seek  
11 to identify suitable samples to do so in future versions of PsyMaptic.  
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19 Our best-fitting overall model demonstrated excellent external validity for predicting sex-specific FEP  
20 cases in our *validation region* (i.e. SEPEA). It performed less well across age- and ethnic-specific stratum  
21 in this region. With respect to age, this discrepancy is most likely to be a function of EIS provision itself,  
22 which seeks to intervene as early as possible in the onset of psychosis. The effect of this will reduce  
23 median age at onset in comparison to studies conducted prior to the introduction of EIS, such as the  
24 ÆSOP and ELFEP studies, upon which our models are based. Future versions of PsyMaptic will  
25 incorporate empirical data from post-EIS studies to improve age-specific predictions. The validity of our  
26 model in some ethnic groups also requires further refinement. Much of the prediction data underlying  
27 our models came from urban environments with large proportions of ethnic minority groups. The  
28 sociodemographic profile and sociocultural experiences of these groups may be very different to those  
29 of their counterparts in other, less urban, parts of England, thus altering risk of psychosis according to  
30 ethnicity. In our observed data, a larger proportion of cases were white British than predicted by our  
31 model. If ethnicity is a partial proxy for exposure to deleterious socio-environmental experiences, such  
32 as the combined effect of social inequality, fragmentation, deprivation and population density,<sup>31</sup> then  
33 simultaneously incorporating such factors into our models may improve their predictive validity by  
34 ethnicity. Alternatively, risk by ethnic group may be conditional upon (i.e. interact with) environmental  
35 factors in urban areas (as with the ethnic density effect<sup>32, 33</sup>), but whether such interactions exist in less  
36 urban regions is not known. Forthcoming SEPEA and PsyMaptic data will explore such possibilities as  
37 2011 census data become available.  
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53 All prediction models had reasonable apparent validity, although our proposed model performed slightly  
54 worse (most noticeably for AIC) than models which included deprivation (i.e. models 2-4) instead of  
55 population density. Our decision to use model 6 as our proposed candidate for the prediction tool was  
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3 supported by the fact that it produced the most accurate external forecasts of any model, despite  
4 considerable socioenvironmental differences between regions in our *prediction* and *validation* samples.  
5 We were unable to predict the expected incidence of psychotic disorder in geographical areas smaller  
6 than LADs, such as electoral wards (N~6000), or to other parts of the UK, because appropriate  
7 denominator data was not published as mid-term census estimates. The 2011 census will provide small  
8 area and national data for the whole of the UK, scheduled for release by ONS in mid-2013. This will allow  
9 us to update our tool to the latest population estimates for the UK, and refine our PsyMaptic tool at a  
10 smaller geographical level for fine-grained healthcare commissioning. We will then be able to develop  
11 models to explore cross-level interactions, such as the association between individual ethnicity and  
12 neighbourhood-level ethnic density. Small area prediction models will require a multilevel approach, not  
13 attempted here, because obtaining predictions from multilevel random effects models is not  
14 straightforward and requires active statistical development.  
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26 We believe case ascertainment in our *validation sample* led to a reliable estimate of the incidence of  
27 psychotic disorder for people aged 16-35 years old. EIS were the only mental health service for people  
28 aged 14-35 years experiencing a first episode of psychosis in East Anglia, minimising the potential for  
29 under-ascertainment in the population at-risk when derived from careful epidemiological design.<sup>13</sup> We  
30 are confident that our *validation sample* also contained few false positive cases for any clinically-  
31 relevant psychoses, since participants were excluded who failed to meet acceptance criteria for EIS or  
32 who did not receive a clinical diagnosis of psychotic disorder during the first six months from initial  
33 referral. It is important to recognise that while our prediction models are based on diagnosed clinically  
34 relevant psychotic disorders, service commissioning will also need to account for additional pre-clinical  
35 or non-psychotic psychiatric morbidity presenting to EIS, particularly in services which operate early  
36 detection models or implement “watch-and-wait” briefs. The SEPEA data used to validate our models do  
37 not predict (1) the number of “false positive” subjects who may require psychiatric triage and  
38 assessment even though they are not accepted by EIS, or (2) the number of “true positive” subjects  
39 accepted by services, but who did not meet epidemiological criteria for inclusion in the *validation*  
40 *sample* of the SEPEA study (those living outside the catchment area at first contact, or those transferred  
41 from other services); these people will consume varying degrees of service resources which needs to be  
42 considered in service planning.  
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3 We also note that pathways to care may affect the level of incidence observed in EIS, since many filters  
4 are likely to operate before subjects come to the attention of EIS. These will include local level service  
5 organisation and the relationship between Community Mental Health Teams [CMHTs], Child and  
6 Adolescent Mental Health [CAMHs] and EIS. Furthermore, acceptance criteria for entry to EIS vary,  
7 which will have a downstream effect on the number of new cases of clinically relevant psychoses  
8 received in each team. Future versions of PsyMaptic will include forecasts for specific psychotic  
9 disorders, as standardised research-based diagnoses (using OPCRIT<sup>34</sup>) are currently being collected in  
10 the ongoing SEPEA study in order to provide more detailed forecasts. Acceptance rates to EIS may also  
11 be influenced by local community awareness of such services. While our prediction models  
12 outperformed the current gold standard for EIS commissioning in England when restricted to clinically  
13 relevant caseloads, we recommend that our models are best interpreted as forecasts of the expected  
14 burden of first episode psychosis in given populations, and not the expected burden which will  
15 necessarily be seen through EIS given these issues.  
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27 We estimated prediction intervals from first principles [DJ] since their derivation is an area of statistical  
28 development.<sup>35</sup> We used a bootstrap-like methodology to produce 95% PI accounting for natural  
29 variation in the *validation sample*, but ignoring parameter uncertainty in the coefficients included in  
30 prediction models, which we assumed to be the true coefficients of risk in the population. Our approach  
31 therefore naturally led to slightly artificially narrow 95% PIs. This was not necessarily undesirable for the  
32 purpose of model validation and the precise prediction of expected counts because we wished to apply  
33 stringent criteria. Ideally, prediction intervals should take into account both these sources of variation,  
34 although we note that parameter uncertainty is usually small compared to the natural variation of the  
35 quantities of interest. The addition of more empirical data in the *prediction sample* would not lead to  
36 narrower PIs, though would tend to move the point estimate of risk for each coefficient closer to the  
37 true value in the population. We do not believe we have mis-estimated point estimates of risk across  
38 major sociodemographic groups, since our results accord with the wider literature.<sup>17, 21, 22</sup> We sought  
39 independent confirmation that our development of 95% PI were correct (personal communication with  
40 Prof Ian White, MRC Biostatistics Unit). We recommend that all prediction point estimates from our  
41 PsyMaptic model are considered with their 95% PIs, which provide information about the natural  
42 variance in expected rates in the population.  
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### 57 **Meaning of the findings**

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3 If commissioners are to meet the Department of Health's vision to orientate health services around local  
4 need,<sup>1, 2, 5</sup> differences in demand for EIS and other mental and physical health services will need to be  
5 taken into account to allocate finite resources where they are most needed. The PsyMaptic prediction  
6 model provides proof-of-concept that when robust empirical epidemiological data is combined with  
7 accurate population at-risk estimates this can be realised. As such, our modelling approach could have  
8 utility in many other settings and for many disorders. Our translational approach demonstrated good  
9 validity to predict the expected incidence of first episode psychosis, particularly through EIS, where 76%  
10 and 63% of all male and female adult-onset FEP cases, respectively, will typically present.<sup>18</sup> Since their  
11 inception in 2002, EIS in England and Wales have reported both lower<sup>11</sup> and higher<sup>10</sup> caseloads than they  
12 were originally envisioned to manage,<sup>5</sup> with shortfalls or excesses in anticipated demand for services  
13 aligned to the degree of urbanisation in the underlying catchment area. Others have noted that EIS  
14 provision in rural areas may be difficult to implement effectively,<sup>14, 15</sup> and while the MH-PIG  
15 acknowledged that "...[a]n understanding of local epidemiology is needed as the size of population  
16 covered will depend on a number of different factors" (p.55),<sup>5</sup> no further elaboration on how to achieve  
17 this was provided. We believe PsyMaptic provides a possible tool to overcome this challenge, improving  
18 the description and prediction of local population need beyond the MH-PIG and including individual-  
19 and neighbourhood-level indicators of local need.<sup>17</sup> From an aetiological perspective, we acknowledge  
20 that variables such as ethnicity or population density are likely to be markers for a suite of more  
21 complex, interactive social, genetic and environmental determinants of psychosis.<sup>36</sup>

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38 Our models are not the first to be used to forecast mental illness needs in England and Wales,<sup>37</sup> though  
39 we believe this is the first attempt to forecast incidence rather than prevalence in the community. We  
40 recommend that our prediction methodology is used in conjunction with the wide range of public health  
41 observatory data available,<sup>38</sup> as well as the caveats presented above. PsyMaptic has been included with  
42 other indicators in the Joint Commissioning Panel for Mental Health's forthcoming guidance for  
43 commissioning of public mental health services.<sup>39</sup> Ongoing monitoring and audit of EIS will be vital to  
44 ensure services meet the fidelity criteria upon which they were originally commissioned,<sup>11, 40</sup> including  
45 ensuring that service capacity matches local need as closely as possible. As part of this process, we will  
46 need to externally validate our models in a wider range of settings, refining them based on empirical  
47 observation.

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3 We note that advocacy expressed for EIS by healthcare professionals in England and Wales broadly  
4 correlates with demand for services as predicted by PsyMaptic.<sup>41</sup> Though by no means universal,  
5 proponents of EIS tend to be located in major conurbations – such as London,<sup>42</sup> Birmingham<sup>43</sup> or  
6 Manchester<sup>7,44</sup> – where demand for EIS will be highest, while those who suggest EIS resources could be  
7 used more effectively elsewhere tend to work in more rural communities,<sup>15,41</sup> where but a handful of  
8 young people would be expected to come to the attention of EIS each year. It is possible that both sides  
9 are correct and that more resources are required to help with the tide of psychotic illness in inner cities.  
10 Resources might be used more effectively in other ways, elsewhere, so long as the needs of the small  
11 number of young people who suffer a FEP each year are met; a dedicated specialist EIS may not be the  
12 most effective approach when anticipated demand will be very low.  
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22 Given the significant downstream economic savings associated with spending on EIS as estimated in an  
23 urban setting,<sup>8</sup> PsyMaptic could be used to highlight regions where sufficient investment to appropriate  
24 mental health services would lead to greatest economic gains in terms of mental healthcare expenditure  
25 (assuming sustained intervention also leads to improved social and clinical benefit for patients<sup>6,7</sup>).

26 PsyMaptic can also be used to highlight regional variation in demand according to age and sex and, in  
27 future versions, by ethnicity. This will allow service planners to tailor provision around the socio-cultural  
28 characteristics of their local populations. Our prediction tool for first episode psychosis, which translates  
29 robust empirical epidemiological data on psychosis risk to the population structure of different regions,  
30 offers a methodology for improving the allocation of finite mental health resources based around local  
31 need.  
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**Box 1: Description of included socioenvironmental variables**<sup>1 2</sup>

Variable	Classification & description
Multiple deprivation	Weighted data from routine national sources across 7 domains: income, employment, education, health, barriers to housing & services, living environment, crime. Continuous, z-standardised scores for analysis.
Extent of deprivation	Proportion of LAD population living in 20% most deprived SOA in England (%)
Income deprivation	Proportion of all people in LAD classified as income deprived (%)
Employment deprivation	Proportion of adults of working age in LAD classified as employment deprived (%)
Population density	Population density at LAD level (people per hectare).

IMD: Index of Multiple Deprivation; LAD: Local authority district; SOA: super output area; IQR: inter-quartile range

<sup>1</sup>*Prediction sample* sources: Population density – 2001 census estimates; Deprivation variables: 2004 Indices of Deprivation, predominantly collected from data sources close to A&SOP & ELFEP case ascertainment periods (i.e. 1997-2000)

<sup>2</sup>*Validation sample* sources: Population density – 2009 mid-year census estimates; Deprivation variables: 2010 Indices of Deprivation, predominantly collected from data sources just prior to SEPEA case ascertainment period (2008)

Table 1: Prediction models, covariates and fit: all clinically relevant psychoses (F10-39)

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Variable	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)	IRR (95%CI)
Age group*sex interaction <sup>1</sup>	p=0.07	p=0.06	p=0.06	p=0.06	p=0.06	p=0.06
Ethnicity						
White British	1	1	1	1	1	1
Non-British white	2.0 (1.5, 2.5)	1.7 (1.4, 2.2)	1.7 (1.3, 2.2)	1.7 (1.3, 2.2)	1.8 (1.4, 2.3)	1.7 (1.3, 2.2)
Black Caribbean	6.0 (4.9, 7.3)	5.3 (4.3, 6.5)	5.2 (4.3, 6.4)	5.2 (4.3, 6.4)	5.4 (4.5, 6.6)	5.1 (4.2, 6.3)
Black African	4.1 (3.3, 5.1)	3.6 (2.9, 4.5)	3.5 (2.8, 4.4)	3.5 (2.8, 4.4)	3.7 (3.0, 4.6)	3.5 (2.8, 4.3)
Indian	1.7 (1.2, 2.5)	1.5 (1.1, 2.2)	1.5 (1.0, 2.2)	1.5 (1.0, 2.1)	1.6 (1.1, 2.3)	1.6 (1.1, 2.2)
Pakistani	1.8 (1.2, 2.5)	1.6 (1.0, 2.5)	1.6 (1.0, 2.4)	1.6 (1.0, 2.4)	1.6 (1.1, 2.5)	1.8 (1.3, 2.7)
Bangladeshi	2.1 (1.5, 2.8)	1.7 (1.2, 2.3)	1.7 (1.2, 2.3)	1.6 (1.2, 2.2)	1.8 (1.3, 2.5)	1.8 (1.4, 2.4)
Mixed white & black Caribbean	4.3 (2.8, 6.7)	3.9 (2.5, 6.0)	3.9 (2.5, 6.0)	3.9 (2.5, 6.0)	4.0 (2.6, 6.1)	3.9 (2.5, 6.1)
Mixed, other ethnicities	1.3 (0.8, 2.3)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)
Other ethnicities	2.2 (1.6, 3.0)	1.9 (1.4, 2.7)	1.9 (1.4, 2.6)	1.9 (1.4, 2.6)	2.0 (1.4, 2.7)	1.9 (1.4, 2.7)
Socioenvironmental variables						
IMD (z-score)	-	1.184 (1.101, 1.274)	-	-	-	-
Extent of deprivation (%)	-	-	1.008 (1.004, 1.011)	-	-	-
Income deprivation (%)	-	-	-	1.025 (1.015, 1.035)	-	-
Employment deprivation (%)	-	-	-	-	1.062 (1.032, 1.093)	-
Population density (pph)	-	-	-	-	-	1.005 (1.003, 1.007)
Model fit diagnostics						
AIC <sup>2</sup>	2571.8	2552.4	2551.3	2549.6	2556.4	2556.3
Mean Lin's CCC (95%CI) <sup>3</sup>	0.75 (0.74, 0.77)	0.77 (0.75, 0.78)	0.77 (0.75, 0.79)	0.77 (0.75, 0.78)	0.77 (0.75, 0.78)	0.76 (0.74, 0.77)
Mean RMSE (s.d.) <sup>4</sup>	0.75 (0.11)	0.74 (0.11)	0.74 (0.10)	0.74 (0.10)	0.74 (0.11)	0.76 (0.13)

IRR: Incidence rate ratio; AIC: Akaike's Information Criterion; CCC: Lin's correlation concordance coefficient; RMSE: Root mean squared error.

<sup>1</sup>All models fitted with age group by sex interaction given *a priori* evidence for effect modification.<sup>18, 45</sup> Likelihood ratio test p-values reported between models with and without an interaction term fitted between age group and sex. Specific IRR not been reported for clarity, but available on request

<sup>2</sup>— lower scores denote improved model fit

<sup>3</sup>Higher scores indicate greater correlation between observed & predicted count of cases in the *prediction sample*. Mean CCC and 95%CI reported following *h*=20 trials during cross-validation.

<sup>4</sup>Lower scores indicate lower prediction error. Mean RMSE and standard deviation (s.d.) reported following *h*=20 repeats of *k*-fold cross-validation, where *k*=10.

EIS	Observed	Model 1	Model 2	Model 3	Model 4
		Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)
<b>Overall total, 16-35 years</b>	<b>521</b>	<b>641.2 (586.0, 696.1)</b>	<b>468.5 (422.0, 518.0)</b>	<b>474.7 (429.0, 522.0)</b>	<b>487.5 (441.0, 535.0)</b>
Cameo North	55	84.7 (66.0, 106.0)	68.5 (52.0, 87.0)	67.8 (51.0, 86.0)	70.2 (53.0, 90.0)
Cameo South	134	163.6 (135.0, 192.0)	105.5 (84.0, 129.0)	111.7 (89.0, 134.0)	110.9 (90.0, 132.0)
West Norfolk	26	29.2 (18.0, 41.0)	23.0 (13.0, 35.0)	22.0 (12.0, 32.0)	23.4 (14.0, 34.0)
Central Norfolk	120	162.6 (136.0, 191.0)	122.6 (99.0, 148.0)	123.0 (100.0, 149.0)	128.3 (104.0, 152.0)
Great Yarmouth & Waveney	60	49.1 (34.0, 65.0)	41.6 (28.0, 55.0)	39.9 (27.0, 53.0)	42.9 (30.0, 57.0)
Suffolk	126	151.9 (126.0, 178.0)	107.4 (85.0, 128.0)	110.3 (88.0, 133.0)	111.7 (90.0, 136.0)
Overall total, 36-64 years	-	332.2 (292.0, 373.0)	244.0 (213.0, 276.0)	248.6 (216.0, 280.0)	256.3 (228.0, 291.0)
EIS	Observed	Model 5	Model 6	Model 7	
		Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)	
<b>Overall total, 16-35 years</b>	<b>521</b>	<b>477.1 (428.0, 523.0)</b>	<b>508.5 (459.0, 559.0)</b>	<b>715.6 (664.0, 769.0)</b>	
Cameo North	55	69.1 (52.0, 88.0)	64.5 (48.0, 82.0)	92.1 (74.0, 111.0)	
Cameo South	134	100.7 (79.0, 123.0)	131.1 (108.0, 157.0)	169.0 (144.0, 195.0)	
West Norfolk	26	24.7 (16.0, 35.0)	22.3 (13.0, 33.0)	35.8 (25.0, 48.0)	
Central Norfolk	120	128.2 (105.0, 153.0)	132.5 (108.0, 157.0)	187.7 (161.0, 215.0)	
Great Yarmouth & Waveney	60	47.7 (35.0, 63.0)	38.0 (26.0, 51.0)	59.1 (44.0, 74.0)	
Suffolk	126	106.6 (86.0, 128.0)	120.0 (96.0, 143.0)	172.1 (147.0, 198.0)	
Overall total, 36-64 years	-	249.7 (221.0, 284.0)	262.9 (233.0, 297.0)	1175.4 (1109.0, 1243.0)	

<sup>1</sup>Numbers in green denote where observed count fell within 95% prediction interval [95% PI] for people aged 16-35 years. Observed data for people aged 36-64 years in the *validation sample* was not available.

Model 1: Age group, sex, their interaction and ethnicity

Model 2: Model 1 + IMD

Model 3: Model 1 + extent of deprivation

Model 4: Model 1 + income deprivation

Model 5: Model 1 + employment deprivation

Model 6: Model 1 + population density

Model 7: Department of Health uniform figure for EIS of 15 new cases per 100,000 people per year.

**Table 3: External model validation diagnostics<sup>1</sup>**

Model	Observed case count within SEPEA overall prediction intervals? [rank]	EIS (N=6)		LAD (N=21)		Mean ranking [rank of mean ranking]
		Number correct [rank]	RMSE [rank]	Number correct [rank]	RMSE [rank]	
Model 1	No [5]	3 [6]	27.0 [6]	18 [2]	8.9 [6]	5.0 [6]
Model 2	No [5]	4 [4]	16.8 [4]	18 [2]	6.4 [4]	4.8 [5]
Model 3	Yes [1]	5 [1]	14.9 [2]	17 [5]	6.1 [2]	2.2 [2]
Model 4	Yes [1]	4 [4]	14.9 [2]	17 [5]	6.1 [2]	2.8 [3]
Model 5	Yes [1]	5 [1]	17.8 [5]	18 [2]	6.7 [5]	2.8 [3]
Model 6	Yes [1]	5 [1]	11.5 [1]	19 [1]	6.0 [1]	1.0 [1]
Model 7	No [5]	2 [7]	39.6 [7]	13 [7]	11.7 [7]	6.6 [7]

<sup>1</sup>For each diagnostic, models are placed in rank order [1=best model, 7=worst model] with ties given the same ranking. The mean ranking and rank provide an estimate of the overall performance of various models.

RMSE: Root mean squared error (lower scores indicate lower error); EIS: Early Intervention in Psychosis Service; LAD: Local Authority District

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## Data sharing statement

Extra data is available at our prediction website, PsyMaptic: [www.psymaptic.org](http://www.psymaptic.org). We have made a large array of prediction data freely available to interested users, who can visualise prediction data in maps and tables for a range of psychotic disorder predictions by major sociodemographic subgroup and by LAD. Future versions of PsyMaptic will release data for other regions and at other geographical levels. Users can also download LAD-specific and national summaries of prediction data from our models in tabular form. Finally, additional explanatory material about how to use the data and the PsyMaptic website is also available at [www.psymaptic.org](http://www.psymaptic.org). Bespoke data not provided freely on our website may be requested from the authors at the cost of data extraction. The empirical data underlying the prediction models (ÆSOP and ELFEP) or the validation sample (SEPEA) is not freely available as the studies are ongoing, but papers detailing the main findings from these studies have previously been published elsewhere.

## Competing interests statement

All authors have completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare that (i) JBK has support from the Wellcome Trust for the submitted work (grant number WT085540) and PBJ has support from the NIHR (grant RP-PG-0606-1335); (ii) DJ, JP, FW, DF, JC, RMM have no relationships with any company that might have an interest in the submitted work in the previous 3 years; (iii) their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and (iv) no author holds non-financial interests that may be relevant to the submitted work.



### Role of funders

The funders were not involved in the design, collection, analysis, interpretation of the data, writing the report or the decision to submit the article for publication. All authors were independent from the funders in contributing to this work.

### Ethical approval

Ethical approval to conduct the original AESOP and East London First Episode Psychosis studies was granted from local research ethics committees in their respective centres prior to the original date of onset of the study. We were granted ethical approval to conduct the work related to the present manuscript, including use of data from the SEPEA study, from the Cambridgeshire 3 REC (09/H0306/39).

### Guarantorship

JBK takes full responsibility for the work and conduct of the study, had access to the data, and controlled the decision to publish.

### Contributorship

JBK was responsible for concept, design, analysis, data extrapolation, interpretation of the data, drafting the report and developing the content for the websites [www.psymaptic.org](http://www.psymaptic.org), [www.psymaptic.com](http://www.psymaptic.com) and [www.psymaptic.co.uk](http://www.psymaptic.co.uk). JBK was also the chief investigator of the SEPEA study, where the *validation sample* data was obtained. He gave final approval of this version of the manuscript to be published.

DJ was responsible for developing and initially implementing the statistical approach with regard to prediction intervals from count-based regression. He also contributed to drafting and editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

JP is principal collaborator on the SEPEA study in the CAMEO early intervention in psychosis services. He also contributed to editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

DF is co-principal collaborator on the SEPEA study in the Norfolk and Suffolk Foundation Trust. He also contributed to editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

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### 41 **STROBE statement**

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43 Our STROBE statement is provided as a supplementary file.  
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9 **A population-level prediction tool for the incidence of first episode psychosis: translational**  
10 **epidemiology based on cross-sectional data**

11 Kirkbride JB<sup>1\*</sup>, Jackson D<sup>2</sup>, Perez J<sup>3</sup>, Fowler D<sup>4</sup>, Winton F<sup>5</sup>, Coid JW<sup>6</sup>, Murray RM<sup>7</sup>, Jones PB<sup>8</sup>

14 **For submission to BMJ Open**

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48 ~~relevant prediction data on these pages so only editors and peer reviewers can access this data until the peer~~  
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## Abstract

*Objectives:* Specialist early intervention services [EIS] for people aged 14-35 years with first episodes of psychosis [FEP] have been commissioned throughout England since 2001. A single estimate of population need was used everywhere, but true incidence varies enormously according to sociodemographic factors. We sought to develop a realistically-complex, population-based prediction tool for FEP, based on precise estimates of epidemiological risk.

*Design & participants:* Data from 1037 participants in two cross-sectional population-based FEP studies were fitted to several negative binomial regression models to estimate risk coefficients across combinations of different sociodemographic and socioenvironmental factors. We applied these coefficients to the population at-risk of a third, socioeconomically different region to predict expected caseload over 2.5 years, where observed rates of ICD-10 F10-39 FEP had been concurrently ascertained via EIS.

*Setting:* Empirical data from London, Nottingham and Bristol predicted counts in the population at-risk in the East Anglia region of England.

*Main outcome measures:* Observed counts compared with predicted counts (with 95% prediction intervals) at regional, EIS and local authority district [LAD] levels in East Anglia to establish predictive validity of each model.

*Results:* A model with age, sex, ethnicity and population density performed most strongly, predicting 508 FEP participants in EIS in East Anglia (95%PI: 459, 559), compared with 521<sup>8</sup> observed participants. This model predicted correctly in 5/6 EIS and 19/21 LAD. All models performed better than the current gold standard for EIS commissioning in England (716 cases; 95%PI: 664-769).

*Conclusions:* We have developed a prediction tool for incidence of psychotic disorders in England and Wales, made freely available online ([www.psymaptic.org](http://www.psymaptic.org)) to provide healthcare commissioners with accurate forecasts of FEP based on robust epidemiology and anticipated local population need. Initial assessment of some people who do not require subsequent EIS care means additional service resources, not addressed here, will be required.

## Background

Commissioners of health and social care require precise information on the health needs of their local populations<sup>1</sup>, especially if parity of mental and physical health is to be realised.<sup>2</sup> Mental health disorders alone represent the leading disease burden in the UK (22.8%).<sup>3</sup> They contribute substantially to healthcare expenditure and societal costs even before physical ill health is taken into account. The Centre for Mental Health estimated total costs of mental health to British health services and society at £105 billion in 2009/10,<sup>4</sup> a figure expected to double over the next 20 years.<sup>2</sup> These are serious challenges compounded by a paucity of information on which to commission appropriate services. Early intervention in psychosis services [EIS] for people aged 14-35 years with a first episode of psychosis [FEP] offer a useful example of failure to map services to local need.

EIS are a major evidence-based innovation, systematically commissioned throughout England and Wales over the past decade.<sup>5</sup> When EIS intervention is sustained there is evidence that people with psychosis achieve better functional and social outcomes.<sup>6, 7</sup> Such services are also highly cost-effective.<sup>4, 8, 9</sup> However, EIS were originally commissioned on an anticipated rate of 150 new cases of any psychotic disorder per 1,000,000 of the total population per year in the Department of Health's Mental Health Policy Implementation Guide [MH-PIG].<sup>5</sup> In 2001 in England and Wales, 29.3% of the population were aged 14-35 years old, meaning that the MH-PIG commissioned incidence rate was approximately 51 cases per 100,000 person-years in the age range covered by EIS. Following their deployment, anecdotal reports began to emerge from EIS in different regions to suggest that a uniform figure for commissioning was simultaneously under-<sup>10</sup> and over-estimating<sup>11</sup> actual observed need in urban and rural populations, respectively. Recent epidemiological evidence of FEP incidence in rural communities in England has suggested that rates are somewhat lower than the uniform figure upon which services were commissioned,<sup>12, 13</sup> confirming previous calls that a "one-size-fits-all" prescription for EIS implementation is unlikely to lead to the efficient allocation of finite mental health resources.<sup>14, 15</sup>

Using rich epidemiological data on variation in the incidence of first episode psychosis according to major sociodemographic risk factors,<sup>16-19</sup> we describe the development and validation of a population-level prediction tool capable of accurately estimating the expected incidence of psychiatric disorder, based on the sociodemographic structure of the population in a given region. Applied to FEP as proof-of-concept, we show it is possible to closely predict expected incidence in a given population, where the observed count of cases was within the prediction intervals forecast by our models. We applied our

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most precise prediction model to the population of England and Wales to provide health commissioners with a translational epidemiological prediction tool to underpin information-based service planning.

## Methods

Our prediction models were based on epidemiological data from the Aetiology and Ethnicity in Schizophrenia and Other Psychoses [ÆSOP] and the East London First Episode Psychoses [ELFEP] studies,<sup>18,20</sup> two methodologically-similar population-based FEP studies. We fitted various count-based regression models with different combinations of sociodemographic and socioenvironmental factors, well-established in the literature to be associated with the incidence of psychotic disorder.<sup>21,22</sup> We first established the relative ~~internal~~*internal* ~~validity~~*apparent* validity of each model by estimating ~~internal~~ model fit diagnostics to assess how well each model fitted the empirical data (henceforth, the *prediction sample*). We next sought to estimate the *external validity* of each model by applying model-based parameter coefficients to the population structure of a purposefully different region of England, East Anglia (henceforth, the *validation sample*). This out-of-sample prediction technique allowed us to obtain the expected incidence of disorder in this region forecast by each model, which we compared with observed rates simultaneously ascertained in this region via the ongoing Social Epidemiology of Psychoses in East Anglia [SEPEA] study.<sup>13</sup> We performed various model fit diagnostics to identify which, if any, model demonstrated utilisable predictive capability.

### Empirical data underlying prediction models (*prediction sample*)

#### *Case ascertainment (numerator)*

The designs of the ÆSOP and ELFEP studies have been described in detail elsewhere,<sup>18,20</sup> with features relevant to the present paper summarised here. Case ascertainment took place over two years in ELFEP (Newham: 1996-8; Tower Hamlets & Hackney: 1998-2000) and the Southeast London and Nottingham centres of the ÆSOP study (1997-9), and over the first 9 months of 1997 in Bristol (ÆSOP). All service bases were screened regularly for potential new contacts aged 16-64 years (18-64 in ELFEP) resident within these catchment areas. Leakage studies were conducted to identify participants missed by this initial screen, but meeting inclusion criteria for FEP.<sup>18,20</sup> All participants who received an ICD-10 F10-39 diagnosis for psychotic disorder following assessment via the Schedules for Clinical Assessment in Neuropsychiatry were included in the incident sample, except those with an organic medical basis to their disorder or profound learning difficulty. Data on age-at-contact, sex and ethnicity were collected on included participants. We geocoded participants' residential postcode at first contact to their

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9 corresponding local authority district [LAD] to allow us to model possible neighbourhood effects  
10 associated with the incidence of psychotic disorder, such as population density or socioeconomic  
11 deprivation.  
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#### 13 *Population at-risk*

14 We estimated the population at-risk using the 2001 Census of Great Britain, adjusted for study duration,  
15 and stratified by age group (16-17, 18-19, then 5-year age bands), sex and ethnicity. Ethnicity was based  
16 on self-ascription according to one of ten categories derived from the census: white British, non-British  
17 white, black Caribbean, black African, Indian, Pakistani, Bangladeshi, mixed white & black Caribbean,  
18 other mixed ethnic backgrounds and all other ethnicities.  
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#### 23 *Socioenvironmental variable estimation*

24 We estimated LAD -level deprivation using the 2004 Index of Multiple Deprivation [IMD] in England,  
25 which estimated domains of deprivation using measures predominantly collected close to the time of  
26 our case ascertainment periods (see Box 1).<sup>23</sup> We z-standardised English LAD IMD scores to have a mean  
27 of zero and standard deviation of one, and extracted IMD z-scores for the 14 LADs in the ÆSOP and  
28 ELFEP studies. To inspect whether any particular deprivation domain was a better predictor of psychosis  
29 incidence than IMD, we also considered LAD-level income deprivation, employment deprivation and the  
30 extent of deprivation in our models (Box 1). We estimated population density by dividing LAD usual  
31 resident population by its area (in hectares), using ArcGIS 9.3 software.  
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38 <Box 1 about here>  
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#### 40 **Observed data for external validation of prediction models (*validation sample*)**

41 Observed participants and population at-risk data for our *validation sample* was obtained from the  
42 SEPEA study, an ongoing study of the incidence of psychotic disorders incepted over three years (2009-  
43 12) through one of six EIS covering 20 LAD and a subsection of one LAD (the town of Royston,  
44 Hertfordshire) in Norfolk (three EIS: West, Central and Great Yarmouth & Waveney), Suffolk (one EIS)  
45 and Cambridgeshire, Royston & Peterborough (CAMEO North and South EIS).<sup>13</sup>  
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#### 50 *Case ascertainment*

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To establish the incepted incidence of first episode psychosis as seen through EIS, entry criteria for the SEPEA study were:

- Referral to an EIS in East Anglia for suspected first episode of psychosis
- Aged 16-35 years old at first referral to EIS (17-35 years in CAMEO services)
- Resident within the catchment area at first referral
- First referral during case ascertainment period (2009-12)

At six months after EIS acceptance, or discharge from the service, whichever was sooner, we asked the clinician responsible for care to provide an ICD-10 F10-39 psychiatric diagnosis using all information available. We excluded participants without a clinical FEP diagnosis, or participants presenting with an organic basis to their disorder or profound learning disability. For remaining participants, basic sociodemographic and postcode information was recorded and classified in the same way as in the *prediction sample*. We included participants presenting to EIS during the first 2.5 years of the ongoing SEPEA study.

#### *Population at-risk*

We estimated the population at-risk of East Anglia using 2009 mid-year census estimates published by the Office for National Statistics [ONS] at LAD-level, by age group, sex and ethnicity.<sup>24</sup> These estimates used the 2001 census base, adjusted for immigration, births and deaths each year. It was not possible to obtain 2009 mid-year estimates for the town of Royston, because data were only published at LAD level. Here, we thus used denominator data from the 2001 census data, in order to estimate the population at-risk in Royston. We do not believe this would have substantially invalidated our results as this town represented 0.6% of the overall population at-risk (n=9,555) in the SEPEA study. Denominator data were multiplied by 2.5 to account for person-years of exposure in the *validation sample*.

#### *Socioenvironmental variable estimation*

For each LAD in the SEPEA study we obtained corresponding socioenvironmental variables to those included in our *prediction sample*, using updated data collected as close to the SEPEA case ascertainment period as possible. Population density was estimated using 2009 mid-term population estimates. Our measures of deprivation were derived from the IMD 2010,<sup>25</sup> which was estimated in an analogous way to 2004 data, but collected from sources obtained immediately prior to the SEPEA study.



## Statistical techniques

### Dataset generation

We constructed a dataset for the regression analysis of count data by pooling data from the AEsOP & ELFEP studies (the *prediction sample*). Data were stratified by age group, sex, ethnicity and LAD, such that each stratum (N=2,536) represented the total count of FEP cases in a unique sociodemographic group for a given LAD, with a corresponding estimate of the population at-risk, treated as an offset in our models. Our socioenvironmental measures (population density, deprivation) were adjoined to the dataset for each LAD.

Population at-risk data from the *validation sample* were stratified in the same way and retained in a separate database. ~~Here, the~~ count of cases, which we wished to predict, was entered as a vector of variable with missing data values, which would be populated with predicted case estimates following prediction modelling we could predict into, given the model coefficients and population at risk.

### Prediction models

We used the *prediction sample* data to fit negative binomial regression models to obtain parameter coefficients of incidence for the sociodemographic and socioenvironmental factors included in each model. We considered the internal and external predictive capabilities of six models, all of which contained age group, sex, an age-sex interaction term and ethnicity. Model 1 contained no further covariates. Model 2 also included IMD. We replaced IMD with either income, employment or the extent of deprivation, respectively, in models 3-5. Model 6 included population density. Initial exploration of the *prediction sample* data indicated the presence of possible over-dispersion (variance ( $\delta^2=1.37$ ) exceeded mean ( $\mu=0.4$ ) count of cases) so negative binomial regression was preferred to Poisson regression since it explicitly models any over-dispersion with an extra dispersion parameter.

### Internal model cross-validation & prediction

We assessed ~~internal~~apparent model validity in three ways. First we used Akaike's Information Criterion [AIC] to assess the respective overall fit of each model to the data. Second, we conducted K-fold cross-validation to assess each model's ~~internal~~apparent validity to predict cases within the *prediction sample*. This method randomly allocated strata in the *prediction sample* into  $K$  subsets. Each model was then re-estimated on  $K-1$  subsets (the *training data*) to predict expected counts of cases in the  $K^{\text{th}}$  subset (the

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9 *test data*). This was repeated over  $K$  trials, such that each stratum in the dataset appeared exactly once  
10 as the *test data*. At the end of this process, we derived Lin's concordance correlation coefficient [CCC]  
11 and 95% confidence intervals [95%CI] to estimate the correlation between predicted and observed  
12 counts of cases across all strata in the *prediction sample*. Finally, we estimated the root mean squared  
13 error [RMSE] to determine the average error between fitted and observed values from each model,  
14 where lower RMSE scores indicated smaller prediction error. The RMSE is derived as  
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$$17 \quad RMSE = \sqrt{\frac{\sum_{i=1}^n (y_i - \hat{y}_i)^2}{n}}$$

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23 where  $y_i$  and  $\hat{y}_i$  are the observed and predicted count of cases in the  $i^{\text{th}}$  stratum, respectively, and  $n$  is  
24 the number of strata.  
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27 We repeated  $K$ -fold cross-validation  $h$  times, generating  $K$  new random divisions of the data each time.  
28 We retained model fit diagnostics across  $Kh$  iterations, and reported the mean of Lin's CCC and RMSE to  
29 provide summary cross-validation statistics for each model. We specified  $K=10$  and  $h=20$ , as  
30 recommended for cross-validation to obtain precise model fit diagnostics.<sup>26</sup>  
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### 33 *External model prediction & validation*

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35 We retained parameter coefficients from each model (using the full *prediction sample* data) and applied  
36 these to the corresponding population at-risk in the *validation sample* dataset. This gave out-of-sample  
37 prediction estimates for the expected count of cases in each stratum of the *validation sample*, given the  
38 model. We summed expected counts across relevant strata to estimate the (i) total predicted count of  
39 cases in the SEPEA region, (ii) predicted counts in each EIS, and (iii) predicted counts by LAD. These  
40 counts were further stratified by broad age group (16-35, 36-64 and 16-64 years). Because census  
41 (denominator) data was unavailable for 35 year olds alone (needed to estimate their contribution to  
42 predicted counts in the age range for EIS, 16-35 years) we assumed the risk coefficient was the same  
43 across all ages within the 35-39 year old age group. We apportioned predicted counts on a 1:4 ratio (35  
44 years: 36-39 years) to their respective broad age groups.  
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9 To determine how well the MH-PIG<sup>5</sup> figure of 51 new cases per 100,000 people per year for EIS  
10 performed as a predictive tool, we also estimated the predicted count of cases in the *validation sample*  
11 under this scenario, which we termed “Model 7”.  
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14 We derived prediction intervals [95% PIs] for all summary predictions from first principles for each  
15 negative binomial regression model, since their derivation is not straightforward, nor routinely  
16 implemented by statistical software. Prediction intervals are similar to confidence intervals, but account  
17 for standard errors introduced in both the *prediction* and *validation* samples. We developed a  
18 bootstrap-like approach to obtain prediction intervals from each model by simulating 1000 model-based  
19 realisations of the quantities we wished to predict, where we took the parameters to be the maximum  
20 likelihood estimates. We obtained the lower and upper bounds of the prediction intervals as the  
21 corresponding quantiles of the simulated realisations (see Appendix for full details).  
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27 To assess each model’s external predictive capabilities, we considered five markers of predictive  
28 accuracy. We compared the number of times the observed count of cases in the SEPEA study fell within  
29 the prediction intervals estimated from each model for (i) the SEPEA region, (ii) at EIS level, and (iii) at  
30 LAD level. We also derived EIS- and LAD-level RMSE scores to estimate prediction error from each model  
31 in our *validation sample*. We ranked model performance (1: best, 7: worst) on these five measures, and  
32 estimated an overall mean rank to determine the overall predictive validity of each model.  
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36 Observational data on first episode psychosis in our *validation sample* were not available for the age  
37 range 36–64 years, so external validation was restricted to the 16–35 year old group. For completeness,  
38 however, we also reported overall predicted count of cases for this age group from each model.  
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#### 42 *Extrapolation to the United Kingdom*

43 Guided by our validation procedures, we identified which model had the greatest overall predictive  
44 validity, and proposed this as a candidate for FEP incidence prediction in England and Wales. We  
45 repeated out-of-sample prediction on the sociodemographic and socioenvironmental population  
46 characteristics of each LAD in England and Wales to obtain national and LAD-level predictions.  
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49 Denominator data was obtained from the ONS 2009 mid-term estimates and stratified as previously  
50 described. Overall counts were derived for three broad age groups (16–35, 36–64 and 16–64 years), and  
51 for each of these, by sex and ethnicity. 95% PIs were estimated as before. We visualised this data on  
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maps and in tables to provide healthcare planners and commissioners with an easy-to-use tool to forecast the expected incidence of psychosis in England and Wales. We have made this available as a free, open-use prediction tool, known as PsyMaptic (version 0.54) (Psychiatric Mapping Translating Innovations into Care; [www.psymaptic.org](http://www.psymaptic.org)). Counts of cases predicted by our model were compared with those obtained under the Department of Health's uniform rate in each LAD. We expressed these comparisons as ratios with 95% CIs derived using the same method as for standardised morbidity ratios [SMR]. This approach was conservative because here we substituted the usual numerator in an SMR, the observed, O, for a predicted count. Unlike an observed count, no sampling variation is present for the predicted count, only uncertainty due to the model from which the prediction was estimated. Since variance in the prediction is therefore much smaller than the variance normally present for the numerator (O) this led to conservative estimates of 95% CI. Ratios in LAD where 95% CI did not span unity could therefore be interpreted as regions where there was strong evidence that the predictions from our model differed significantly from those predicted by the Department of Health's uniform rate.

#### Software

All negative binomial regression models, out-of-sample prediction and estimation of 95% PI were conducted in R (version 2.15.1). ~~Internal-C~~cross-validation and model-fit diagnostics were conducted in Stata (version 11). Prediction maps for England and Wales were created using StatPlanet Plus (version 3.0) visualisation software.<sup>27</sup>

## Results

### Prediction sample

Our prediction models contained data on 1,037 persons with a first episode psychosis in the ÆSOP (n=553; 53.3%) and ELFEP (n=484; 46.7%) studies, ascertained from over 2.4m person-years at-risk. Twelve participants were excluded from the original ÆSOP sample because they were of no fixed abode and could not be geocoded to an LAD.<sup>18</sup>

The population at-risk in the *prediction sample* came from LAD with higher median levels of multiple and employment deprivation, extent of deprivation and population density than the population at-risk in the *validation sample*, though there were no statistically significant differences in median income deprivation between the two samples (Supplemental Table 1).

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9 <Supplemental Table 1 about here>

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11 Parameter coefficients obtained from the full prediction sample following negative binomial regression  
12 are shown in Table 1. As previously reported from these data,<sup>20,28</sup> incidence rates were generally raised  
13 in ethnic minority groups compared with the white British population. Models 2-6 included a measure of  
14 LAD deprivation (Models 2-5) or population density (Model 6), which were all significantly associated  
15 with increased incidence of psychotic disorder, after control for individual-level confounders. Each of  
16 these models produced a lower AIC score than a model fitted solely with individual-level covariates  
17 (Model 1), indicating better internal fit. Internal cross-validation suggested all models achieved good  
18 CCC agreement between predicted and observed cases, with low RMSE values (Table 1).  
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24 <Table 1 about here>

#### 25 26 **Validation sample**

##### 27 *Observed participants*

28 We identified 572 participants over the first 30 months of the SEPEA study, aged 16-35 years old, who  
29 met acceptance criteria for EIS in East Anglia. We excluded 5144 participants (8.90%) who did not meet  
30 clinical criteria for ICD-10 psychotic disorder. This left an incidence sample of 5218 participants from  
31 nearly 1.4m person-years at risk (37.38 per 100,000 person-years; 95%CI: 34.72, 40.64). A further  
32 2.3m person-years at-risk accrued in the same region for people aged 36-64 years over this period.  
33 Median levels of multiple, income and employment deprivation in the region did not differ significantly  
34 from the remainder of England, although median population density and extent of deprivation in East  
35 Anglia were lower than elsewhere in England (Supplemental Table 1).  
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42 <Table 2 about here>

##### 43 *External model prediction & validation*

44 The overall observed count of cases, aged 16-35 years, in the validation sample (n=528) fell within 95%  
45 prediction intervals in four only two of seven tested models (Models 34 and 6, Table 2). Of these, the  
46 observed count (N=521) was closest to the point estimate for Model 6 (508.5; 95% PI: 449.0, 559.0),  
47 fitted with age group, sex, their interaction, ethnic group and LAD population density. The observed  
48 count of cases also fell within prediction intervals from this model in five of six EIS in the study region,  
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and 19 of 21 LADs, the most of any model (Table 3). This model had the lowest error scores at EIS (RMSE=11.59) and LAD (RMSE=6.05-9) levels of any model. Overall, Model 6 was ranked highest across all external model fit diagnostics (Table 3). All models outperformed the Department of Health's uniform figure of 51 cases per 100,000 people per year (Model 7), which generally overestimated cases in the *validation sample* (overall prediction: 715.7 cases; 95% PI: 664.0, 769.0).

[<Table 3 about here>](#)

We also reported predicted cases aged 36-64 years old from our models (Table 3), although we could not test these in the *validation sample*. Model 6 predicted an additional 262.9 cases aged 36-64 years over a 2.5 year period in East Anglia (95% PI: 233.0, 297.0).

We also inspected the stratum-specific external validity of our best-fitting model (Model 6, Supplementary Table 2), which performed accurately for sex-specific predictions, but less well in age- and ethnicity-specific strata. Thus, our model tended to under-predict observed cases in people aged 16-19 years, but over-predicted cases observed in people over 25 years old. With respect to ethnicity, model predictions were consistent with observed FEP cases for people of non-British white, black African, Bangladeshi and mixed ethnicities. However, our model under-predicted observed rates in the white British group, and over-predicted rates in black Caribbean, Indian and Pakistani populations.

[<Supplemental Table 2 about here>](#)

#### *Extrapolation to England and Wales*

We predicted the expected count and incidence of first episode psychosis per annum in each LAD in England and Wales based on Model 6, and visualised this data in maps and tables freely available at [www.psymaptic.org](http://www.psymaptic.org). Many maps can be visualised (for example, Supplemental Figure 1), including overall predicted incidence counts and rates for each broad age group at LAD level, and-by sex. We will make PsyMaptic data -available by and ethnic group when we can improve the validity of future versions of these models for these strata, as well as a variety of population and socioenvironmental data.

According to our model, the annual number of new FEP cases in England and Wales would be 8745 (95% PI: 8558, 8933), of which our model predicted 67.9% (N=5939; 95% PI: 5785, 6102) would be seen through EIS. Only 176 (95% PI: 151, 203) cases aged 16-64 years were forecast in Wales per annum.

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9 Assuming our prediction model is accurate, it indicated that the Department of Health's current uniform  
10 rate of 51 per 100,000 person-years was higher than the predicted point estimates for rates forecast by  
11 our PsyMaptic model in 351 LAD (93%) in England and Wales, but was lower than predicted by our  
12 model in Birmingham and several London boroughs (Supplemental Figure 2, left hand map). Under a  
13 conservative approach, these differences achieved statistical significance in parts of London (where the  
14 Department of Health's model underestimated need as predicted by PsyMaptic), and in some more rural  
15 parts of England and Wales (where the Department of Health's model over-estimated need)  
16 (Supplemental Figure 2, right hand map).  
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21 [<Supplemental Figures 1 & 2 about here>](#)  
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## 24 Discussion

### 25 Principal findings

26  
27 We have developed and tested several epidemiological prediction models to forecast FEP incidence in  
28 England and Wales, having taken into account regional differences in the sociodemographic and  
29 socioenvironmental profile of different populations. Inspection of our data suggested that a model fitted  
30 with age group, sex, their interaction, ethnic group and LAD-level population density provided the  
31 greatest external predictive validity when compared with the observed FEP caseload ascertained  
32 through EIS in our *validation sample*. This model also had good [internal apparent](#) validity across the  
33 entire age range (16-64 years). All models performed significantly better in predicting the incidence of  
34 clinically relevant first episode psychosis than the Department of Health's current gold standard for EIS  
35 commissioning,<sup>5</sup> based on a uniform incidence rate. Our data suggested the figure used to commission  
36 EIS over-estimated the likely true incidence rates of FEP in rural areas, and under-estimated them in  
37 urban settings, although we acknowledge that commissioning decisions will need to be based on several  
38 additional factors, including the level of pre-clinical or non-psychotic psychopathology requiring  
39 assessment at initial referral to EIS, and variation in service organisation, remit and delivery.  
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### 46 Limitations & future development

47 Our prediction models were based on epidemiological data obtained from large, robust population-  
48 based FEP studies for people aged 16-64 years.<sup>18, 19</sup> ~~The Our~~ best-fitting model, [overall](#), had good  
49 [internal apparent](#) validity over this age range, and good external validity over the age range 16-35 years.  
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51 While this covered the majority of adult onset psychosis cases seen in mental health services, including  
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9 EIS, we recognise that some EIS teams incept people from 14 years old. We were unable to extrapolate  
10 our models to this age range, given the current absence of incidence data for this group in England. Data  
11 from Scandinavia suggest that the incidence of such “early onset” psychoses is absolutely low,<sup>29</sup>  
12 although the rate may have been increasing in the last few decades, probably as a result of movement  
13 towards earlier detection. We were also unable to externally validate prediction models for people aged  
14 36-64 years, because comparable observed incidence data was not available in our *validation sample*.  
15 We have no reason to believe our predictions will be invalid for this group, however, since the empirical  
16 data which underpinned our models was ascertained from the same two large, well-conducted studies  
17 as for data on the younger age group.<sup>18, 19, 28</sup> Furthermore, unpublished findings from these studies are  
18 consistent with the wider epidemiological literature for psychosis in England and internationally.<sup>17, 21, 30</sup> It  
19 will be important to validate the predictive capability of our model(s) in this age range, and we will seek  
20 to identify suitable samples to do so in future versions of PsyMaptic.  
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27 Our best-fitting overall model demonstrated excellent external validity for predicting sex-specific FEP  
28 cases in our validation region (i.e. SEPEA). It performed less well across age- and ethnic-specific stratum  
29 in this region. With respect to age, this discrepancy is most likely to be a function of EIS provision itself,  
30 which seeks to intervene as early as possible in the onset of psychosis. The effect of this will reduce  
31 median age at onset in comparison to studies conducted prior to the introduction of EIS, such as the  
32 ÆSOP and ELFEP studies, upon which our models are based. Future versions of PsyMaptic will  
33 incorporate empirical data from post-EIS studies to improve age-specific predictions. The validity of our  
34 model in some ethnic groups also requires further refinement. Much of the prediction data underlying  
35 our models came from urban environments with large proportions of ethnic minority groups. The  
36 sociodemographic profile and sociocultural experiences of these groups may be very different to those  
37 of their counterparts in other, less urban, parts of England, thus altering risk of psychosis according to  
38 ethnicity. In our observed data, a larger proportion of cases were white British than predicted by our  
39 model. If ethnicity is a partial proxy for exposure to deleterious socio-environmental experiences, such  
40 as the combined effect of social inequality, fragmentation, deprivation and population density,<sup>31</sup> then  
41 simultaneously incorporating such factors into our models may improve their predictive validity by  
42 ethnicity. Alternatively, risk by ethnic group may be conditional upon (i.e. interact with) environmental  
43 factors in urban areas (as with the ethnic density effect<sup>32, 33</sup>), but whether such interactions exist in less  
44 urban regions is not known. Forthcoming SEPEA and PsyMaptic data will explore such possibilities as  
45 2011 census data become available.  
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10 | All prediction models had reasonable internal/external validity, although our proposed model  
11 performed slightly worse (most noticeably for AIC) than models which included deprivation (i.e. models  
12 2-4) instead of population density. Our decision to use model 6 as our proposed candidate for the  
13 prediction tool was supported by the fact that it produced the most accurate external forecasts of any  
14 model, despite considerable socioenvironmental differences between regions in our *prediction* and  
15 *validation* samples. We were unable to predict the expected incidence of psychotic disorder in  
16 geographical areas smaller than LADs, such as electoral wards (N~6000), or to other parts of the UK,  
17 because appropriate denominator data was not published as mid-term census estimates. The 2011  
18 census will provide small area and national data for the whole of the UK, scheduled for release by ONS  
19 in mid-2013. This will allow us to update our tool to the latest population estimates for the UK, and  
20 refine our PsyMaptic tool at a smaller geographical level for fine-grained healthcare commissioning. We  
21 will then be able to develop models to explore cross-level interactions, such as the association between  
22 individual ethnicity and neighbourhood-level ethnic density. Small area prediction models will require a  
23 multilevel approach, not attempted here, because obtaining predictions from multilevel random effects  
24 models is not straightforward and requires active statistical development.  
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32 We believe case ascertainment in our *validation sample* led to a reliable estimate of the incidence of  
33 psychotic disorder for people aged 16-35 years old. EIS were the only mental health service for people  
34 aged 14-35 years experiencing a first episode of psychosis in East Anglia, minimising the potential for  
35 under-ascertainment in the population at-risk when derived from careful epidemiological design.<sup>13</sup> We  
36 are confident that our *validation sample* also contained few false positive cases for any clinically-  
37 relevant psychoses, since participants were excluded who failed to meet acceptance criteria for EIS or  
38 who did not receive a clinical diagnosis of psychotic disorder during the first six months from initial  
39 referral. It is important to recognise that while our prediction models are based on diagnosed clinically  
40 relevant psychotic disorders, service commissioning will also need to account for additional pre-clinical  
41 or non-psychotic psychiatric morbidity presenting to EIS, particularly in services which operate early  
42 detection models or implement “watch-and-wait” briefs. The SEPEA data used to validate our models do  
43 not predict (1) the number of “false positive” subjects who may require psychiatric triage and  
44 assessment even though they are not accepted by EIS, or (2) the number of “true positive” subjects  
45 accepted by services, but who did not meet epidemiological criteria for inclusion in the *validation*  
46 *sample* of the SEPEA study (those living outside the catchment area at first contact, or those transferred  
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from other services); these people will consume varying degrees of service resources which needs to be considered in service planning.

We also note that pathways to care may affect the level of incidence observed in EIS, since many filters are likely to operate before subjects come to the attention of EIS. These will include local level service organisation and the relationship between Community Mental Health Teams [CMHTs], Child and Adolescent Mental Health [CAMHs] and EIS. Furthermore, acceptance criteria for entry to EIS vary, which will have a downstream effect on the number of new cases of clinically relevant psychoses received in each team. Future versions of PsyMaptic will include forecasts for specific psychotic disorders, as standardised research-based diagnoses (using OPCRIT<sup>34</sup>) are currently being collected in the ongoing SEPEA study in order to provide more detailed forecasts. Acceptance rates to EIS may also be influenced by local community awareness of such services. While our prediction models outperformed the current gold standard for EIS commissioning in England when restricted to clinically relevant caseloads, we recommend that our models are best interpreted as forecasts of the expected burden of first episode psychosis in given populations, and not the expected burden which will necessarily be seen through EIS given these issues.

We estimated prediction intervals from first principles [DJ] since there derivation is an area of statistical development.<sup>35</sup> We used a bootstrap-like methodology to produce 95% PI accounting for natural variation in the *validation sample*, but ignoring parameter uncertainty in the coefficients included in prediction models, which we assumed to be the true coefficients of risk in the population. Our approach therefore naturally led to slightly artificially narrow 95% PIs. This was not necessarily undesirable for the purpose of model validation and the precise prediction of expected counts because we wished to apply stringent criteria. Ideally, prediction intervals should take into account both these sources of variation, although we note that parameter uncertainty is usually small compared to the natural variation of the quantities of interest. The addition of more empirical data in the *prediction sample* would not lead to narrower PIs, though would tend to move the point estimate of risk for each coefficient closer to the true value in the population. We do not believe we have mis-estimated point estimates of risk across major sociodemographic groups, since our results accord with the wider literature.<sup>17, 21, 22</sup> We sought independent confirmation that our development of 95% PI were correct (personal communication with Prof Ian White, MRC Biostatistics Unit). We recommend that all prediction point estimates from our

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9 PsyMaptic model are considered with their 95% PIs, which provide information about the natural  
10 variance in expected rates in the population.  
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### 12 13 **Meaning of the findings**

14 If commissioners are to meet the Department of Health's vision to orientate health services around local  
15 need,<sup>1,2,5</sup> differences in demand for EIS and other mental and physical health services will need to be  
16 taken into account to allocate finite resources where they are most needed. The PsyMaptic prediction  
17 model provides proof-of-concept that when robust empirical epidemiological data is combined with  
18 accurate population at-risk estimates this can be realised. As such, our modelling approach could have  
19 utility in many other settings and for many disorders. Our translational approach demonstrated good  
20 ~~internal and external~~ validity to predict the expected incidence of first episode psychosis, particularly  
21 through EIS, where 76% and 63% of all male and female adult-onset FEP cases, respectively, will typically  
22 present.<sup>18</sup> Since their inception in 2002, EIS in England and Wales have reported both lower<sup>11</sup> and  
23 higher<sup>10</sup> caseloads than they were originally envisioned to manage,<sup>5</sup> with shortfalls or excesses in  
24 anticipated demand for services aligned to the degree of urbanisation in the underlying catchment area.  
25 Others have noted that EIS provision in rural areas may be difficult to implement effectively,<sup>14,15</sup> and  
26 while the MH-PIG acknowledged that "...[a]n understanding of local epidemiology is needed as the size  
27 of population covered will depend on a number of different factors" (p.55),<sup>5</sup> no further elaboration on  
28 how to achieve this was provided. We believe PsyMaptic provides a possible tool to overcome this  
29 challenge, improving the description and prediction of local population need beyond the MH-PIG and  
30 including individual- and neighbourhood-level indicators of local need.<sup>17</sup> From an aetiological  
31 perspective, we acknowledge that variables such as ethnicity or population density are likely to be  
32 markers for a suite of more complex, interactive social, genetic and environmental determinants of  
33 psychosis.<sup>36</sup>  
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43 Our models are not the first to be used to forecast mental illness needs in England and Wales,<sup>37</sup> though  
44 we believe this is the first attempt to forecast incidence rather than prevalence in the community. We  
45 recommend that our prediction methodology is used in conjunction with the wide range of public health  
46 observatory data available,<sup>38</sup> as well as the caveats presented above. PsyMaptic has been included with  
47 other indicators in the Joint Commissioning Panel for Mental Health's forthcoming guidance for  
48 commissioning of public mental health services.<sup>39</sup> Ongoing monitoring and audit of EIS will be vital to  
49 ensure services meet the fidelity criteria upon which they were originally commissioned,<sup>11,40</sup> including  
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9 ensuring that service capacity matches local need as closely as possible. As part of this process, we will  
10 need to externally validate our models in a wider range of settings, refining them based on empirical  
11 observation.  
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14 We note that advocacy expressed for EIS by healthcare professionals in England and Wales broadly  
15 correlates with demand for services as predicted by PsyMaptic.<sup>41</sup> Though by no means universal,  
16 proponents of EIS tend to be located in major conurbations – such as London,<sup>42</sup> Birmingham<sup>43</sup> or  
17 Manchester<sup>7,44</sup> – where demand for EIS will be highest, while those who suggest EIS resources could be  
18 used more effectively elsewhere tend to work in more rural communities,<sup>15,41</sup> where but a handful of  
19 young people would be expected to come to the attention of EIS each year. It is possible that both sides  
20 are correct and that more resources are required to help with the tide of psychotic illness in inner cities.  
21 Resources might be used more effectively in other ways, elsewhere, so long as the needs of the small  
22 number of young people who suffer a FEP each year are met; a dedicated specialist EIS may not be the  
23 most effective approach when anticipated demand will be very low.  
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30 Given the significant downstream economic savings associated with spending on EIS as estimated in an  
31 urban setting,<sup>8</sup> PsyMaptic could be used to highlight regions where sufficient investment to appropriate  
32 mental health services would lead to greatest economic gains in terms of mental healthcare expenditure  
33 (assuming sustained intervention also leads to improved social and clinical benefit for patients<sup>6,7</sup>).

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35 PsyMaptic can also be used to highlight regional variation in demand according to age and, sex and in  
36 future versions, by ethnicity group. This will, allowing service planners to tailor provision around the  
37 socio-cultural characteristics of their local populations. Our prediction tool for first episode psychosis,  
38 which translates robust empirical epidemiological data on psychosis risk to the population structure of  
39 different regions, offers a methodology for improving the allocation of finite mental health resources  
40 based around local need.  
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**Box 1: Description of included socioenvironmental variables <sup>1 2</sup>**

Variable	Classification & description
Multiple deprivation	Weighted data from routine national sources across 7 domains: income, employment, education, health, barriers to housing & services, living environment, crime. Continuous, z-standardised scores for analysis.
Extent of deprivation	Proportion of LAD population living in 20% most deprived SOA in England (%)
Income deprivation	Proportion of all people in LAD classified as income deprived (%)
Employment deprivation	Proportion of adults of working age in LAD classified as employment deprived (%)
Population density	Population density at LAD level (people per hectare).

IMD: Index of Multiple Deprivation; LAD: Local authority district; SOA: super output area; IQR: inter-quartile range

<sup>1</sup>*Prediction sample* sources: Population density – 2001 census estimates; Deprivation variables: 2004 Indices of Deprivation, predominantly collected from data sources close to AESOP & ELFEP case ascertainment periods (i.e. 1997-2000)

<sup>2</sup>*Validation sample* sources: Population density – 2009 mid-year census estimates; Deprivation variables: 2010 Indices of Deprivation, predominantly collected from data sources just prior to SEPEA case ascertainment period (2008)



Table 1: Prediction models, covariates and fit: all clinically relevant psychoses (F10-39)

Variable	Model 1 IRR (95%CI)	Model 2 IRR (95%CI)	Model 3 IRR (95%CI)	Model 4 IRR (95%CI)	Model 5 IRR (95%CI)	Model 6 IRR (95%CI)
Age group*sex interaction <sup>1</sup>	p=0.07	p=0.06	p=0.06	p=0.06	p=0.06	p=0.06
<b>Ethnicity</b>						
White British	1	1	1	1	1	1
Non-British white	2.0 (1.5, 2.5)	1.7 (1.4, 2.2)	1.7 (1.3, 2.2)	1.7 (1.3, 2.2)	1.8 (1.4, 2.3)	1.7 (1.3, 2.2)
Black Caribbean	6.0 (4.9, 7.3)	5.3 (4.3, 6.5)	5.2 (4.3, 6.4)	5.2 (4.3, 6.4)	5.4 (4.5, 6.6)	5.1 (4.2, 6.3)
Black African	4.1 (3.3, 5.1)	3.6 (2.9, 4.5)	3.5 (2.8, 4.4)	3.5 (2.8, 4.4)	3.7 (3.0, 4.6)	3.5 (2.8, 4.3)
Indian	1.7 (1.2, 2.5)	1.5 (1.1, 2.2)	1.5 (1.0, 2.2)	1.5 (1.0, 2.1)	1.6 (1.1, 2.3)	1.6 (1.1, 2.2)
Pakistani	1.8 (1.2, 2.5)	1.6 (1.0, 2.5)	1.6 (1.0, 2.4)	1.6 (1.0, 2.4)	1.6 (1.1, 2.5)	1.8 (1.3, 2.7)
Bangladeshi	2.1 (1.5, 2.8)	1.7 (1.2, 2.3)	1.7 (1.2, 2.3)	1.6 (1.2, 2.2)	1.8 (1.3, 2.5)	1.8 (1.4, 2.4)
Mixed white & black Caribbean	4.3 (2.8, 6.7)	3.9 (2.5, 6.0)	3.9 (2.5, 6.0)	3.9 (2.5, 6.0)	4.0 (2.6, 6.1)	3.9 (2.5, 6.1)
Mixed, other ethnicities	1.3 (0.8, 2.3)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)	1.2 (0.7, 2.1)
Other ethnicities	2.2 (1.6, 3.0)	1.9 (1.4, 2.7)	1.9 (1.4, 2.6)	1.9 (1.4, 2.6)	2.0 (1.4, 2.7)	1.9 (1.4, 2.7)
<b>Socioenvironmental variables</b>						
IMD (z-score)	-	1.184 (1.101, 1.274)	-	-	-	-
Extent of deprivation (%)	-	-	1.008 (1.004, 1.011)	-	-	-
Income deprivation (%)	-	-	-	1.025 (1.015, 1.035)	-	-
Employment deprivation (%)	-	-	-	-	1.062 (1.032, 1.093)	-
Population density (pph)	-	-	-	-	-	1.005 (1.003, 1.007)
<b>Internal model fit diagnostics</b>						
AIC <sup>2</sup>	2571.8	2552.4	2551.3	2549.6	2556.4	2556.3
Mean Lin's CCC (95%CI) <sup>3</sup>	0.75 (0.74, 0.77)	0.77 (0.75, 0.78)	0.77 (0.75, 0.79)	0.77 (0.75, 0.78)	0.77 (0.75, 0.78)	0.76 (0.74, 0.77)
Mean RMSE (s.d.) <sup>4</sup>	0.75 (0.11)	0.74 (0.11)	0.74 (0.10)	0.74 (0.10)	0.74 (0.11)	0.76 (0.13)

IRR: Incidence rate ratio; AIC: Akaike's Information Criterion; CCC: Lin's correlation concordance coefficient; RMSE: Root mean squared error.

<sup>1</sup>All models fitted with age group by sex interaction given *a priori* evidence for effect modification.<sup>18, 45</sup> Likelihood ratio test p-values reported between models with and without an interaction term fitted between age group and sex. Specific IRR not been reported for clarity, but available on request

<sup>2</sup>AIC: Akaike's Information Criterion— lower scores denote improved model fit

<sup>3</sup>CCC: Lin's correlation concordance coefficient. Higher scores indicate greater correlation between observed & predicted count of cases in the prediction sample. Mean CCC and 95%CI reported following *h*=20 trials during cross-validation.

<sup>4</sup>RMSE: Root mean squared error. Lower scores indicate lower prediction error. Mean RMSE and standard deviation (s.d.) reported following *h*=20 repeats of *k*-fold cross-validation, where *k*=10.

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**Table 2: Observed versus predicted cases in SEPEA study for all clinically relevant psychoses, 16-35 years<sup>1</sup>**

EIS	Observed	Model 1	Model 2	Model 3	Model 4
		Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)
<b>Overall total, 16-35 years</b>	<b>521<del>8</del></b>	<b>641.2 (586.0, 696.1)</b>	<b>468.5 (422.0, 518.0)</b>	<b>474.7 (429.0, 522.0)</b>	<b>487.5 (441.0, 535.0)</b>
Cameo North	55	84.7 (66.0, 106.0)	68.5 (52.0, 87.0)	67.8 (51.0, 86.0)	70.2 (53.0, 90.0)
Cameo South	134 <del>7</del>	163.6 (135.0, 192.0)	105.5 (84.0, 129.0)	111.7 (89.0, 134.0)	110.9 (90.0, 132.0)
West Norfolk	26 <del>5</del>	29.2 (18.0, 41.0)	23.0 (13.0, 35.0)	22.0 (12.0, 32.0)	23.4 (14.0, 34.0)
Central Norfolk	124 <del>0</del>	162.6 (136.0, 191.0)	122.6 (99.0, 148.0)	123.0 (100.0, 149.0)	128.3 (104.0, 152.0)
Great Yarmouth & Waveney	60	49.1 (34.0, 65.0)	41.6 (28.0, 55.0)	39.9 (27.0, 53.0)	42.9 (30.0, 57.0)
Suffolk	126 <del>30</del>	151.9 (126.0, 178.0)	107.4 (85.0, 128.0)	110.3 (88.0, 133.0)	111.7 (90.0, 136.0)
Overall total, 36-64 years	-	332.2 (292.0, 373.0)	244.0 (213.0, 276.0)	248.6 (216.0, 280.0)	256.3 (228.0, 291.0)

EIS	Observed	Model 5	Model 6	Model 7
		Predicted (95% PI)	Predicted (95% PI)	Predicted (95% PI)
<b>Overall total, 16-35 years</b>	<b>521<del>8</del></b>	<b>477.1 (428.0, 523.0)</b>	<b>508.5 (459.0, 559.0)</b>	<b>715.6 (664.0, 769.0)</b>
Cameo North	55	69.1 (52.0, 88.0)	64.5 (48.0, 82.0)	92.1 (74.0, 111.0)
Cameo South	134 <del>7</del>	100.7 (79.0, 123.0)	131.1 (108.0, 157.0)	169.0 (144.0, 195.0)
West Norfolk	26 <del>5</del>	24.7 (16.0, 35.0)	22.3 (13.0, 33.0)	35.8 (25.0, 48.0)
Central Norfolk	124 <del>0</del>	128.2 (105.0, 153.0)	132.5 (108.0, 157.0)	187.7 (161.0, 215.0)
Great Yarmouth & Waveney	60	47.7 (35.0, 63.0)	38.0 (26.0, 51.0)	59.1 (44.0, 74.0)
Suffolk	126 <del>30</del>	106.6 (86.0, 128.0)	120.0 (96.0, 143.0)	172.1 (147.0, 198.0)
Overall total, 36-64 years	-	249.7 (221.0, 284.0)	262.9 (233.0, 297.0)	1175.4 (1109.0, 1243.0)

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<sup>1</sup>Numbers in green denote where observed count fell within 95% prediction interval [95% PI] for people aged 16-35 years. Observed data for people aged 36-64 years in the validation sample was not available.

Model 1: Age group, sex, their interaction and ethnicity  
 Model 2: Model 1 + IMD  
 Model 3: Model 1 + extent of deprivation  
 Model 4: Model 1 + income deprivation

Model 5: Model 1 + employment deprivation  
 Model 6: Model 1 + population density  
 Model 7: Department of Health uniform figure for EIS of 15 new cases per 100,000 people per year.

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**Table 3: External model validation diagnostics<sup>1</sup>**

Model	Observed case count within QSEPEA overall correct prediction intervals? [rank]	EIS (N=6)		LAD (N=21)		Mean ranking [rank of mean ranking]
		Number correct [rank]	RMSE [rank]	Number correct [rank]	RMSE [rank]	
Model 1	No [53]	34 [62]	27.056 [6]	18 [2]	8.94 [6]	5.038 [64]
Model 2	No [53]	43 [64]	168.84 [4]	18 [25]	6.49 [4]	43.48 [56]
Model 3	Yes/No [13]	54 [21]	146.94 [32]	178 [25]	6.135 [32]	23.602 [32]
Model 4	Yes [1]	4 [42]	14.963 [2]	187 [25]	6.14 [2]	24.868 [23]
Model 5	Yes/No [31]	54 [12]	179.48 [5]	186 [62]	6.74 [5]	24.82 [53]
Model 6	Yes [1]	5 [1]	11.59 [1]	19 [1]	65.90 [1]	1.0 [1]
Model 7	No [53]	42 [7]	398.16 [7]	13 [7]	11.70 [7]	6.62 [7]

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<sup>1</sup>For each diagnostic, models are placed in rank order [1=best model, 7=worst model] with ties given the same ranking. The mean ranking and rank provide an estimate of the overall performance of various models.  
 RMSE: Root mean squared error (lower scores indicate lower error); EIS: Early Intervention in Psychosis Service; LAD: Local Authority District

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Article Summary
<b>Article Focus</b>
<ul style="list-style-type: none"> <li>Commissioners require precise information on the health needs of their local populations to effectively plan health services</li> <li>A failure to arm mental health commissioners with precise epidemiological data led to mis-estimation of actual activity in early intervention in psychosis services [EIS]</li> <li>We sought to develop a prediction tool for the incidence of first episode psychosis [FEP], by applying precise estimates of epidemiological risk in various sociodemographic groups to the structure of the population at-risk in a second region, where the observed incidence had been concurrently ascertained</li> </ul>
<b>Key Messages</b>
<ul style="list-style-type: none"> <li>A model of psychosis incidence which included age, sex, ethnicity and population density yielded precise FEP predictions in our second region, out-performing the Department of Health in England's current gold standard for EIS commissioning.</li> <li><u>While our model provides forecasts of the burden of FEP in different populations, initial assessment of some people who do not require subsequent EIS care means additional service resources, not addressed here, will be required.</u></li> <li>We have translated this model into a freely available prediction tool (<a href="http://www.psymaptic.org">www.psymaptic.org</a>) to facilitate evidence-based healthcare commissioning of socioculturally relevant services according to local need</li> <li><del>Our tool could be extended to many international settings and other disorders to inform healthcare commissioning, when epidemiological risk can be well characterised and the structure of the underlying population at risk is known</del></li> </ul>
<b>Strengths and limitations</b>
<ul style="list-style-type: none"> <li>Our modelling approach used robust epidemiological data from two large studies of first episode psychosis in England to provide estimates of incidence in a third study region, producing accurate FEP forecasts</li> <li>While our models provide estimates of the expected clinical burden of FEP in the community, services may see a broader range of psychopathology consuming resources, or incepted rates may be influenced by supply-side organisational factors</li> <li>Due to data availability it was not possible to validate our prediction tool in settings outside of England and Wales, or for specific psychotic disorders. As data become available we will extend the capability of our prediction tool, <u>including into other settings and disorders.</u></li> </ul>

Supplemental Table 1: Socioenvironmental variables at local authority district [LAD] level considered in epidemiological prediction models

Variable		England <sup>1</sup>	Prediction sample <sup>2</sup>	Validation sample <sup>1</sup>	Mann-Whitney test <sup>3</sup> : Z; p-value	
					Prediction vs. Validation	Validation vs. England
Number of LAD	-	326	14	20 (+1 partial)	-	-
Multiple deprivation (z-standardised)	Median (IQR): Min/Max:	<u>0 (1)</u> <sup>4</sup> -1.7 / 2.9	1.0 (-0.5, 2.4) -1.1 / 2.9	-0.7 (-1.0, 0.3) -1.4 / 1.0	2.4; p=0.02	1.5; p=0.12
Extent of deprivation (%)	Median (IQR): Min/Max:	9.0 (1.3, 23.9) 0.0 / 83.6	28.0 (4.0, 63.0) 0.0 / 83.0	1.4 (.4, 12.8) 0.0 / 29.7	2.4; p=0.02	2.2; p=0.03
Income deprivation (%)	Median (IQR): Min/Max:	11.7 (8.6, 16.1) 3.9 / 32.8	15.5 (8.2, 24.7) 5.9 / 34.4	9.0 (8.2, 14.9) 6.0 / 19.1	1.5; p=0.14	1.3; p=0.19
Employment deprivation (%)	Median (IQR): Min/Max:	8.0 (5.8, 10.8) 2.1 / 18.8	11.6 (6.1, 14.1) 6.1 / 14.1	6.4 (5.4, 10.1) 3.9 / 13.9	2.5; p=0.01	1.4; p=0.17
Population density (people per hectare)	Median (IQR): Min/Max:	5.1 (1.8, 17.4) 0.2 / 137.1	19.4 (9.3, 81.9) 2.6 / 106.4	1.5 (1.2, 3.1) 0.9 / 30.0	3.7; p<0.001	3.4; p=0.001

IQR: inter-quartile range; LAD: Local Authority District

<sup>1</sup>Sources: Population density – 2009 mid-year census estimates; Deprivation variables: 2010 Indices of Deprivation, predominantly collected from data sources just prior to SEPEA case ascertainment period (2008)

<sup>2</sup>Sources: Population density – 2001 census estimates; Deprivation variables: 2004 Indices of Deprivation, predominantly collected from data sources close to A&ESOP & ELFEP case ascertainment periods (i.e. 1997-2000).

<sup>3</sup>Mann-Whitney test performs test that the median LAD socioenvironmental scores for the prediction & validation data come from the same population distribution; p<0.05 indicates evidence that the median scores are significantly different

<sup>4</sup>For England we displayed the mean and s.d. of the z-score of deprivation (as shown, underlined), instead of the median and IQR.

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**Supplementary Table 2: Stratum-specific external validity of our PsyMaptic prediction model in people aged 16-35 years old (Model 7)**

	Observed N <sup>1</sup> (SEPEA)	Predicted N <sup>2</sup> (Model 7)	95% PI <sup>3</sup>	Observed N within 95% PI? <sup>4</sup>
<b>Sex</b>				
Men	345	338.9	(299.0, 382.0)	Yes
Women	176	169.5	(144.0, 196.0)	Yes
<b>Age group</b>				
16-17	66	24.8	(15.0, 36.0)	No
18-19	95	72.1	(55.0, 90.0)	No
20-24	183	159.8	(131.0, 189.0)	Yes
25-29	107	152.4	(128.0, 179.0)	No
30-34	65	85.3	(66.0, 105.0)	No
35	5	14.2	(7.0, 22.0)	No
<b>Ethnicity</b>				
White British	410	335.2	(299.0, 375.0)	No
Non-British white	44	43.7	(31.0, 57.0)	Yes
Black Caribbean	5	18.3	(10.0, 27.0)	No
Black African	14	20.3	(12.0, 31.0)	Yes
Indian	1	20.9	(13.0, 31.0)	No
Pakistani	6	13.8	(7.0, 22.0)	No
Bangladeshi	6	3.8	(0.0, 8.0)	Yes
Mixed, white & black Caribbean	5	10.6	(5.0, 18.0)	Yes
Mixed, other ethnicities	12	7.5	(3.0, 13.0)	Yes
Other ethnicities	18	34.5	(23.0, 46.0)	No

<sup>1</sup>Observed number of cases meeting SEPEA criteria for FEP over 2.5 years (n=521).

<sup>2</sup>Predicted caseloads over 2.5 years based on model estimates from AEsOP & ELFEP data extrapolated to the population at-risk, aged 16-35 years, in the SEPEA study

<sup>3</sup>95% prediction intervals

<sup>4</sup>Reports whether the observed number of cases falls within the prediction intervals given by the model

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9 **Appendix (supplementary): Development of 95% prediction intervals for negative binomial regression**  
10 **models**  
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13 To obtain 95% prediction intervals from each model, we took all parameter estimates from the fitted  
14 negative binomial regression, including the over-dispersion parameter  $\theta$ , as the true values when  
15 constructing prediction intervals. We then used a Monte Carlo procedure, where we simulated  
16 realisations using the Gamma-Poisson representation of the negative binomial distribution. For each  
17 iteration, we first simulated the random components of the linear predictors from  $\text{Gamma}(\theta, \theta)$ , which  
18 were multiplied by the point predictions (or equivalently  $e^{\upsilon}$ , where  $\upsilon$  is the non-random component of  
19 the linear predictor) to give the Poisson rates for the counts that comprised the predictions. We then  
20 simulated Poisson counts using these rates and summed them to provide one realisation of the quantity  
21 we wished to predict. By repeating this process many ( $n=1000$ ) times the distribution of the quantity to  
22 be predicted was obtained, from which 95% prediction intervals were obtained using the 2.5% and  
23 97.5% quantiles.  
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## Data sharing statement

Extra data is available at our prediction website, PsyMaptic: [www.psymaptic.org](http://www.psymaptic.org). We have made a large array of prediction data freely available to interested users, who can visualise prediction data in maps and tables for a range of psychotic disorder predictions by major sociodemographic subgroup and by LAD. Future versions of PsyMaptic will release data for other regions and at other geographical levels. Users can also download LAD-specific and national summaries of prediction data from our models in tabular form. Finally, additional explanatory material about how to use the data and the PsyMaptic website is also available at [www.psymaptic.org](http://www.psymaptic.org). Bespoke data not provided freely on our website may be requested from the authors at the cost of data extraction. The empirical data underlying the prediction models (ÆSOP and ELFEP) or the validation sample (SEPEA) is not freely available as the studies are ongoing, but papers detailing the main findings from these studies have previously been published elsewhere.

## Competing interests statement

All authors have completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare that (i) JBK has support from the Wellcome Trust for the submitted work (grant number WT085540) and PBJ has support from the NIHR (grant RP-PG-0606-1335); (ii) DJ, JP, FW, DF, JC, RMM have no relationships with any company that might have an interest in the submitted work in the previous 3 years; (iii) their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and (iv) no author holds non-financial interests that may be relevant to the submitted work.



**Role of funders**

The funders were not involved in the design, collection, analysis, interpretation of the data, writing the report or the decision to submit the article for publication. All authors were independent from the funders in contributing to this work.

**Ethical approval**

Ethical approval to conduct the original AESOP and East London First Episode Psychosis studies was granted from local research ethics committees in their respective centres prior to the original date of onset of the study. We were granted ethical approval to conduct the work related to the present manuscript, including use of data from the SEPEA study, from the Cambridgeshire 3 REC (09/H0306/39).

**Guarantorship**

JBK takes full responsibility for the work and conduct of the study, had access to the data, and controlled the decision to publish.

**Contributorship**

JBK was responsible for concept, design, analysis, data extrapolation, interpretation of the data, drafting the report and developing the content for the websites [www.psymaptic.org](http://www.psymaptic.org), [www.psymaptic.com](http://www.psymaptic.com) and [www.psymaptic.co.uk](http://www.psymaptic.co.uk). JBK was also the chief investigator of the SEPEA study, where the *validation sample* data was obtained. He gave final approval of this version of the manuscript to be published.

DJ was responsible for developing and initially implementing the statistical approach with regard to prediction intervals from count-based regression. He also contributed to drafting and editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

JP is principal collaborator on the SEPEA study in the CAMEO early intervention in psychosis services. He also contributed to editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

DF is co-principal collaborator on the SEPEA study in the Norfolk and Suffolk Foundation Trust. He also contributed to editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

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FW is co-principal collaborator on the SEPEA study in the Norfolk and Suffolk Foundation Trust. He also contributed to editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

JC is chief investigator of the ELFEP study and provided part of the empirical dataset underlying the prediction model for use in this project. He also contributed to editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

RMM is co-chief investigator of the ÆSOP study and provided part of the empirical dataset underlying the prediction model for use in this project. He also contributed to editing the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

PBJ is co-chief investigator of the ÆSOP study and provided part of the empirical dataset underlying the prediction model for use in this project. He contributed to the development of the prediction methodology and edited the final version of this manuscript. He gave final approval of this version of the manuscript to be published.

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#### **STROBE statement**

Our STROBE statement is provided as a supplementary file.

Supplemental Figure 1: Screenshot of web-based PsyMaptic prediction tool

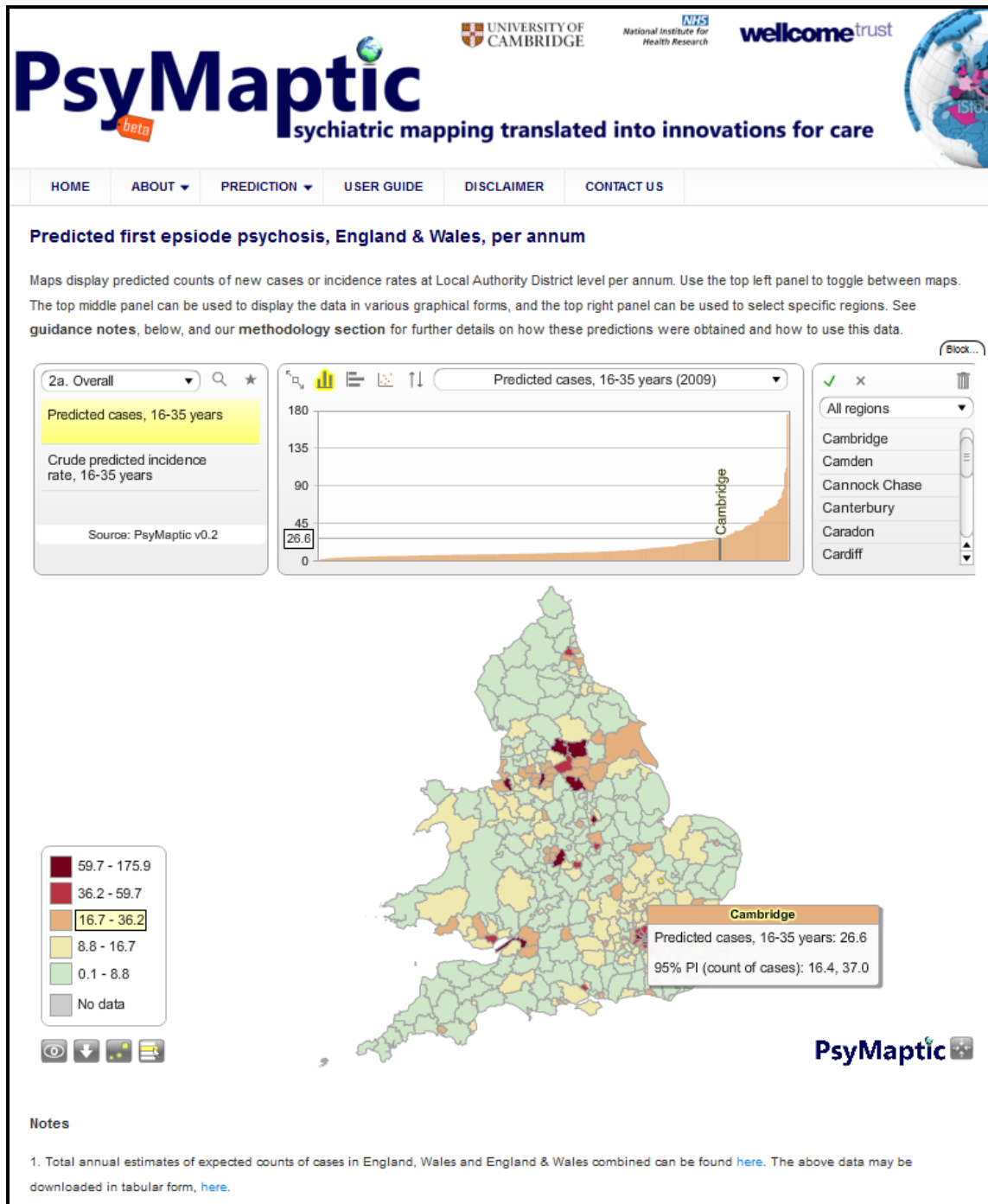


Figure legend: Screenshot shows the PsyMaptic prediction tool made freely available at [www.psymaptic.org](http://www.psymaptic.org). This example shows a prediction map of the annual expected count of new cases of psychotic disorder for people aged 16-35 years across 376 Local Authority Districts [LAD] in England & Wales from our candidate prediction model (Model 6). Each prediction is presented with corresponding 95% prediction intervals. Count data are categorised into the following percentiles: green: 0-50% of LAD; yellow: 50.1-75%; orange: 75.1-90%; red: 90.1-95%; dark red: 95.1-100%. Our PsyMaptic prediction maps are provided with additional graphical utility (histograms, scatterplots, region selection) and are freely available at [www.psymaptic.org](http://www.psymaptic.org)

Supplemental Figure 2: PsyMaptic predicted incidence rate of psychotic disorder in England and Wales, aged 16-35 years old, compared with Department of Health uniform rate for EIS commissioning

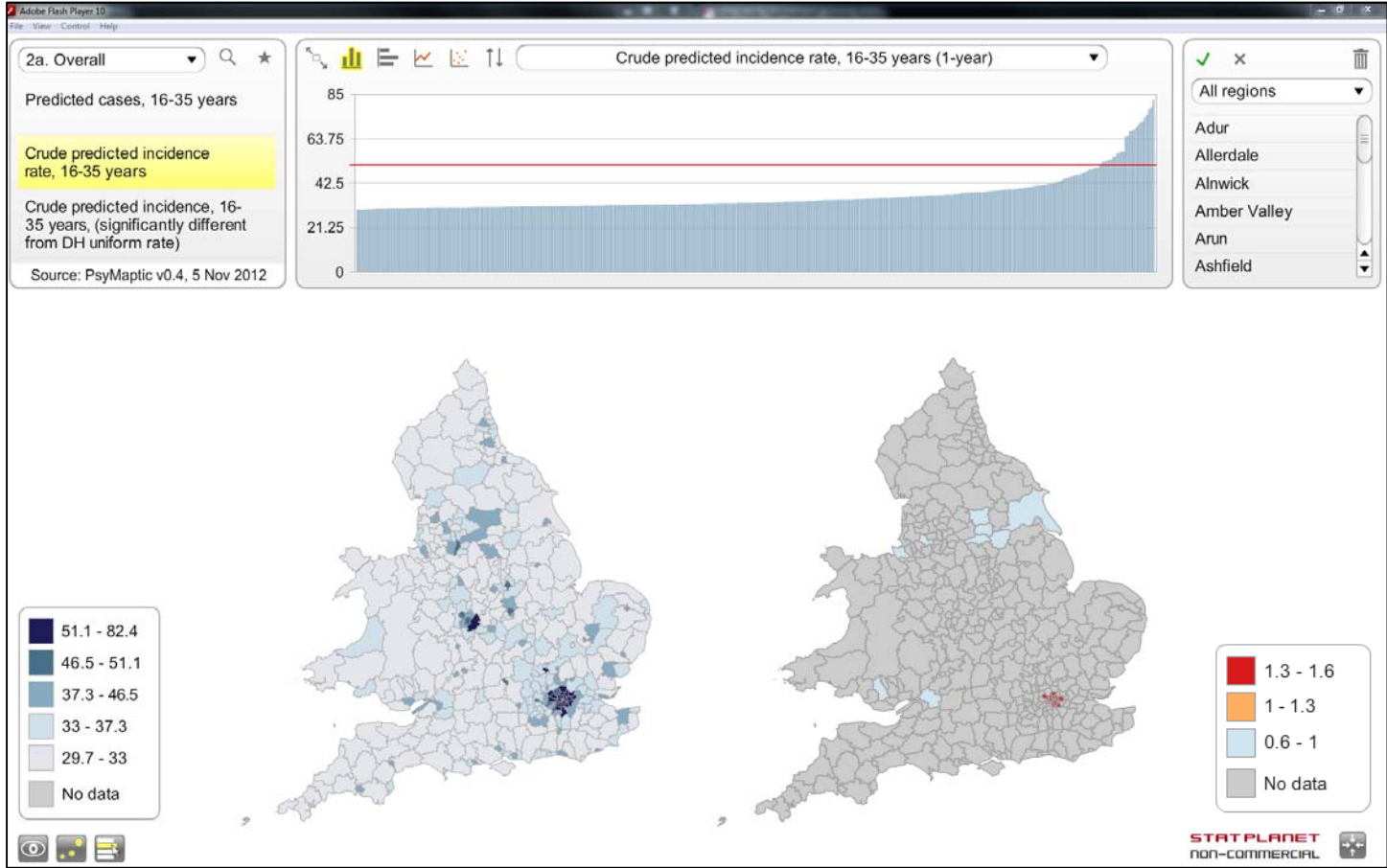


Figure legend: The graph (top) plots all LADs according to predicted incidence rates in people aged 16-35 years (per 100,000 person-years) using PsyMaptic (model 6). The red line is the uniform rate (51 cases per 100kpy), used to commission EIS. Our predicted rates fall below this in 93% of LAD in England & Wales (n=351), indicating that the Department of Health's [DH] uniform rate may have over-estimated incidence in these regions. Predicted incidence rates are plotted geographically on the left hand map, The darkest shading indicates LAD (in London and Birmingham) where the point estimate of incidence exceeded the DH uniform rate. The right hand map plots the ratio between predicted cases from PsyMaptic & the DH uniform rate. Ratios significantly exceeding unity (in orange & red) show regions where the DH rate under-estimated incidence; ratios significantly less than unity (in blue) show regions where the DH rate over-estimated incidence. This method is conservative (see methodology).

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
<b>Title and abstract</b>	1	<p>(a) Indicate the study's design with a commonly used term in the title or the abstract</p> <p>We entitled our paper <b>A population-level prediction tool for first episode psychosis: development and validation</b>. While our paper uses cross-section data to base prediction models on, the central study design is in reference to prediction <u>modelling using epidemiological data, which we have duly referred to.</u></p> <hr/> <p>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</p> <p>Our abstract was written in the structured style required by the British Medical Journal for publication and included information on <i>background, objectives, design, setting, main outcome measures, results and conclusions.</i></p>
<b>Introduction</b>		
Background/rationale	2	<p>Explain the scientific background and rationale for the investigation being reported</p> <p>Health care planners and commissioners require accurate data on the incidence of psychotic disorder to anticipate the burdens faced by different populations in different regions. Only by using precise predictions, which take into account local need, will it be possible for health care funders and commissioners to allocate finite resources where they are most needed. There is evidence that Early Intervention in Psychosis services [EIS] were commissioned on an erroneously low uniform rate, and that commissioners were unable to satisfactorily take into local population need based on established sociodemographic and environmental risk factors for disorder. This led to misestimation of demand for EIS services in many parts of the UK. We sought to improve the information available for health care commissioners in psychosis, and particularly EIS, by developing an epidemiological prediction tool for disorder.</p>
Objectives	3	<p>State specific objectives, including any prespecified hypotheses</p> <p>To develop a population-based epidemiological prediction tool for first episode psychosis [FEP]. Our hypothesis was that our best prediction model, using informed empirical epidemiological data, should be more valid than the current gold standard for EIS planning, based on the Department of Health's Mental Health Policy Implementation Guide figure of 51 new cases per year per 100,000 people.</p>
<b>Methods</b>		
Study design	4	<p>Present key elements of study design early in the paper</p> <p>Pooled data from two large epidemiological studies of First Episode Psychosis [FEP] conducted with similar methodologies (the Aetiology and Ethnicity in Schizophrenia and Other Psychoses [AESOP] study, and the East London First Episode Psychosis [ELFEP] study) were used to generate risk coefficients from six negative binomial regression models, which tested different combinations of sociodemographic (i.e. age, sex, ethnicity) and socioenvironmental factors (deprivation, population density at local authority district [LAD] level) associated with psychosis incidence. Coefficients were applied to the population at-risk of a third, markedly different region, to predict expected FEP counts over a 2.5 year period, where the observed incidence had also been ascertained.</p>
Setting	5	<p>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</p> <p>Empirical data from the AESOP (1997-9) and ELFEP (1996-8 &amp; 1998-2000) studies</p>

in London, Nottingham and Bristol was used in regression models to estimate out-of-sample predictions for the expected count of new FEP cases in the population at-risk of East Anglia over a 2.5 year period (2009-2012), where the observed count of cases incepted through EIS has also been ascertained through a third study, the Social Epidemiology of Psychoses in East Anglia [SEPEA] study.

Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants
<p>All participants in the AESOP and ELFEP studies, aged 16-64 years old at referral, were identified using the same study design based on the principles of the World Health Organisation Ten-Country study. Any participant presenting to services in each study's defined catchment areas with a suspected first episode of psychotic disorder over the case ascertainment period were screened. Participants were included if they were diagnosed by consensus with an ICD-10 F10-39 first episode of psychotic disorder, using standardised diagnostic data from the Schedule for the Clinical Assessment of Neuropsychiatry [SCAN] presented to a panel of clinicians blind to the ethnicity of the subject. A leakage study was conducted to identify participants missed by the initial screen.</p>		
<p>Participants in the SEPEA study, aged 16-35 years old, were identified if they were referred to one of six EIS in East Anglia for the first time with a suspected first episode of psychosis in the defined catchment area of these services over a 2.5 year period. Participants were excluded if they did not meet clinical criteria for acceptance into EIS or if, at six months after referral, a clinical diagnosis of ICD-10 F10-39 psychosis had not been observed. Observational data in people aged 36-64 years old could not be obtained as this was not part of the SEPEA study objective and no routine surveillance of this group was in place.</p>		
<p>Participants from any study were excluded if they were found to have a profound learning disability or an organic basis to their psychotic episode.</p>		
<p>The denominator populations for AESOP and ELFEP were estimated from the 2001 Census of Great Britain, while the latest mid-term census estimates (2009) stratified by age, sex and ethnicity were obtained for the denominator population in the SEPEA study.</p>		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
<p>All clinically relevant psychotic disorders as per ICD-10 F10-39 psychotic disorders were included as the main outcome variable. We included age group (16-19, then 5 year age groups until 60-64 years), sex and ethnic group (ten categories based on the 2001 census 16-category variable to include: white British, non-British white, black Caribbean, black African, Indian, Pakistani, Bangladeshi, mixed white &amp; black Caribbean, other mixed ethnicities and all other ethnicities). Given evidence of effect modification of the risk of psychotic disorder over age by sex, we considered an <i>a priori</i> interaction between these variables. All individual level variables are known to be associated with the incidence of psychotic disorder and were therefore considered important predictors in our models. Additionally, for some prediction models (see</p>		

below), we also included various socioenvironmental measures at the Local Authority District [LAD] level, such as socioeconomic deprivation or population density, since there is evidence that the incidence of psychotic disorder varies by urbanicity and deprivation. Population density was measured by dividing total population size (2001 or 2009) by LAD area. The Indices of Deprivation (2004/2010) were used to include the potential effects of four domains of deprivation relevant to psychosis incidence – multiple deprivation, the extent of deprivation in the LAD (i.e. an inequality-like measure), income deprivation and employment deprivation. These domains were obtained from the 2004 and 2010 indices of deprivation for the AESOP/ELFEP and SEPEA studies, respectively, with the source data originating from national surveys and other data sources predominantly collected close to the case ascertainment periods of each study.

Data sources/ measurement	<p>8* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group</p> <p>For numerator participants: Age was based on age at first referral for suspected psychotic disorder. Ethnicity and sex were assigned by self-ascription. Neighbourhood-level socioenvironmental factors were assigned to participants based on their residential address at first referral to services.</p> <p>For denominator (census) participants: Age was defined as age at the time of the census or mid-term census estimate. Sex and ethnicity were defined through self-ascription. LAD population density was based on the total census/mid-term population in each LAD, divided by each LAD's area (in hectares) estimated using ArcGIS software. Deprivation domains were assessed by the 2004/2010 indices of deprivation, which use a comparable methodology to assess changes in deprivation over time, integrating data from a range of nationally-collected routine data sources.</p>
Bias	<p>9 Describe any efforts to address potential sources of bias</p> <p>To minimise the risk of missing incidence participants from the AESOP and ELFEP studies leakage studies were conducted to identify all subjects with a potential FEP, not picked up by the initial screen. This was achieved by close contact with other services where FEP subjects may present, including prisons, the judicial systems, homeless shelters and so forth. In the SEPEA study, EIS provide the only service base for people experiencing FEP up to 35 years old. No leakage study was possible in SEPEA, but all services engaged in active outreach to ensure missing participants were minimised in their communities. One potential source of bias in the SEPEA study is the over-estimation of incidence rates given that EIS do not tend to diagnose participants at referral to avoid stigmatisation and to allow the full course of symptoms to emerge. We minimised the possibility of over-inclusion here by excluding all participants who did not meet clinical criteria for entry to EIS (clear evidence of psychotic symptoms, no previous referral, no previous antipsychotic treatments) and by restricting the sample only to those participants who were given a clinician-rate ICD-10 F10-39 diagnosis of psychotic disorder at first episode.</p>

1 2 3 4 5 6 7 8 9 10	Study size	10	<p>Explain how the study size was arrived at</p> <p>Studies of incidence rates have a sample size equivalent to the ability of the study to identify all true instances of first episode psychosis in a defined catchment area and population over a given time period. Thus, the sample size for all studies here is a function of these factors. We included data from the SEPEA study for 2.5 years of the 3 year study, since it was presently ongoing at the time of these analyses. We included 14 LADs in our empirical prediction data (AESOP/ELFEP) and 21 LADs in our SEPEA study region.</p>
11 12 13 14 15 16 17 18 19 20 21 22	Quantitative variables	11	<p>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</p> <p>Variable groupings for individual level variables have been described in Section 7. For LAD-level variables, population density was entered as a continuous variable. Multiple deprivation and the extent of deprivation were entered as continuous z-standardised variables (across variation in these scores over England) to have a mean of zero and standard deviation of one. Income and employment deprivation were classified as the proportion of people in a given LAD classed as income or employment deprived.</p>
23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60	Statistical methods	12	<p>(a) Describe all statistical methods, including those used to control for confounding</p> <p>A summary of our statistical methodology is provided here. Full details are provided at <a href="http://www.psymaptic.org">www.psymaptic.org</a> or in the accompanying paper to this checklist:</p> <p>[i] Six negative binomial regression models were fitted to the empirical data (AESOP/ELFEP). Model 1 was fitted with age group, sex, their interaction and ethnic group. Models 2-5 included the variables in Model 1 plus a single LAD deprivation measure (multiple deprivation, extent of deprivation, income and employment deprivation, respectively). Model 6 included the variables in Model 1 plus LAD population density.</p> <p>[ii] Apparent predictive error for the whole sample, aged 16-64 years, was estimated using repeat k-fold validation to obtain estimates of the Residual Mean Squared Error and Lin's Correlation Concordance Coefficient (correlation between model predictions and the observed count of cases in the data). For each full</p> <p>[iii] Regression coefficients from each model obtained in [i] were applied to the population structure of the population at-risk, aged 16-35 years old, in the SEPEA study to obtain out-of-sample predictions of the expected count of cases in East Anglia over 2.5 years as seen in the age range for EIS. Predicted counts for each model were obtained for the (1) overall predicted count (2) EIS-specific counts and (3) LAD-specific counts in East Anglia. For every prediction, 95% prediction intervals were estimated, using a bootstrap-like method developed from first principles to take into account prediction error in both the prediction data and the out-of-sample dataset.</p> <p>[iv] We obtained similar predictions to [iii] based on a "model" (Model 7) which fitted the Department of Health's current gold standard incidence rate for EIS commissioning (51 per 100000 per year) to the SEPEA data and obtained predictions [iii](1-3) as before.</p>



[v] The predicted counts from each model obtained in [iii] (1-3) were compared with the observed counts of cases for each grouping. We considered the number of times the observed count fell within the 95% prediction intervals from the model prediction to indicate satisfactory model fit. RMSE estimates of model fit between the predicted and observed counts at the EIS- and LAD-levels were obtained for external model validation and comparison. For each of the five diagnostics (overall fit to the observed data, number of times fitted correctly to six EIS, number of times fitted correctly to the 21 LAD, EIS-level RMSE, LAD-level RMSE) we ranked models in terms of performance (1: best, 7: worst). Ranks were averaged across these 5 diagnostics to give an overall ranking for the model which had the greatest predictive power.

[vi] Using the best model obtained in [v] we extrapolated our findings to the population structure (2009 mid-term estimates) of every LAD in England and Wales to produce a freely available prediction tool for commissioners, which forecasts (with 95% Prediction Intervals) the expected incidence of psychotic disorder in every LAD, across all major sociodemographic groups, based on empirical risk coefficients and applied to each LAD's unique population structure. This prediction data was visualised using software known as StatPlanet and uploaded to our website [www.psymaptic.org](http://www.psymaptic.org) to provide Psychiatric Mapping Translated into Innovations for Care [PsyMaptic], a free, online commissioning tool for health care planners, providers and commissioners.

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(b) Describe any methods used to examine subgroups and interactions

We used the full empirical dataset aged 16-64 years to predict the expected count of cases in our validation sample (SEPEA), where the observed caseload had been restricted to the ages 16-35 years old, consistent with the age range covered by EIS. SEPEA did not identify an incidence sample in this region for people aged 36-64 years old and so we could not externally validate our models in this age range. However apparent validity of our models across the entire age range, 16-64 years old, was good, and we have no reasons to believe our empirical data in the older age range would be any less valid for prediction than at younger age ranges given it was obtained from the same two studies (AESOP/ELFEP).

Interactions between age group and sex were entered into our regression models as a multiplicative statistical interaction.

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(c) Explain how missing data were addressed

There were no missing data in this dataset

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(d) If applicable, describe analytical methods taking account of sampling strategy

N/A

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(e) Describe any sensitivity analyses

95% prediction intervals were developed for negative binomial regression prediction and reported for all predicted counts and incidence rates of FEP. These intervals give a measure of the confidence we have in our prediction estimates.

**Results**

Participants	13*	<p>(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</p> <p>1037 participants with a first episode psychosis were included in the prediction sample of an initial sample of 1049, where 12 participants were of no fixed abode at time of entry to the study. For the SEPEA study 521 cases were observed over the study period who met entry criteria for the study from an initial sample of 572. Those excluded did not meet clinical criteria for FEP.</p> <p>(b) Give reasons for non-participation at each stage</p> <p>See above</p> <p>(c) Consider use of a flow diagram</p> <p>Not necessary</p>
Descriptive data	14*	<p>(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders.</p> <p>See previously published papers on the AESOP, ELFEP and SEPEA studies as this is not directly relevant here. Of more relevance are the risk coefficients for psychosis incidence across sociodemographic and socioenvironmental groups, as reported in Table 1 of the paper accompanying to this Strobe statement includes. This table confirms the typical risk coefficients seen across these variables.</p> <p>(b) Indicate number of participants with missing data for each variable of interest</p> <p>12 participants were excluded because of no fixed abode in the AESOP. These subjects were more likely to be men, but otherwise did not differ from the remainder of the sample.</p>
Outcome data	15*	<p>Report numbers of outcome events or summary measures</p> <p>N/A – see below for full results</p>
Main results	16	<p>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included.</p> <p>A model with age, sex, ethnicity and population density performed strongest overall, predicting 508 FEP participants in EIS in East Anglia (95%PI: 459, 559) compared with an observed count of 521 over the same period. This model predicted correctly in 5 of 6 EIS (83.3%) and 19 of 21 LAD (90.5%). This model achieved the highest ranking on all external diagnostic measures of any model, and reasonable apparent RMSE (0.76; s.d.: 0.13) and CCC (0.76; 95% CI: 0.74, 0.77) estimates across the entire age range. All models performed better than the current gold standard for EIS service commissioning (716 cases; 95%PI: 664-769).</p> <p>Inspection of stratum-specific predictions of our best model in the SEPEA region suggested results were accurate by sex. For age, our models tended to underpredict caseloads at younger ages, but over predict caseloads at older ages (up to 35 years old). This was probably due to the nature of EIS themselves, which alter i.e. lower the median age at onset. Our prediction data was based on pre-EIS epidemiological data, so future versions of PsyMaptic need to incorporate new EIS data. Results by ethnicity were mixed with accurate predictions in some, but not all ethnic groups. This will continue to be refined.</p>

		(b) Report category boundaries when continuous variables were categorized <a href="#">Age groups – see above</a>
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period <a href="#">Not relevant</a>
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
<b>Discussion</b>		
Key results	18	<p>Summarise key results with reference to study objectives</p> <p>We have developed several epidemiological prediction models to forecast expected incidence of first episode psychosis in England and Wales, and assessed their relative apparent and external validity, taking into account regional differences in the sociodemographic and socioenvironmental profile of different populations. Inspection of the data suggested that a model fitted with age group, sex, their interaction, ethnic group and LAD-level population density provided the best external predictive capabilities compared with the observed caseload ascertained through EIS in our <i>validation sample</i>. This model also had good apparent validity across the entire age range considered here (16-64 years). All prediction models performed significantly better than the Department of Health’s current gold standard for EIS resource allocation, based on a low uniform anticipated incidence rate.</p>
Limitations	19	<p>Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias</p> <p>Our predictions are based upon the assumed true rate of disorder in the population aged 16-64, 16-35 or 36-64 years old. This may differ from the caseloads observed by services, due to supply-side and demand-side issues. For example, services may see a broader range of referrals who are not psychotic or in the prodromal stage of disorder. Additional resources for false positive caseloads need to be considered in any commissioning decisions. Furthermore, demand for services may differ from the true underlying rate of FEP in the community if people are not aware of the relevant mental health services available to them. Services vary considerably in organisation, remit and structure and such factors may also affect the incepted (versus true) rate of disorder seen in EIS and other mental health services.</p> <p>Prediction intervals for count-based regression models are not computationally-straightforward to derive. We estimated prediction intervals from first principles [DJ], using a bootstrap-like methodology to produce 95%PI accounting for uncertainty in the <i>validation sample</i>, but ignoring parameter uncertainty in the coefficients included in prediction models, which were assumed to be the true coefficients of risk in the population. This approach naturally leads to narrow 95%PIs given ignorance of parameter uncertainty, and is therefore desirable for model validation and the precise prediction of expected counts. The addition of more empirical data to the prediction model would thus not lead to narrower PIs, though might move the point estimate of risk for each coefficient closer to the true value in the population. We sought independent confirmation that our formula was correct (Prof Ian White, MRC Biostatistics Unit) and full details of our methodology are made available in the</p>

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2 Appendix. We recommend that all prediction point estimates made available in our  
3 PsyMaptic model are considered with their 95%PIs, which provide information about  
4 the natural variance in expected rates in the population.  
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7 We could not externally validate our prediction models for people aged 36-64 years  
8 because comparable observed incidence data was not available in our *validation*  
9 *sample*. We have no reason to believe our predictions will be invalid for this group,  
10 however, since the empirical data which underpinned our models was ascertained  
11 from the same two large, well-conducted studies of first episode psychosis in England  
12 as the data for the younger age group, and published findings from these studies are  
13 consistent with the wider epidemiological literature for psychosis from England and  
14 internationally. It will be important to ascertain the predictive capability of our  
15 model(s) where we could not externally validate our model, and we will seek to  
16 identify suitable samples to do so in future versions of PsyMaptic.  
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20 All prediction models had reasonable apparent validity, although our proposed model  
21 had slightly poorer apparent validity (most noticeably in terms of AIC) than models  
22 which included deprivation instead of population density (i.e. Models 2-4). Model 4  
23 (including income deprivation) had marginally greater apparent validity than our  
24 candidate prediction model, but performed worse during *external validation* (Table 4),  
25 which we considered more important for the development of a prediction tool. This  
26 decision was supported by the fact that despite considerable socioenvironmental  
27 differences between regions in our *prediction* and *validation samples*, our prediction  
28 model produced accurate forecasts in a markedly different population. We were  
29 unable to predict the expected incidence of psychotic disorder in geographical areas  
30 smaller than LADs, such as electoral wards (N~6000), or to other parts of the UK,  
31 because the appropriate denominator data was not published as mid-term census  
32 estimates. The 2011 census will provide small area and national data for the whole of  
33 the UK and will be released by ONS in mid-2013. This will allow us to update our  
34 tool to the latest population estimates for the UK, and refine our PsyMaptic tool at a  
35 smaller geographical level for fine-grained healthcare commissioning. Small area  
36 prediction models will require a multilevel approach, not attempted here, because  
37 obtaining predictions from multilevel random effects models is not straightforward  
38 and requires active statistical development.  
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44 We believe case ascertainment in our *validation sample* led to a reliable estimate of  
45 the incidence of psychotic disorder for people aged 16-35 years old. EIS are the only  
46 mental health service for people aged 14-35 years experiencing a first episode of  
47 psychosis, minimising the potential for under-ascertainment in the population at-risk  
48 when derived from a careful epidemiological design. We are confident that our  
49 *validation sample* also contained few false positive cases for any clinically-relevant  
50 psychoses, since participants were excluded who failed to meet acceptance criteria for  
51 EIS or who did not receive a clinical diagnosis of psychotic disorder at six months  
52 after referral. Future versions of PsyMaptic will include forecasts for specific  
53 psychotic disorders, but these are unavailable at present because standardised  
54 research-based diagnostic data (using OPCRIT) needed to obtain specific reliable  
55 diagnoses are currently being collected in the ongoing SEPEA study.  
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59 Interpretation 20 Give a cautious overall interpretation of results considering objectives, limitations,  
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multiplicity of analyses, results from similar studies, and other relevant evidence. If commissioners are to meet the Department of Health's vision to orientate health services around local need, differences in demand for EIS and other mental and physical health services will need to be taken into account to allocate finite resources where they are most needed. The PsyMaptic prediction model provides proof-of-concept that when robust empirical epidemiological data is combined with accurate population at-risk estimates this can be realised. Our translational approach demonstrated good apparent and external validity to predict the expected incidence of first episode psychosis, particularly through EIS where 76% and 63% of all male and female adult-onset FEP cases, respectively, would typically present. Since their inception in 2002, EIS in England and Wales have reported both lower and higher caseloads than they were originally typically commissioned to manage, usually depending on the urbanicity of the population. Rural communities saw much lower demand for EIS than urban services. The Mental Health-Policy Implementation Guide [MH-PIG] anticipated a uniform rate of 51 per 100,000 people per year. While the MH-PIG also acknowledged that "...[a]n understanding of local epidemiology is needed as the size of population covered will depend on a number of different factors" (p.55), no further elaboration on how to achieve this was provided for commissioners. We believe PsyMaptic provides one possible exemplar to overcome this challenge.

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Generalisability	21	Discuss the generalisability (external validity) of the study results We believe our results are generalisable to the populations of England and Wales. The empirical data we used is consistent with the wider international and national literature regarding the pattern of incidence rates across different sociodemographic and socioenvironmental subgroups. Our model had good external validity in the age range 16-35 years, and we have no reason to doubt its validity for the entire adult age range for psychosis, 16-64 years old given the reasonable apparent validity demonstrated. That our prediction data was based on a very different environment (urban London, Nottingham and Bristol) but still produced valid forecasts in a markedly more diverse, rural and less deprived region overall (East Anglia), suggests our model will have good validity in England and Wales. This will make our prediction model a valuable tool for mental health service planning and commissioning, based on local need and translational epidemiology, when the prediction intervals we produce here are also taken into account. Service commissioners must also provide allowances for differing structure of services and the extra (false positive) referrals that may consume service resources but do not meet clinical criteria for FEP.
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#### Other information

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Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based James Kirkbride was supported by a Sir Henry Wellcome Research Fellowship from the Wellcome Trust (grant number WT085540), through which the SEPEA study ( <a href="http://www.sepea.org">www.sepea.org</a> ) was established. Peter Jones directs the NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC) for Cambridgeshire & Peterborough and is supported by NIHR grant RP-PG-0606-1335. The SEPEA study has been adopted by the Mental Health Research Network [MHRN]. The authors are grateful to the clinical services and staff participating in the SEPEA study, and the MHRN for their support. We are grateful to Professor Ian White of the MRC
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Biostatistics Unit (University of Cambridge) for his guidance on developing our prediction interval methodology for negative binomial regression.

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\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

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