




A public early intervention approach to first-episode psychosis: Treated incidence over 7 years in the Emilia-Romagna region

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Abstract

Aim: To estimate the treated incidence of individuals with first-episode psychosis (FEP) who contacted the Emilia-Romagna public mental healthcare system (Italy); to examine the variability of incidence and user characteristics across centres and years.

Methods: We computed the raw treated incidence in 2013–2019, based on FEP users aged 18–35, seen within or outside the regional program for FEP. We modelled FEP incidence across 10 catchment areas and 7 years using Bayesian Poisson and Negative Binomial Generalized Linear Models of varying complexity. We explored associations between user characteristics, study centre and year comparing variables and socioclinical clusters of subjects.

Results: Thousand three hundred and eighteen individuals were treated for FEP (raw incidence: 25.3 / 100.000 inhabitant year, IQR: 15.3). A Negative Binomial location-scale model with area, population density and year as predictors found that incidence and its variability changed across centres (Bologna: 36.55; 95% CrI: 30.39–43.86; Imola: 3.07; 95% CrI: 1.61–4.99) but did not follow linear temporal trends or density. Centers were

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associated with different user age, gender, migrant status, occupation, living conditions and cluster distribution. Year was associated negatively with HoNOS score ($R = -0.09$, $p < .001$), duration of untreated psychosis ($R = -0.12$, $p < .001$) and referral type.

Conclusions: The Emilia-Romagna region presents a relatively high but variable incidence of FEP across areas, but not in time. More granular information on social, ethnic and cultural factors may increase the level of explanation and prediction of FEP incidence and characteristics, shedding light on social and healthcare factors influencing FEP.

KEYWORDS

first-episode psychosis, incidence, schizophrenia, untreated psychosis

1 | INTRODUCTION

Psychotic disorders are relatively rare, but have a profound, long-lasting impact on the individual trajectory. Thus, patients with the first episode of psychosis (FEP) need early detection and specific clinical management. Analysing data from a large geographical area where this approach is widely implemented, such as the Emilia-Romagna region, may provide useful information.

When a person shows the first signs of a psychotic disorder, a timely, proactive and appropriate specialist care is crucial to increase the odds of reaching satisfactory outcomes. Ample evidence supports this approach. Early intervention programs improve clinical outcomes and prevent severe psychosocial deterioration to a greater extent than usual care (Correll et al., 2018; Shah et al., 2022). The call for early intervention on psychosis has been received across countries worldwide which provide tailored, community-based, multidisciplinary psychosocial intervention to promote personal and vocational recovery (McDonagh et al., 2022). This approach takes into account that for each individual psychosis is shaped by an idiosyncratic array of factors spanning the familial, peer, work and community social domains (Heinz et al., 2013).

Similar considerations can be made at the population level. Knowing specific population characteristics should make it possible to tailor public mental healthcare for the specific local needs in terms of detection, prevention and management (Kirkbride, 2015). Indeed, the distribution and combination of risk factors for FEP can be extremely variable. Similarly, there is high variability in the incidence, course and outcomes of psychosis across different communities or countries (Jongsma et al., 2018). Not surprisingly, studies have identified a number of associations between patterns of sociodemographic characteristics, substance use and social deprivation, and changes in the incidence, clinical features or outcomes of individuals with FEP (Anglin et al., 2021; Heinz et al., 2013; Jongsma et al., 2021; Leighton et al., 2019; Mascayano et al., 2020; Suvisaari et al., 2018). More recently, studies have begun to translate epidemiological knowledge on risk factors into models that predict the incidence (or features) of psychosis at the individual level, or within specific catchment areas (Lee et al., 2022; McDonald et al., 2021; Suvisaari et al., 2018). For instance, the incidence of psychosis in various areas of England is accurately forecasted using data on age, sex, ethnicity, social

deprivation and population density (Kirkbride, 2015). Another model uses individual clinical data and area-level information to predict the outcomes of patients with FEP during treatment (Leighton et al., 2019). Similar instruments may be of crucial help for policy-makers to plan resource allocation (Aceituno et al., 2019; Campion et al., 2019) as well as for clinicians to identify high-risk individuals/populations (Belvederi Murri et al., 2022).

Building actionable epidemiological or risk prediction models for psychosis requires that one identifies what causes the variability of FEP incidence and patient clinical heterogeneity. Examining data from a homogenous healthcare system has the advantage of reduce confounding due to healthcare-related variables (e.g. detection of cases and pathways to care) and some heterogeneity due to social factors (e.g. cultural and economic characteristics). The first sensible step towards the characterization of local FEP services is represented by the analysis of the heterogeneity of incidence and user characteristics across geographic subareas, or time fluctuations (March et al., 2008; Singh et al., 2000). Then, further investigations may pinpoint the specific contribution of individual risk factors.

The aim of this study was to estimate the treated incidence, and describe the user characteristics of individuals with FEP that had contact with the Emilia-Romagna regional healthcare system. This study makes use of data from the Emilia-Romagna Region Program for First-Episode Psychosis (RER-FEP) that has been implemented since 2012 (Belvederi Murri et al., 2020; Ferrara et al., 2019). The RER-FEP is one of the few large-scale public healthcare initiatives in Italy to address this condition in a coordinated way. In particular, we sought to analyse the variability of incidence across the region catchment areas, over the first 7 years since the establishment of the RER-FEP, including both users who entered the program and those who did not (Ajnakina et al., 2017).

2 | METHODS

2.1 | Setting and organization of the study

The Emilia-Romagna region is one of the largest in Northern Italy (4.5 million residents), with a high density (about 200 inhabitants per square km). The region presents with a varied demographic and

economic census: a rather old population and steadily increasing immigration fluxes (ISTAT Italian Institute of Statistics, 2020). It is among the top 10 regions for the highest average gross income in Europe (Annuario Statistico Regionale, 2020), and has an overall low prevalence of social deprivation (Regione Emilia Romagna, 2021). However, it ranks high for substance use in Italy. The region comprises nine administrative provinces: Bologna (approximately one million inhabitants), Modena (700 000), Reggio Emilia (530 000), Parma (450 000), Forli-Cesena (400 000), Ravenna (390 000), Ferrara (350 000), Rimini (340 000) and Piacenza (290 000). They correspond to 11 Local Health Trusts (Forli and Cesena have separate Trusts as well as Imola, a city in the province of Bologna), from which 10 final groupings resulted.

Since the 1978 reform, mental healthcare in Italy is provided by publicly funded Departments of Mental Health (DMH) within the Local Health Trusts. Currently, 45 early intervention services for psychosis are active within the national healthcare system although they are still unevenly distributed in the territory (Cocchi et al., 2018). The Emilia Romagna regional system has been one pioneer delivering evidence-based care for FEP in the Italian public sector. The RER-FEP represents the first region-wide coordinated program to provide routine early intervention for individuals aged 15–35 manifesting a psychiatric condition pertaining the clinical high risk for, or the onset of psychosis (Regione Emilia Romagna, 2016). Various aspects of care for individuals for FEP, and of the RER-FEP program have been previously described for the provinces of Bologna (Tarricone et al., 2012, 2016), Modena (Ferrara et al., 2019), Reggio Emilia (Pelizza et al., 2019), Parma (Leuci et al., 2020) and Ferrara (Belvederi Murri et al., 2020).

The RER-FEP program allows each DMH to tailor the implementation and the delivery of the FEP service (FES) according to the local organization and workforce availability (Regione Emilia Romagna, 2016). Each FES is organized either as follows: (i) FEP stand-alone service with full-time specialists dedicated to FEP patients only and geographically distant from the general CMHC, (ii) dedicated staff, but not-exclusive for FEP, or (iii) 'specialist within generalist service', corresponding to FEP-trained professionals within the individual general CMHC (Ferrara et al., 2019). A FES usually includes a minimum of three professional categories: a psychiatrist, a psychotherapist, and a case manager (nurse or rehabilitation therapist). Over the past decade, the composition of each FES and the caseload has varied due to changes in local policies, and staff turnover (Meneghelli et al., 2023).

2.2 | Detection of FEP cases in adults

The region applies a coordinated approach to the detection of adult individuals with FEP (Regione Emilia Romagna, 2016). Guidelines eligibility for the RER-FEP program in adults is based on the following inclusion criteria: aged 18–35 years; Duration of Untreated Psychosis (DUP) shorter than 2 years; the absence of prior treatment with antipsychotic medications, fluency in the Italian language. Using the ICD-9 system, the following diagnostic codes are admissible:

affective psychosis (295.34, 296.24, 296.44, 296.14, 296.54, and 296.64) and non-affective psychosis (295.0–295.95, 299.9, 297, and 298). Subjects are also excluded from the multi-component intervention if they present severe intellectual disability. Subjects who are not eligible for the RER-FEP interventions because of longer DUP, substance-induced psychosis, or intellectual disability are referred to the CMHC for Treatment As Usual (TAU). Patients are also excluded if they lack linguistic fluency, as communication in Italian is necessary to access the cognitive behavioural treatment, a key component of FEP service. However, CMHCs are equipped with translators for routine visits.

Pathways to care to the RER-FEP programme or to TAU include self-referrals, referrals from other services within the DMH, such as psychiatric inpatient units, eating disorders units and addiction units, referrals from the general hospital, particularly the emergency room (ER). General practitioners (GPs) in particular were trained in the recognition of early psychosis and encouraged to refer patients to mental health services, in the context of a liaison programme (Curcetti et al., 2005). In addition, local services such as social service and local police can sometimes be the first who come into contact with people with FEP advising a referral to the ER or to the CMHC.

Ethical approval was obtained by the Area Vasta Emilia Centro Ethical Committee (CE-AVEC); the study conforms to principles expressed in the Declaration of Helsinki. Participants gave their informed consent prior to their inclusion.

2.3 | Data collection

Incidence data was available for 7 years (January 1st, 2013 to December 30th, 2019) at the level of 10 Local Health Trusts: Bologna, Ferrara, Forli-Cesena, Modena, Parma, Piacenza, Ravenna, Reggio Emilia, Rimini, and Imola. We obtained data on the size of the population at risk (18–35 years old) in each catchment area, per year from the ISTAT census (ISTAT Italian Institute of Statistics, 2020). Population density was calculated as the total number of inhabitants per square kilometre, and log-transformed.

Data for sociodemographic and clinical variables was obtained during clinical consultations and recorded on the electronic or physical charts. Additional information was collected by clinicians on migrant status (either first- or second-generation), current substance misuse, and personality disorder in comorbidity (ICD-9 diagnosis of personality disorder in comorbidity). For descriptive purposes, we report data on the Italian version of the Health of the Nation Outcome Scale (HoNOS) (Lora et al., 2001) which was used to rate the severity of behavioural, impairment, social problems and symptoms over the previous 2 weeks (Starace & Mazzi, 2012).

2.4 | Data analyses

First, we report the raw estimates of incidence of psychosis, calculated as the number of the newly treated cases per 100 000 persons/year in the region and each departmental catchment area.

Second, we estimated the incidence of FEP using a Bayesian modelling framework. The Bayesian approach assumes that observed data are a noisy indicator of a “true” generating process: it estimates both the parameter(s) and its level of uncertainty, expressed as a posterior probabilistic distribution. Different from null hypothesis testing, Bayesian models provide the probabilities a whole range of parameter values, thus conveying richer information. When data are measured from multiple centres from the same population it is recommended to use generalized hierarchical models (a.k.a. “mixed” models) because they reduce the sensitivity to noise in data. In such models, differences of incidence between centres may depend on different distribution of unmeasured risk factors (McElreath, 2018). By accounting for the level of uncertainty and by combining information from multiple centres (partial pooling), Bayesian models proved particularly successful for the prediction and forecasting of the incidence of rare events such as FEP (McDonald et al., 2021).

In this study, we used different Generalized Linear Models of increasing complexity to estimate the distribution and time-related changes of FEP incidence rate. In particular, we modelled data using both a Poisson and Negative Binomial distribution. The latter assumes there could be overdispersion of data. Poisson models have one outcome parameter, the ratio of incident cases over the at-risk population (offset). This main single parameter represents the mean count of events: its variance is constrained to be equal to the mean. In the first model, the population density and study year served as the predictors. In the subsequent models, we used a hierarchical approach, allowing: (1) the intercept; (2) the intercept and longitudinal slope, to vary by centre. Then, we used a Negative-Binomial distribution, where the mean incidence and its variance (a.k.a. *shape*) are distinct parameters that serve as dependent variables. Each can be associated with an individual set of predictors. For instance, such models may be able to detect if time is associated with increase or decreases of the *variability* of incident cases, even if the mean incidence remains the same (Williams et al., 2019). We explored the different incidence rates between centres by comparing posterior predictions and overlaps in their 95% credible intervals. Default, non-informative priors were used for all models. Models were compared evaluating based on their out-of-sample predictive accuracy using Leave-One-Out Cross Validation, where higher values of the expected log pointwise predictive density (ELPD-LOO) indicate better predictive accuracy. Influential cases were identified using the *pareto-k*-diagnostic. However, we also provide Bayesian R^2 values as an intuitive measure of model fit, calculated as predicted variance divided by predicted variance plus error variance (Gelman et al., 2019). Analyses were conducted with the 2.1.16 *brms* R package (Bürkner, 2017) and reported with the *tidy-bayes* 3.0.2 (Kay, 2021).

Third, we compared user sociodemographic and clinical characteristics between centres and study years. Chi-square and non-parametric analyses were used to compare single categorical and continuous variables, respectively, while the supplement reports detailed plots for each variable for visual aid.

Fourth, we re-examined the association between user characteristics, study centre and year using clusters of patients based on a basic

set of sociodemographic features (age, gender, migrant status and substance use). Cluster analysis was based on Gower distance and the Partitioning Around Medoids (PAM) method; the number of clusters was identified examining silhouette width. This analysis was performed with the *cluster* R package (Maechler et al., 2022).

3 | RESULTS

3.1 | Raw incidence of treated cases

The program included 1454 individuals with FEP (Figure S1). This corresponds to a grand mean incidence of 25.3 cases/100 000 inhabitants per year, Interquartile Range (IQR) = 15.3, using the reference 2016 census size of the population at risk (18–35 years old, 781.172 inhabitants).

The raw incidence of FEP in the regional program did not reveal specific longitudinal temporal patterns. There was relatively lower incidence in 2013, 2016 and 2019 (Figure 1, Table S1). There were large differences in the average incidence of each centre (from 11.76 Imola to 39.54 / 100.000 inhabitants per year in Parma, Table S2). However, by examining the temporal changes within each centre (depicted as diamonds in Figure 2) no clear temporal pattern emerged.

3.2 | Bayesian models of FEP incidence

The incidence data were modelled using a series of Bayesian models. Based on the out-of-sample predictive accuracy, a Hierarchical model based on the Negative Binomial distribution resulted as the most accurate (Table S3). The model used population density and study year to predict the mean incidence rate, nesting temporal trends within study centre (grouping factor). In addition, the dispersion of incidence rates was allowed to vary by study centre. The model converged well, with good posterior predictive checks and *rhat* values equal to 1.00. Accounting for both random and fixed effects, the model explained 64.3% of the variance in incidence rates (Bayesian R^2 ; Error: 6.6%, 95% CrI: 49.5%–75.3%); based only on fixed effects, that is, not accounting for centre variability, it explained 37.2% (Error: 9.9% 95% CrI: 17%–6%–56.5%). The model did not detect evidence of linear temporal trend in the general regional population. Similarly, there was no evidence of an effect of population density, with a very weak trend for a negative effect on incidence (Table S3. ‘fixed’ effects and Figure S5). Variability of FEP incidence rates could be largely attributed to study centre, rather than year (Figure 1, S3, S4, and S6). For instance, in 2016 Imola had the lowest incidence (incidence: 3.07; 95% Credible Intervals: 1.61–4.99), followed by Ravenna (8.15; 95% Cr.I.: 2.95–17.31), Piacenza (10.41; 95% Cr.I.: 7.73–13.41), Rimini (11.36; 95% Cr.I.: 8.56–14.60), Forli-Cesena (11.98; 95% Cr.I.: 8.92–15.25), Ferrara (15.38; 95% Cr.I.: 12.11–19.11), Reggio Emilia (25.81; 95% Cr.I.: 15.66–39.33), Parma (29.04; 95% Cr.I.: 18.18–40.18), Modena (29.39; 95% Cr.I.: 22.53–37.50) and Bologna (36.55; 95% Cr.I.: 30.39–43.86). Imola, Rimini, Piacenza were characterized by low

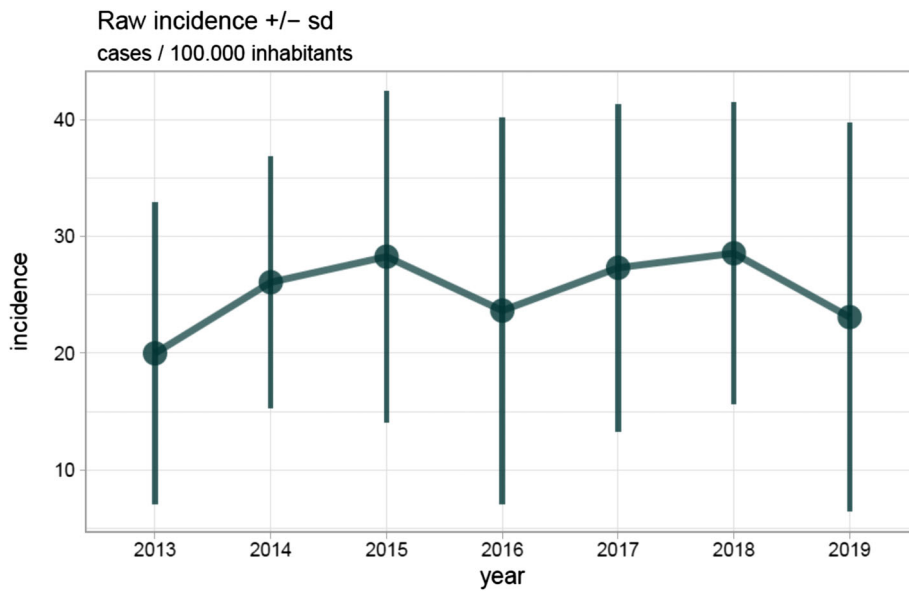


FIGURE 1 Raw incidence of treated cases per 100 000 inhabitant year.

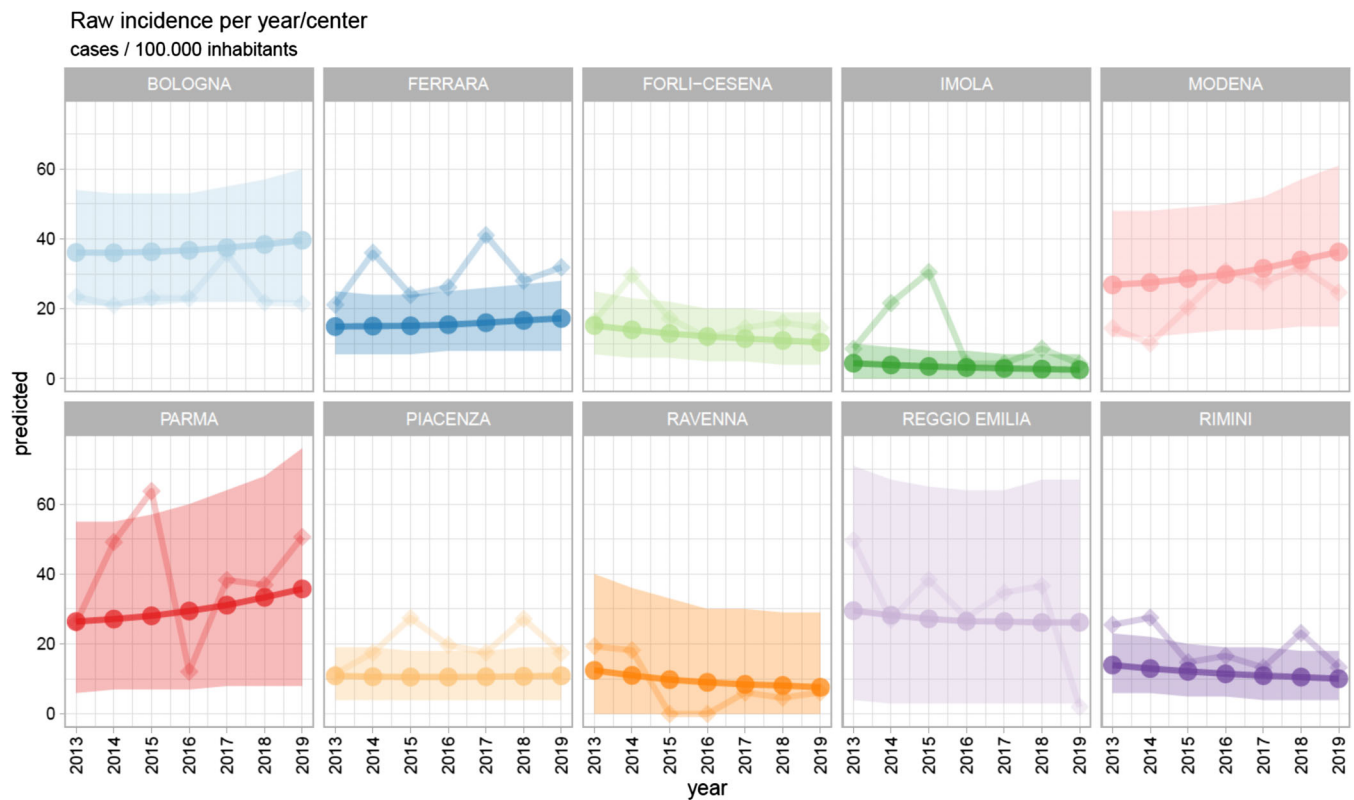


FIGURE 2 Raw and modelled incidence of treated cases per 100 000 inhabitant year. Observed values are diamonds; circles and shaded areas represent mean values predicted by the model with 95% Credible Intervals.

degrees of uncertainty around the median (Figure S3). Compared posterior predictions and 95% Credible Intervals across centres for the year 2016: the model predicted that Bologna had a larger incidence of FEP than Ferrara, Forli-Cesena, Imola, Piacenza and Rimini. Imola had a lower incidence than Ferrara, Modena and Parma (the full list of comparisons is reported in Table S5). In addition, Rimini had a larger dispersion than Ravenna and Reggio Emilia.

3.3 | User characteristics

The entire sample (1318 individuals) comprised 69% of males; the median age of 22 and 21% of the sample were migrants (Table S6). The vast majority was single, with a middle- or high-school education level and living with the family of origin (62%). The median DUP was 5 months.

We compared user characteristics across centres. Users had significant differences in mean age ($p < .001$), gender ($p < .001$), migrant status ($p < .001$), occupation ($p = .009$) and living conditions ($p < .001$), but not in education levels ($p = .13$) or civil status ($p = 0.24$) (Table 1 and Figures S7–S13). Considering clinical characteristics, there were significant differences in the percentage of users displaying personality disorders, substance use, as well as HoNOS total and subscale scores. Moreover, users differed across centres in terms of referrals to the program and length of the DUP (Table 2 and Figures S14–S18).

The same comparisons were drawn by study year: the differences were not significant in mean age, gender, migrant status, occupation, education levels, civil status, personality disorder and substance use but they were in terms of living conditions ($p = .01$), referral type ($p = .006$), HoNOS total and subscale scores ($p < .01$) and DUP length ($p = .002$; Tables S7 and S8). In addition, there was a significant negative association between study year and HoNOS total score ($R = -0.09$, $p < .001$) and between study year and DUP length ($R = -0.12$, $p < 0.001$) (Figures S19 and S20).

Cluster analysis identified a seven-cluster solution as the one with the highest silhouette width. Clusters were differentiated by almost all possible permutations of gender, migrant status and substance use, with smaller differences in age (Table S9). They comprised: Male users (M), not migrant (migrant-), not substance users (substance-) ($n = 343$), M, migrant+, substance+ ($n = 304$), Females (F), migrant-, substance- ($n = 229$), M, migrant+, substance+ ($n = 95$), M, migrant, substance- ($n = 89$), F, migrant-, substance+ ($n = 72$), F, migrant+, substance- ($n = 69$). The distribution of user clusters displayed a significant variability by study centre (chi square = 123.6, $df = 54$, $p < .0001$) but not by year (chi square = 41.2, $df = 36$, p -value = .253) (Figure 3 and Figure S21).

4 | DISCUSSION

This study describes the incidence and user characteristics of FEP in Emilia-Romagna during the first 7 years when the Regional Program for FEP was active. The treated incidence rates and user characteristics were rather variable across different departments, although deriving from the same region. Whereas, clinical severity of FEP and modality of access to the program were the few factors that may have displayed some variability in relation to the study year. This study is strengthened by a rigorous methodological approach and a large, representative sample.

The incidence of FEP in our study varied between 20 and 30 cases per 100 000 inhabitants in 7 years. This is in line with other estimates from the literature (Kirkbride et al., 2006). The more appropriate comparison is with the European EUGEI study, which adopted similar enrolment criteria and also included the Center of Bologna and other two Italian centres, over a period of 48 months (Jongsma et al., 2018; Tarricone et al., 2016). Our estimates are higher than those from the Bologna and the other Italian centres (Palermo and

Veneto), as well as that of the region of Sicily (Mulè et al., 2017), but they are lower than those from South London and Amsterdam, urbanized areas with high prevalence of risk factors, especially migration and cannabis (Di Forti et al., 2019). Our estimates are also much lower if compared to a recent Australian estimate (102.4 per 100 000 population at-risk) (Pignon et al., 2021). Finally, our estimates are similar to those of a recent meta-analysis (Jongsma et al., 2019) which detected extreme levels of heterogeneity in the incidence of psychosis across countries, and also failed to detect time-related trends. The meta-analysis of Jongsma and colleagues suggested that methodological factors may have influenced incidence rates in that larger studies, especially population-registers of whole countries or cohort studies similar to ours may generally detect higher incidence than first contact studies (Jongsma et al., 2019).

Our study was conducted within one region and assumes some level of homogeneity in sociocultural characteristics, case-selection criteria and healthcare approach that derive from the coordination between departmental areas and from the adoption of shared guidelines (Regione Emilia Romagna, 2016). Nonetheless, we observed large variability in the incidence, sociodemographic and clinical characteristics of individuals with psychosis. This variability was almost entirely attributable to the study centre, while we did not detect an effect of population density, as some studies (Kelly et al., 2010; Kirkbride et al., 2017; March et al., 2008), but not all did (Jongsma et al., 2018). Hence, factors other than population density may explain the differences we observed. Compared with other regions in Italy, the Emilia-Romagna region, in fact, has a relatively high and homogeneous population density. However, its population displays the highest use of substance in Italy (Di Forti et al., 2019), a higher presence of migrants – also internal migrants for work or study reasons (Tarricone et al., 2016), and a high average pro-capita income. The former two factors are associated with higher incidence of FEP, while the latter is expected to reduce the incidence of psychosis, although income inequality would need to be taken in account (Kirkbride et al., 2014). Further analyses of these data will clarify whether, and how the distribution of these factors contributes to shape the risk of psychosis. Based on the previous literature, one should expect non-linear patterns and complex interactions between different factors to shape incidence. For instance, the role of migrant status may interact with ethnic density (Baker et al., 2021; Bosqui et al., 2014), negative personal experiences (Tarricone et al., 2021) and social dynamics (Termorshuizen et al., 2022). Network analyses may aid the process of modelling complex interactions at the clinical and sociocultural levels (Amore et al., 2020).

This study is strengthened by a large sample, representative of well-defined regional catchment area, and ample coverage of cases of FEP. However, it should be considered preliminary, given that data with greater level of detail has still not been collected. We argue that more granular information on social, ethnic and cultural factors may allow to increase the level of explanation and prediction

TABLE 1 Sociodemographic characteristics.

Characteristic	Piacenza, N = 71 ¹	Parma, N = 232 ¹	Reggio emilia, N = 215 ¹	Modena, N = 205 ¹	Bologna, N = 261 ¹	Imola, N = 19 ¹	Ferrara, N = 113 ¹	Ravenna, N = 36 ¹	Forlì- cesena, N = 84 ¹	Rimini, N = 82 ¹
Age*										
N/No. obs. % not missing	70/71 99%	228/232 98%	206/215 96%	-	-	18/19 95%	107/113 95%	35/36 97%	-	-
Mean (SD)	22.8 (5.0)	24.8 (5.4)	22.4 (4.7)	24.0 (4.9)	23.4 (4.5)	22.9 (4.2)	22.2 (4.3)	21.3 (4.1)	24.8 (5.4)	23.0 (5.0)
Sex*										
F	22 (31%)	66 (28%)	83 (39%)	65 (32%)	61 (23%)	8 (42%)	24 (21%)	10 (28%)	36 (43%)	18 (22%)
M	48 (68%)	162 (70%)	123 (57%)	140 (68%)	200 (77%)	10 (53%)	83 (73%)	25 (69%)	48 (57%)	64 (78%)
Missing	1 (1.4%)	4 (1.7%)	9 (4.2%)	0 (0%)	0 (0%)	1 (5.3%)	6 (5.3%)	1 (2.8%)	0 (0%)	0 (0%)
Education										
Elementary	1 (1.4%)	8 (3.4%)	5 (2.3%)	5 (2.4%)	4 (1.5%)	0 (0%)	3 (2.7%)	0 (0%)	4 (4.8%)	0 (0%)
Middle school diploma	29 (41%)	63 (27%)	67 (31%)	74 (36%)	96 (37%)	8 (42%)	33 (29%)	14 (39%)	21 (25%)	23 (28%)
High school diploma	26 (37%)	83 (36%)	72 (33%)	74 (36%)	124 (48%)	7 (37%)	38 (34%)	9 (25%)	42 (50%)	40 (49%)
University degree	5 (7.0%)	17 (7.3%)	6 (2.8%)	16 (7.8%)	31 (12%)	0 (0%)	4 (3.5%)	1 (2.8%)	11 (13%)	5 (6.1%)
Missing	10 (14%)	61 (26%)	65 (30%)	36 (18%)	6 (2.3%)	4 (21%)	35 (31%)	12 (33%)	6 (7.1%)	14 (17%)
Civil status										
Single	46 (65%)	186 (80%)	141 (66%)	162 (79%)	244 (93%)	13 (68%)	72 (64%)	24 (67%)	67 (80%)	58 (71%)
Stable relationship	5 (7.0%)	13 (5.6%)	6 (2.8%)	13 (6.3%)	16 (6.1%)	2 (11%)	3 (2.7%)	1 (2.8%)	8 (9.5%)	1 (1.2%)
Separated	0 (0%)	2 (0.9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.9%)	0 (0%)	2 (2.4%)	1 (1.2%)
Widow	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Missing	20 (28%)	31 (13%)	68 (32%)	30 (15%)	1 (0.4%)	4 (21%)	37 (33%)	11 (31%)	7 (8.3%)	22 (27%)
Migrant*										
No	56 (79%)	158 (68%)	176 (82%)	145 (71%)	194 (74%)	16 (84%)	92 (81%)	28 (78%)	65 (77%)	77 (94%)
Yes	14 (20%)	74 (32%)	38 (18%)	45 (22%)	56 (21%)	3 (16%)	21 (19%)	8 (22%)	19 (23%)	5 (6.1%)
Missing	1 (1.4%)	0 (0%)	1 (0.5%)	15 (7.3%)	11 (4.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Occupation*										
Student or other	25 (35%)	86 (37%)	73 (34%)	55 (27%)	103 (39%)	7 (37%)	42 (37%)	13 (36%)	20 (24%)	30 (37%)
Unemployed	18 (25%)	89 (38%)	52 (24%)	69 (34%)	103 (39%)	6 (32%)	23 (20%)	11 (31%)	39 (46%)	28 (34%)
On disability	0 (0%)	0 (0%)	0 (0%)	2 (1.0%)	0 (0%)	1 (5.3%)	1 (0.9%)	0 (0%)	1 (1.2%)	0 (0%)
Employed	11 (15%)	35 (15%)	23 (11%)	34 (17%)	54 (21%)	3 (16%)	10 (8.8%)	1 (2.8%)	18 (21%)	10 (12%)
Missing	17 (24%)	22 (9.5%)	67 (31%)	45 (22%)	1 (0.4%)	2 (11%)	37 (33%)	11 (31%)	6 (7.1%)	14 (17%)

TABLE 1 (Continued)

Characteristic	Piacenza, N = 71 ¹	Parma, N = 232 ¹	Reggio emilia, N = 215 ¹	Modena, N = 205 ¹	Bologna, N = 261 ¹	Imola, N = 19 ¹	Ferrara, N = 113 ¹	Ravenna, N = 36 ¹	Forlì- cesena, N = 84 ¹	Rimini, N = 82 ¹
Living condition*										
Family of origin	39 (55%)	126 (54%)	127 (59%)	0 (0%)	180 (69%)	12 (63%)	52 (46%)	22 (61%)	60 (71%)	64 (78%)
Acquired family	6 (8.5%)	12 (5.2%)	11 (5.1%)	131 (64%)	30 (11%)	3 (16%)	5 (4.4%)	1 (2.8%)	7 (8.3%)	0 (0%)
Alone	0 (0%)	13 (5.6%)	2 (0.9%)	8 (3.9%)	16 (6.1%)	1 (5.3%)	6 (5.3%)	0 (0%)	5 (6.0%)	1 (1.2%)
Homeless	0 (0%)	2 (0.9%)	0 (0%)	2 (1.0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Residential	0 (0%)	16 (6.9%)	0 (0%)	1 (0.5%)	0 (0%)	0 (0%)	0 (0%)	1 (2.8%)	1 (1.2%)	0 (0%)
Other	9 (13%)	11 (4.7%)	8 (3.7%)	33 (16%)	35 (13%)	1 (5.3%)	19 (17%)	1 (2.8%)	7 (8.3%)	10 (12%)
Missing	17 (24%)	52 (22%)	67 (31%)	30 (15%)	0 (0%)	2 (11%)	31 (27%)	11 (31%)	4 (4.8%)	7 (8.5%)

Note: Categorical data: n (%); Continuous data: mean (SD).

* $p < .001$ in Chi-squared test or Kruskal-Wallis rank sum test.

of psychosis incidence, pathways to care, and clinical characteristics (Fett et al., 2019; Heinz et al., 2013; March et al., 2008). In fact, the distribution of modifiable and non-modifiable risk factors not only changes across countries or at the regional level, but also at the neighbourhood-level (O'Donoghue et al., 2016; Schofield et al., 2022). For example, in our sample educational levels were unevenly distributed across centres, with an overall high level. This might signal some difficulties of access to care by those with a lower socioeconomic level, even within a universal, accessible healthcare system. Thus, in order to reach a youth population with a high risk of psychosis, information campaigns and promotion of referrals should also be strengthened outside the school environment. Heterogeneity across departmental areas, in fact, may crucially depend on factors that are external to the mental health department, such as the efficacy of referrals and the pathways to care, or the knowledge regarding the availability of a specific programme for FEP. In addition, the assumption that the region has homogeneous application of criteria for access to care, and a similar bandwidth of resource allocation, may not entirely hold in clinical practice and should be further investigated (Starace et al., 2018). The present study has not examined the impact of staff resources on the detection of case and their entry into the mental healthcare system. Nonetheless, we have set the grounds for elaborating a robust method of ascertainment of FEP incidence to guide stakeholders on staffing allocation and resources planning (Kirkbride, 2015). In this regard, we did not observe a temporal trend in rising incidence of psychosis at the regional level, however, an increase in number of cases of psychosis due to the COVID-19 pandemic would likely require a modulation of resources (Jauhar et al., 2021).

Other limitations include that we did not collect data of individuals who refused care to minimize interference with routine clinical work. In addition, we did not seek to estimate the rate of subjects with FEP who were treated within other settings than the public DMH (e.g. the private sector or public health agencies outside the Emilia-Romagna region). Thus, the treated incidence estimates of FEP may approximate the true population values, and this prevents to some extent the generalization of our findings from the treated cohort to the general FEP population. However, this latter phenomenon may be marginal, as private practices are generally reluctant to engage with clients with early psychosis. Finally, this study does not distinguish individuals with prodromal schizophrenia, and between the treated incidence of FEP who had access to the RER-FEP program and those who were ineligible for the program (e.g. due to lack of language fluency, low IQ or psychosis due to substance misuse) and received TAU.

In conclusion, the treated incidence of FEP in the Emilia-Romagna regional public healthcare program was relatively high and varied across the different areas, but not according to the population density or time. Further detailed analyses of this data, informed by theory and prior knowledge, may allow examination of psychosocial factors influencing the onset of psychosis and may favour the elaboration of useful prediction models.

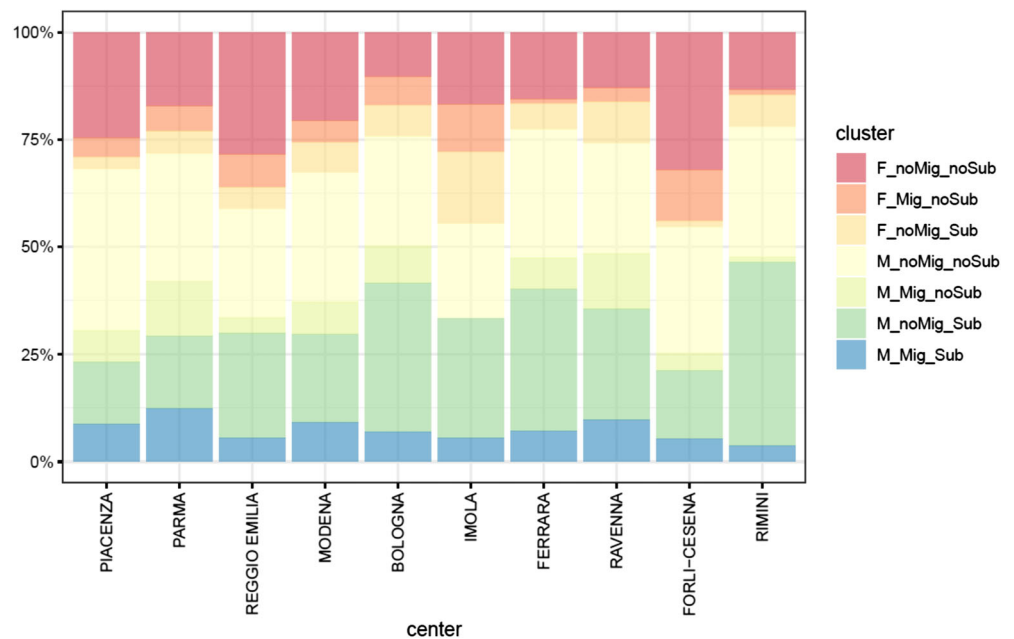
TABLE 2 Clinical characteristics, referrals and DUP.

	Piacenza, N = 71	Parma, N = 232	Reggio emilia, N = 215	Modena, N = 205	Bologna, N = 261	Imola, N = 19	Ferrara, N = 113	Ravenna, N = 36	Forlì- cesena, N = 84	Rimini, N = 82
Personality disorder*	4 (5.6%)	125 (54%)	83 (39%)	34 (18%)	67 (27%)	2 (11%)	57 (51%)	5 (16%)	8 (9.5%)	11 (13%)
Missing	0 (0%)	0 (0%)	1 (0.5%)	18 (8.8%)	17 (6.5%)	0 (0%)	1 (0.9%)	4 (11%)	0 (0%)	0 (0%)
Substance use*	19 (27%)	82 (36%)	77 (36%)	70 (37%)	121 (49%)	10 (53%)	56 (50%)	15 (47%)	19 (23%)	44 (54%)
Missing	0 (0%)	2 (0.9%)	1 (0.5%)	17 (8.3%)	15 (5.7%)	0 (0%)	1 (0.9%)	4 (11%)	0 (0%)	0 (0%)
HONOS_total*	12.92 (6.17)	23.32 (8.44)	17.35 (5.68)	15.80 (6.57)	13.36 (8.84)	14.11 (6.12)	14.58 (6.89)	14.97 (6.45)	18.23 (7.60)	19.21 (6.71)
<i>Subscales</i>										
Behaviour*	1.80 (2.10)	3.84 (2.53)	2.92 (2.12)	2.43 (2.05)	2.39 (2.60)	1.84 (1.26)	2.74 (2.15)	2.94 (1.97)	2.99 (2.53)	3.16 (2.54)
Impairment*	0.94 (1.23)	3.72 (2.02)	1.51 (1.31)	1.40 (1.44)	0.84 (1.33)	1.21 (1.36)	1.42 (1.24)	1.25 (1.23)	1.60 (1.48)	2.11 (1.41)
Psychological*	5.25 (2.42)	7.25 (2.62)	7.53 (2.51)	5.94 (2.61)	4.85 (3.27)	5.63 (2.99)	5.50 (2.50)	5.36 (2.52)	6.65 (2.25)	7.43 (2.54)
Social*	4.92 (3.06)	8.52 (4.01)	5.39 (2.55)	6.03 (3.06)	5.28 (3.92)	5.42 (2.22)	4.91 (3.55)	5.42 (3.50)	6.99 (3.71)	6.51 (2.83)
<i>Referral*</i>										
Self-referral	10 (18%)	20 (11%)	28 (17%)	17 (9.6%)	49 (23%)	3 (21%)	11 (12%)	8 (38%)	11 (15%)	4 (6.6%)
Primary care	7 (12%)	56 (30%)	57 (35%)	60 (34%)	56 (26%)	1 (7.1%)	27 (30%)	1 (4.8%)	23 (32%)	19 (31%)
Public hospital	20 (36%)	14 (7.6%)	30 (19%)	48 (27%)	69 (33%)	6 (43%)	35 (39%)	6 (29%)	31 (44%)	30 (49%)
Private health service	1 (1.8%)	54 (29%)	1 (0.6%)	2 (1.1%)	0 (0%)	0 (0%)	2 (2.2%)	1 (4.8%)	0 (0%)	0 (0%)
Other health service	4 (7.1%)	37 (20%)	26 (16%)	38 (21%)	18 (8.5%)	2 (14%)	8 (9.0%)	1 (4.8%)	1 (1.4%)	7 (11%)
Social service/policer/prison	1 (1.8%)	4 (2.2%)	3 (1.9%)	4 (2.3%)	3 (1.4%)	0 (0%)	0 (0%)	1 (4.8%)	1 (1.4%)	0 (0%)
Other referral	13 (23%)	0 (0%)	16 (9.9%)	8 (4.5%)	17 (8.0%)	2 (14%)	6 (6.7%)	3 (14%)	4 (5.6%)	1 (1.6%)
Missing	15 (21%)	47 (20%)	54 (25%)	28 (14%)	49 (19%)	5 (26%)	24 (21%)	15 (42%)	13 (15%)	21 (26%)
DUP (months)*	3.14 (3.65)	7.83 (7.03)	16.69 (18.11)	6.67 (10.03)	7.74 (9.55)	13.16 (21.93)	4.40 (3.80)	9.50 (8.89)	9.47 (16.19)	4.63 (3.44)
N/No. obs. % not missing	-	-	206/215 95.81%	176/205 85.85%	231/261 88.51%	-	103/113 91.15%	32/36 88.89%	75/84 89.29%	-

Note: Categorical data: n (%); Continuous data: mean (SD).

* $p < .001$ in Chi-squared test or Kruskal-Wallis rank sum test.

FIGURE 3 Distribution of user clusters across centres. F, female; M, male; Mig, migrant; noMig, not migrant; Sub, substance use and noSub, no substance use.



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CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflict of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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