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Pathways to care: Source of referral at first-episode psychosis, a cross-country comparison between Bologna and South London

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ABSTRACT

Objectives: Pathways to Care (PtC) are useful indicators of how patients access mental healthcare, especially in the context of first-episode psychosis (FEP). We explored how PtC: source of referral, is associated with patients' characteristics and clinical presentation and assessed the cross-country differences of the PtC predictors between South London and Bologna.

Methods: This study included 427 FEP individuals in the context of the European Union Gene-Environment Interactions (EU-GEI) study. We performed multinomial logistic regression to test the associations between our outcome variables (PtC) and the independent study variables.

Results: In London, patients were more likely to be referred by GPs or specialists, while in Bologna, most patients followed the emergency route. Despite the study centre differences, older patients were more likely to be referred by GPs; patients referred informally and via specialist services were more likely to be single. Compared with emergency referrals, patients referred by GPs and specialists experienced a longer DUP. We found insufficient evidence of an association between symptoms profile and PtC.

Conclusions: PtC characteristics of FEP patients were associated with several sociodemographic and DUP in both study centres. Our results highlight the importance of social networks and social services and public engagement, and public health initiatives (such as psychoeducation in schools and leisure centres) in easing help-seeking behaviours.

1. Introduction

Psychotic disorders present with a constellation of behavioural, emotional and cognitive signs and symptoms, and they are the most impactful mental disorders in terms of disability and quality of life. These disorders frequently constitute a barrier to productivity and social participation. An early diagnosis is crucial for the prompt establishment of multi-professional treatment plans and for reducing psychosis-related consequences and risks. Pathways to Care (PtC), specifically, source of referral are useful indicators of help seeking and how patients access mental health care, especially in the context of a first-episode psychosis (FEP) (Hodgekins et al., 2017). Studies about them have been increasingly used in FEP research to understand the barriers to access to mental health care (Ferrari et al., 2016). They are defined as "*the sequence of*

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contacts with individuals or organisations determined by the efforts of the ill person, and of his social network, to seek care, and also the care provided following these efforts" (Rogler et al., 1993).

There are several lines of evidence that are developing because of the increasing attention to PtC. The first one is that in the context of mental health services, particularly regarding psychotic disorders, the trajectories of access to care are widely variable and may include several agencies outside the health services, such as school institutions and the justice system (Singh and Grange, 2006). In addition, non-voluntary and negatively experienced contacts (i.e., emergency/urgency services, law enforcement, involuntary admission to hospital) are frequent and may result in subsequent poor treatment compliance (Anderson et al., 2014). Features of PtC, like delays in help-seeking but also in the timing of the diagnosis, may lead to an extension of the Duration of Untreated Psychosis (DUP) (Bechard-Evans et al., 2007). DUP has been consistently inversely correlated with poor clinical and functional outcomes (Norman et al., 2005; Perkins et al., 2005). Many previous studies found no evidence that socio-economic factors are associated with a specific PtC (Anderson et al., 2010), but sociodemographic characteristics such as ethnicity have been shown to be strongly associated with involuntary admission (Oduola et al., 2019). To our knowledge, only a few studies have examined clinical correlations of PtC. From the available research, less severe symptoms and better premorbid functioning are reported to be associated with referral to psychiatric care by general practitioners (Chesney et al., 2016). Moreover, the associations between PtC, DUP and poor clinical and functional outcomes may be impacted by other factors such as cultural and healthcare systems. To date, much of our understanding on these issues have been obtained from single-site or single-country studies, limiting our understanding of whether PtC and DUP estimates are similar or different in different samples and settings according to sociodemographic characteristics. It is, therefore, essential to understand the factors underlying the wide variability of PtC in patients at psychotic onset in different settings and samples.

The aims of this study – conducted in the context of the EU-GEI project in Bologna and South-East London – were: (1) to describe the PtC at first presentation to services for psychosis, (2) to explore how PtC are associated with patients' characteristics, clinical presentation, DUP, and assess the cross-country differences.

2. Materials and methods

This study was carried out in the context of the European Network of National Schizophrenia Networks Studying Gene-Environment Interaction (EU-GEI) project funded by the European Community under the FP7 grants (grant agreement no. HEALTH-F2-2009-24190) across six countries. Data were collected from May 2010 to December 2015, coordinated by Jim van Os of Maastricht University. This is the first large-scale multicentre European study that aims to investigate extensively the genetic, clinical and environmental risk factors and their interactions that contribute to the onset of schizophrenia and correlate with the severity and outcomes of schizophrenia (Gayer-Anderson et al., 2020). We report data from two study sites, i.e., South-East London, UK and Bologna, Italy, which were the EU-GEI sites where data on PtC were collected.

2.1. Study setting

Each Local Health Unit in Italy includes one Mental Health Department, which provides comprehensive psychiatric care for the population. It manages the local network of services on a unitary basis, and these must provide at least the minimum set of services required by national policy documents (Gazzetta Ufficiale, 2023). Italian community mental health centres are universal, tax-funded, and fully integrated within the national health service. They espouse a public health approach, have liberal regulations about involuntary admissions, and offer a minimum set of services provided by a multi-professional team. Integration of mental health care in primary care and rehabilitation through work and employment are priority issues on the national psychiatric agenda (Berardi et al., 2014; Lora et al., 2014). Access to community mental health services (CMHS) is free and open to the whole population, with and without a residence permit; patients can access primary care services even without professional referrals based on the current mental health law and regulations(Tarricone et al., 2012).

Mental health services in the UK are free at the point of use under the National Health Service provision (DHSC, 2022). The South London & Maudsley (SLaM) NHS Foundation Trust, one of the largest mental health providers in Europe, serves a population of over 1.2 million people across four boroughs in south-east London (Stewart et al., 2009). As well as specialist services, SLaM provides a wide range of adult mental health services both in hospital inpatient and community-based services, including those presenting to psychiatric liaison services in accident and emergency departments. Patients can access SLaM services, including community mental health teams, via a range of routes, including General Practitioners (GPs), other health professionals or Accident & Emergency (A&E) etc.

The southeast London participants in this study were residents of the London boroughs of Lambeth and Southwark, which have large minority ethnic populations (Office for National Statistics, 2011). The Bologna participants were residents in Bologna municipality, with around 12 % of ethnic minorities (Censimento, 2011).

All patients with a suspected diagnosis of a first psychotic episode were identified in the Community Mental Health Centres (CMHCs) of the Bologna Mental Health and Pathological Addictions Department and all adult services at the South London & Maudsley (SLaM) NHS Foundation Trust, South-East London. At both sites, researchers made regular contacts with all secondary and tertiary mental health services/professionals and checking clinical records to identify potential cases. The diagnostic evaluations mainly took place between May 2010 and April 2015. The ascertainment period of cases was 12 months in London and 48 months in Bologna. At each site, a psychiatrist or academic experienced in epidemiology research supervised the local team, which was centrally trained to minimise non-differential recruitment bias in the different healthcare systems. Following the assessment, subjects who met the criteria for inclusion in the study were required to sign an informed consent form. The inclusion criteria have been described in previous EU-GEI studies (Jongsma et al., 2018; Gayer-Anderson et al., 2020). In summary, patients were included if they were:

1. Assessed and met diagnostic criteria for FEP according to the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision [ICD-10], codes F20-F33*).
2. Aged between 18 and 64 years.
3. Resident with the study catchment area.

Patients meeting the following criteria were excluded from the study: (a) previous contact with psychiatric services for psychosis; (b) psychotic symptoms with evidence of organic cause, including (c) transient psychotic symptoms on a toxic basis.

2.2. Ethical approval

All participants who agreed to take part in the case-control study provided informed, written consent following a full explanation of the study. Ethical approval for the study was provided by relevant local research ethics committees in each of the study sites (Jongsma et al., 2018).

2.3. Data

Data on age, gender, and sociodemographic characteristics (employment, schooling, marital status, housing situation) were collected using a modified version of the Medical Research Council

Sociodemographic Schedule (Mallett, 1997). When lacking, these data were integrated through information obtained from the Sistema Informatico Territoriale (SIT), an electronic register used in the Bologna Mental Health Department and its province, and the SLaM Clinical Records Interactive Search (CRIS) system (Stewart et al., 2009) which provides fully anonymised access to all SLaM electronic clinical records. Ethnicity was self-reported. For the purpose of multivariable regressions analysis, we dichotomised sociodemographic variables as follows: ethnicity (white vs non-white ethnic group); living circumstances (alone vs other); employment status (unemployed vs employed); relationship status (single vs in a relationship).

DUP was defined as the period between the onset of psychotic symptoms and first contact with services (Register-Brown et al., 2014). It was captured using the Nottingham Onset Schedule (Singh et al., 2005). Data on DUP was dichotomised into short vs long, using a 12-week cut-off, identified in the literature as the optimal DUP limit (Miglietta et al., 2020).

Diagnosis was made using the OPerational CRITeria (OPCRIT) system (McGuffin et al., 1991) by trained interviewers. OPCRIT is an instrument which uses a checklist of psychopathology items to generate diagnoses for psychotic and affective disorders. The absence or presence of symptoms was identified using the OPCRIT checklist, and the 26 specific items for psychotic disorders were grouped into three symptom domains: (a) negative symptoms, (b) positive symptoms, and (c) disorganisation symptoms. This grouping was made in accordance with the literature (Cardno et al., 1996; Quattrone et al., 2019).

We operationalised pathways to care variables, including the source of referral, using the Personal and Psychiatric History Schedule [PPHS] (WHO, 1996) and in keeping with previous studies (Morgan et al., 2005a; Oduola et al., 2019). Source of referral in PPHS comprised seven categories: 1 = General practitioner; 2 = Nurse, other healthcare services/ professionals, addictions services, or social worker; 3 = Accident and Emergency; 4 = Police; 5 = Courts; 6 = Prison; 7 = informal (e.g. family, self). Due to small sample sizes in some of the categories, we collapsed the source of referral as follows: General practitioner, Emergency (Accident and Emergency), Specialist (Nurse, other health professionals, or social worker), Criminal justice system (police, courts, prison, law enforcement), Informal (family, self-referral).

2.4. Statistical analysis

All the statistical analysis was performed using Stata version 15 (StataCorp, 2017). To begin with, we carried out descriptive statistics using chi-squared, t, and the Wilcoxon-Mann-Whitney tests as appropriate to compare study variables by study centre (i.e., Bologna and London). Then, using combined data for South-East London and Bologna, we first addressed missing data through multiple imputations by fully conditional specification using chained equations (Sterne et al., 2009). We performed multinomial logistic regression to test the associations between our outcome variables (PtC: source of referral, [using the emergency route as the reference group]) and the independent study variables (i.e., sociodemographic, socioeconomic, OPCRIT symptoms, DUP). We fitted multinomial logistic regression models for (a) source of referral and sociodemographic characteristics and DUP, (b) source of referral and OPCRIT symptoms, then adjusted for our a priori confounders (age, gender, ethnicity, study centre and DUP).

3. Results

During the study period, a total of 427 patients with FEP presented to services: 262 (61.4 %) in South-East London and 165 in Bologna (38.6 %). The mean age was 33.5 (SD; 11.3) years. A shorter DUP (i.e., <12 weeks) was experienced by 246 (57.9 %) patients. Regarding the pathways to care, the sample was distributed as follows: 148 (34.6 %) made contact via the emergency services, 143 (33.5 %) patients were referred informally, 117 (27.9 %) patients were referred via primary care, and fewer patients (15.2 %) were referred via specialist services. Positive symptoms were experienced by 393 (92.0 %) patients, negative symptoms by 146 (34.2 %) patients and disorganisation by 148 (34.7 %) patients. The sociodemographic and clinical characteristics of the sample are summarised by the study centre in Table 1.

3.1. Comparison between South-East London and Bologna

In South-East London, patients were more likely to be of non-white ethnicity (n = 198, 75.6 %), have a migrant status (n = 123, 52.1 %), be unemployed (n = 127, 56.2 %), and lived alone (n = 72, 28.9 %) than in Bologna (n = 33, 20.0 %; n = 48, 29.1 %; n = 48, 31.0 % and n = 28, 17.8 % respectively). However, patients in Southeast London were less likely to be single (n = 129, 53.7 %) than in Bologna (n = 107, 68.2 %). There were no clear differences between the two study centres regarding age, gender, and education.

In terms of PtC (i.e., source of referral), a greater proportion of patients were referred via primary care (n = 89, 34.0 %) and specialist services (n = 51, 19.5 %) in South-East London compared with those in Bologna (n = 28, 17.7 % and n = 13, 8.2 %, respectively). Conversely, the proportion of patients referred by emergency services was considerably higher in Bologna (n = 66, 41.7 %) compared with South-East London (n = 82, 31.3 %). The two study centres did not differ for informal referrals (n = 96, 36.6 % in South-East London vs n = 47, 29.7 % in Bologna; $\chi^2 = 2.08$; $p = 0.14$).

The DUP was generally longer in South-East London compared with Bologna (South-East London median = 12.3, interquartile range = 3.2–53.8) vs Bologna (median = 4.0, interquartile range = 1.0–14.0; t = 31.1; $p < 0.001$) weeks. Regarding clinical presentation, the OPCRIT checklist showed that patients from South-East London presented with more positive symptoms. However, a greater proportion of patients from Bologna presented with negative, disorganised, depressive, and manic symptoms compared with those from South-East London (Table 1).

3.2. Associations of source of referral with sociodemographic variables

We found that patients referred via primary care were more likely to be older (adj. OR = 1.01, 95%CI = 0.99–1.05), experienced longer DUP (adj. OR = 2.41; 95 % CI: 1.25–4.66) *(vs short DUP)* and less likely to be from the Bologna site (adj. OR = 0.24; 95 % CI: 0.11–0.53) *(vs London site)*. We observed that patients of non-white ethnic backgrounds were twice as likely, and those with a migrant status were 1.14 times more likely to be referred via primary care. However, these associations did not hold after controlling for confounders (Table 2).

We found strong evidence that patients referred via an informal route were more likely to be single (adj. OR = 2.29; 95%CI:1.20–4.37) and less likely to be from the Bologna site (adj. OR = 0.24; 95%CI:0.12–0.49), compared with those in a relationship and the London site respectively, (Table 2). Regarding patients referred via specialist route, they were more likely to be single (adj. OR = 2.70; 95%CI: 1.19–4.44) *(vs in a relationship)* and were less likely to be from the Bologna site (adj. OR = 0.17; 95%CI: 0.06–0.42), *(vs London site)* (Table 2).

3.3. Source of referral and duration of untreated psychosis

We found that in the unadjusted and adjusted analysis, patients referred to psychiatric services by primary care (adj. OR = 2.41, 95%CI = 1.25–4.66) or by a specialist (adj. OR = 2.13, 95%CI = 1.03–4.39) were more likely to experience a longer DUP *(vs short DUP)*. There was no evidence of associations between informal referral routes and DUP (Table 2).

3.4. Associations of source of referral with OPCRIT symptoms

We found that patients experiencing positive symptoms (OR = 4.14, 95%CI = 1.12–15.19) were more likely to be referred by primary care,

Table 1
Comparisons between London and Bologna sociodemographic and clinical characteristics.

	Southeast London, $n = 262$ (%)	Bologna, $n = 165$ (%)	Chi. Sq./t-test (df), p-value
Sex			0.11 (1), 0.73
Male	141 (53.8)	86 (52.1)	
Female	121 (46.2)	79 (47.9)	
Age, mean (sd) years	34.2 (11.2)	33.0 (11.2)	0.004 (1), 0.98
Ethnicity			29.29 (1), <0.001
White British/White	64 (24.4)	132 (80.0)	
Other	198 (75.6)	33 (20.0)	
Migrant status[a]	123 (52.1)	48 (29.1)	21.05, (1), <0.001
Marital status[b]			8.16 (1), 0.004
Single	129 (53.7)	107 (68.2)	
Other (in relationship)	111 (46.3)	50 (31.8)	
Highest level of education[c]			0.12 (5), 0.72
School – no qualification	54 (31.9)	3 (1.9)	
Other school – with qualification	33 (19.5)	48 (31.0)	
Tertiary	41 (24.3)		
Vocational	17 (10.1)	14 (9.0)	
Higher - undergraduate	18 (10.6)	29 (18.7)	
Higher - postgraduate	6 (3.6)	1 (0.6)	
Employment status[d]			23.01 (5), <0.001
Full-time employee	30 (13.3)	46 (29.7)	
Part-time employee	7 (3.1)	10 (6.5)	
Self-employed	7 (3.1)	2 (1.3)	
Economically inactive	28 (12.4)	9 (5.8)	
Unemployed	127 (56.2)	48 (31.0)	
Student	27 (11.9)	39 (25.2)	
Living circumstances[e]			4.92 (6), 0.02
Living alone	72 (28.9)	28 (17.8)	
Living alone with children	23 (9.2)	n/a	
Living with partner	18 (7.2)	14 (8.9)	
Living with partner and children	12 (4.8)	18 (11.5)	
Living with parents	48 (19.3)	62 (39.5)	
Living with other family members	31 (12.5)	13 (8.3)	
Other	45 (18.1)	22 (14.0)	
Pathways to care: source of referral			
Primary care	89 (34.0)	28 (17.7)	12.97 (1), <0.001
Informal	96 (36.6)	47 (29.7)	2.08 (1), 0.14
Emergency	82 (31.3)	66 (41.7)	4.73 (1), 0.02
Specialist	51 (19.5)	13 (8.2)	9.63 (1), 0.002
Criminal justice system	40 (15.3)	4 (3.0)	16.07 (1), <0.001
Diagnosis (OPCRIT)[f]			
Affective psychosis	16 (6.2)	41 (24.8)	22.01 (3), <0.001
Non-affective psychosis	177 (66.3)	124 (75.2)	
Psychosis NOS	71 (27.5)	0	
Duration of untreated psychosis (DUP)			
Median (IQR) weeks	12.3 (3.2–53.8)	4 (1–14)	31.1 (1), <0.001
OPCRIT symptoms			
Positive	252 (96.2)	141 (85.4)	16.80 (1), <0.001
Negative	62 (24.0)	84 (50.9)	32.47 (1), <0.001
Disorganisation	62 (24.0)	86 (52.1)	35.23 (1), <0.001
Depression	180 (69.8)	146 (88.5)	19.76 (1), <0.001
Mania	77 (29.8)	121 (73.3)	76.98 (1), <0.001

List of abbreviations:
Missing values:
London: a = 26 patients; b = 22 patients; c = 93 patients; d = 36 patients; e = 13 patients; f = 4 patients.
Bologna: a = n/a; b = 8 patients; c = 14 patients; d = 11 patients; e = 8 patients; f = 4 patients.

while patients presenting with symptoms of disorganisation (OR = 0.42, 95%CI = 0.25–0.78) or mania (OR = 0.47, 95%CI = 0.26–0.85) were less likely to be referred via this route, compared with patients without these symptoms (Table 3). However, these associations were attenuated when we accounted for potential confounders (Table 3). For informal referral, we observed that patients with depressive symptoms had a reduced likelihood of being referred informally; however, these associations did not hold in the fully adjusted model. Finally, the unadjusted analyses showed that patients referred via the specialist services route were significantly less likely to experience negative, disorganisation or mania symptoms. However, the strength of these associations diminished when we adjusted for confounders (Table 3).

4. Discussion

4.1. Main results

The most important differences that we found between London and Bologna in the pathway to care are the higher proportion of patients referred by the emergency route in Bologna and the higher proportions of GP and specialist routes in London. This may reflect how services are organised at the two sites. For instance, in the UK, GPs are considered the gatekeepers to specialist healthcare including psychiatric care. Hence, initial help-seeking for psychosis from GPs is expected and encouraged, although patients can also access psychiatric care via A&E. In Bologna, Basaglia's psychiatric law allows self-referral or health and social services referrals to psychiatric services. Furthermore, the population density and availability of services could also be important factors when making sense of our findings. For example, at the time of our study, in Bologna, the population density was 2744 per square km and 6162 per square km in SE London, and access to mental healthcare varies. According to the EU Health Programme Access to Mental Health Care in Europe - Consensus Paper, there are 7.8 psychiatrists, 2.6 psychologists, and 19.3 nurses per 100,000 people in Italy compared with 14.6, 12.8 and 67.3 per 100,000 people, respectively, in the UK (Barbato et al., 2016).

Regarding sociodemographic correlations of PtC, our analysis showed that older patients, those who experienced longer DUP, were more frequently referred by GPs. Patients from Bologna were less likely to be referred by GP after adjusting for all potential confounding variables. Patients referred via the informal route were more likely to be single and less likely to be from Bologna. Finally, there was substantial evidence that patients who accessed specialist care were more likely to be single, had a longer DUP and were less likely to be from Bologna.

Considering clinical presentation. We did not find strong evidence of an association between symptom clusters and specific referral sources after potential confounders were considered.

4.2. Comparison with previous evidence

In the literature, the prevalence of referral sources is variable. Our site-specific findings are in accordance with a recent Italian study that showed a prevalence of emergency/urgency services as an entry point to psychiatric care (Miglietta et al., 2020) and with a study from England which found that a majority of patients were referred by GP (Bhui et al., 2014). The fact that the informal route was the second most represented highlights the crucial role of family members as referral sources to mental health care, especially in the Italian social framework. About the evidence from other areas of the world, a recent study from the USA

Table 2
Unadjusted and adjusted odds ratios of associations between source of referral and sociodemographic characteristics and DUP.

	Source of referral					
	Primary care		Informal		Specialist	
Variable	Unadjusted RR (95%CI)	Adjusted RR (95%CI)	Unadjusted RR (95%CI)	Adjusted RR (95%CI)	Unadjusted RR (95%CI)	Adjusted RR (95%CI)
Age	**1.02 (1.00–1.05)**	**1.01 (0.99–1.05)**	0.98 (0.96–1.00)	0.98 (0.95–1.01)	1.00 (0.97–1.03)	0.99 (0.96–1.03)
Sex						
Female	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Male	0.65 (0.36–1.15)	0.52 (0.27–1.01)	0.91 (0.53–1.54)	0.66 (0.36–1.21)	1.00 (0.53–1.88)	0.65 (0.31–1.36)
Ethnicity						
White	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Non-White	**2.83 (1.54–5.12)**	1.45 (0.68–3.06)	**2.33 (1.35–4.01)**	1.41 (0.71–2.80)	**3.97 (2.03–7.75)**	1.78 (0.78–4.08)
Migrant status[a]						
Non-migrant	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Migrant	**1.14 (1.04–3.43)**	1.46 (0.74–2.87)	1.14 (0.66–1.99)	1.05 (0.56–1.96)	1.58 (0.82–3.05)	1.30 (0.62–2.74)
Living circumstances						
Other	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Alone	1.70 (0.87–3.32)	1.24 (0.57–2.68)	0.89 (0.46–1.74)	0.79 (0.37–1.70)	1.58 (0.75–3.31)	1.21 (0.51–2.84)
Employment status						
Other	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Unemployed	1.23 (0.67–2.25)	0.81 (0.40–1.63)	1.18 (0.68–2.06)	0.93 (0.49–1.75)	**2.30 (1.19–4.44)**	1.40 (0.66–2.97)
Relationship status						
In a relationship	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single	0.99 (0.55–1.78)	1.67 (0.83–3.34)	1.65 (0.96–2.85)	**2.29 (1.20–4.37)**	1.68 (0.87–3.25)	**2.70 (1.24–5.86)**
DUP						
<12 weeks	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
≥12 weeks	**3.11 (1.69–5.71)**	**2.41 (1.25–4.66)**	1.46 (0.82–2.59)	1.22 (0.65–2.27)	**3.08 (1.58–5.98)**	**2.13 (1.03–4.39)**
Site						
London	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Bologna	**0.20 (0.11–0.38)**	**0.24 (0.11–0.53)**	**0.26 (0.15–0.46)**	**0.24 (0.12–0.49)**	**0.11 (0.05–0.25)**	**0.17 (0.06–0.42)**

RR: relative risk; 95%CI: 95 % confidence interval; DUP: duration of untreated psychosis.
Adjusted for age, gender, ethnicity, study centre and DUP.
[a] Migrant status was substituted to ethnicity to estimate adjusted RR for migrants.

Table 3
Unadjusted and adjusted odds ratios of associations between source of referral and OPCRIT symptoms domains.

	Source of referral					
	Primary care		Informal		Specialist	
Symptoms domains	Unadjusted RR (95%CI)	Adjusted RR (95%CI)[a]	Unadjusted RR (95%CI)	Adjusted RR (95%CI)[a]	Unadjusted RR (95%CI)	Adjusted RR (95%CI)[a]
Positive	**4.14 (1.12–15.19)**	2.10 (0.54–8.13)	1.69 (0.69–4.10)	1.04 (0.41–2.64)	0.98 (0.37–2.57)	0.39 (0.13–1.16)
Negative	0.66 (0.36–1.19)	1.03 (0.54–1.97)	0.48 (0.28–0.84)	0.69 (0.38–1.25)	**0.42 (0.21–0.83)**	0.73 (0.34–1.54)
Disorganisation	**0.42 (0.22–0.78)**	0.69 (0.35–1.37)	0.67 (0.39–1.15)	0.87 (0.48–1.58)	**0.39 (0.19–0.78)**	0.66 (0.30–1.44)
Depression	0.58 (0.25–1.13)	0.80 (0.36–1.81)	**0.46 (0.21–0.84)**	0.66 (0.31–1.37)	0.51 (0.23–1.15)	1.00 (0.41–2.41)
Mania	**0.47 (0.26–0.85)**	0.97 (0.47–2.00)	1.02 (0.60–1.74)	2.04 (1.06–3.94)	**0.45 (0.23–0.88)**	1.24 (0.56–2.76)

RR: relative risk; 95%CI: 95 % confidence interval.
[a] Adjusted for age, gender, ethnicity, study centre and DUP.

highlighted a prevalence of emergency referral (Chesney et al., 2016), a finding consistent with a previous systematic review that showed that six of the seven North American studies examined found that emergency services were the referral source for the largest proportion of patients (Anderson et al., 2010). The findings regarding the Asian countries are more variable and less consistent, with a high prevalence of various informal referral sources (e.g. traditional healers and families) (Al Fayez et al., 2017; Nishii et al., 2010).

Regarding the sociodemographic and socioeconomic variables associated with PtC, another study regarding patients with FEP in Singapore found an association between age and referral through primary care, but inverse to that found by us (Chesney et al., 2016). Being male has been correlated with a decreased likelihood of referral by a GP and inversely to an increased probability of making first contact with the emergency department (Archie et al., 2010; Morgan et al., 2005b), but we didn't find any association between gender and PtC.

Non-white ethnicity was associated with all the sources of referral compared with the emergency route. However, the strength of the association diminished when we adjusted for confounding variables. There are many studies showing that minority ethnic groups experience more frequently "adverse" trajectories to mental health care (Anderson et al., 2014; Bhui et al., 2003; Oduola et al., 2019). Our finding about the association between relationship status and access through specialist services and informal routes may reflect the mode of onset of psychosis. An acute onset of psychosis might alarm other healthcare professionals, family members, partners, or co-habitants, as suggested in a recent paper (Oduola et al., 2021), and result in prompt help-seeking and access to mental health services.

The body of literature regarding the clinical determinants of PtC is much less consistent. Less severe symptoms and better functioning correlate with an increased likelihood of being referred by a GP (Chesney et al., 2016). In our study, we found that patients experiencing positive symptoms were more likely to be referred by primary care. This evidence was attenuated when we adjusted for confounders. These findings are hard to explain. It could be that mild to moderate positive symptoms with limited effect on behaviour do not prompt evaluation in an emergency context. In fact, initiating help-seeking has been inversely associated with positive symptom severity in several studies (Kaminga et al., 2020; O'Callaghan et al., 2010). It has also been pointed out that an initial presentation with psychosis-unrelated complaints such as

depression, anxiety, and somatic concerns is common in FEP (Kvig et al., 2017). Patients not experiencing severe positive symptoms and perhaps an insidious onset could start help-seeking conduct via entry points such as private specialists, addiction services, clinical psychology services or GPs. Moreover, we found that patients with mania were more likely to access through informal routes. Symptom recognition is a predictor of help-seeking not only in psychiatric illnesses (Smith et al., 2005), and lack of awareness of symptoms are important determinants of help-seeking among first-episode psychotic patients (Chiang et al., 2005). Insight impairment is common in patients with manic symptoms (Aspiazu et al., 2010), and thus help-seeking could be more easily prompted by family members. We found insufficient evidence of associations between negative symptoms and specialist referral; disorganisation and primary care or specialist referral; depression and informal referral; or mania and primary care and specialist referral.

Finally, regarding the association between PtC and DUP, we found that patients referred to psychiatric services by primary care and specialist routes more frequently experienced a longer DUP. This finding has been replicated several times in the literature (Anderson et al., 2014; Bhui et al., 2014; Oduola et al., 2019) and could be correlated to what has been previously underlined, pointing to the fact that symptoms not immediately associated with psychosis, such as anxiety and somatic concerns, could determine the initiation of the first help-seeking behaviours in patients with more insidious onset, thus causing diagnostic difficulties in general practitioners (Kvig et al., 2017). The importance of this is highlighted in the evidence that, conversely, emergency referral which is associated with a reduced DUP, nevertheless points to psychiatric service disaffection and disengagement (Anderson et al., 2014).

4.3. Methodological considerations

The sample size and the diverse social framework of the catchment areas are strengths of this work, particularly regarding the generalizability of the findings. The use of multiple imputations to address missing data is another strength. In addition, although several studies have assessed the impact of sociodemographic variables on pathways to care, very few have focused on the effect of clinical variables. To our knowledge, this is the first study to examine the association between specific symptom clusters and pathways to care. Furthermore, the Bologna Mental Health and Pathological Addictions Department and SLAM are the main mental health providers at both study sites. People presenting with major mental health issues such as psychosis tend to present to specialist mental health services directly or are referred by their GP, other healthcare professionals or emergency department, as private sector provision is minimal. This means that FEP cases and PtC data in our study can be considered complete case ascertainment, and the likelihood of selection bias is minimal. The present work has some limitations, the main one being the partial analysis of the pathways undertaken by the patients prior to their presentation to mental health services. Our data collection was limited to the identification of the last referral source, thus preventing the evaluation of the first contact and the quality and number of intermediate nodes of the pathways to care. In addition, the assessment of symptoms by OPCRIT allowed the evaluation of their presence/absence but not their severity. Furthermore, OPCRIT does not cover some relevant aspects of negative symptoms (passive social withdrawal, lack of motivation, difficulties in abstract/symbolic thinking), leading to a potential underestimation of this symptom cluster (Quattrone et al., 2019). While we compared and adjusted for sociodemographic factors between the two sites, it is possible that our results may still be confounded by unmeasured factors, such as socioeconomic status and previous service use for other mental health difficulties.

5. Conclusions

Pathways to care of people expereincing FEP were found to be correlated with several sociodemographic and clinical variables in both centres, despite local differences in health services organisations. These results highlight the importance of individual sociodemographic and clinical characteristics in shaping the pathway to care (social network, social services, informal sector, primary care). Furthermore, public engagement and public health initiatives targeted at non-health professionals (such as psychoeducation in school and leisure centres) could play an important role in easing help-seeking behaviours. Finally, further training for general practitioners and other healthcare professionals on the issues of psychotic disorders, particularly in recognising non-positive symptoms and their signs, could significantly shorten the latency of referral to mental health services during the first episode of psychosis. One possible approach could be a shift toward pragmatic screening thresholds that are sensitive to the prodromal context of the early development of psychosis, which are often less noticeable (e.g. social withdrawal, isolation, anxiety, or depression) when assessing FEP patients.

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CRediT authorship contribution statement

Sherifat Oduola: Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Giuseppe D'Andrea:** Conceptualization, Formal analysis, Methodology, Writing – review & editing. **Danilo Smimmo:** Conceptualization, Writing – original draft, Writing – review & editing. **Marco Menchetti:** Conceptualization, Supervision, Writing – original draft, Writing – review & editing. **Domenico Berardi:** Conceptualization, Funding acquisition, Writing – review & editing. **Roberto Muratori:** Conceptualization, Funding acquisition, Writing – review & editing. **Robin Murray:** Conceptualization, Funding acquisition, Methodology, Writing – review & editing. **Marta Di Forti:** Conceptualization, Funding acquisition, Writing – review & editing. **Fabio Lucchi:** Conceptualization, Funding acquisition, Writing – review & editing. **Craig Morgan:** Conceptualization, Funding acquisition, Methodology, Writing – review & editing. **Ilaria Tarricone:** Conceptualization, Funding acquisition, Methodology, Writing – review & editing.

Declaration of competing interest

None.

Data availability

No additional data are available.

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