# **Review Article**

# The incidence of psychotic disorders in the Republic of Ireland: a systematic review

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# Abstract

**Objectives:** Despite a substantial epidemiological literature on the incidence of psychotic disorders in Ireland, no systematic review has previously been undertaken. Such evidence can help inform understanding of need for psychosis care.

**Methods:** We conducted a prospectively registered systematic review (PROSPERO: CRD42021245891) following PRISMA guidelines. We searched four databases (Medline, PsycInfo, Web of Science, Embase) for papers containing incidence data on non-organic psychotic disorders, in people 16–64 years, published between 1950 and 2021 in the general adult population. We conducted duplicate screening, risk of bias assessments, and extracted data to a standardised template. We undertook a narrative synthesis for each major diagnostic outcome. Random effects meta-analyses were conducted for comparisons with  $\geq 5$  incidence rates.

**Results:** Our search yielded 1975 non-duplicate citations, of which 23 met inclusion criteria, containing incidence data ascertained between 1974 and 2016 (median study quality: 5/8; interquartile range: 4–6). Incidence of all psychotic disorders (N = 4 studies) varied from 22.0 (95% CI: 17.3–28.0) in Dublin to 34.1 per 100,000 person-years (95%CI: 31.0–37.5) in Cavan and Monaghan. The pooled incidence of schizophrenia (N = 6 studies, N = 8 settings) was 20.0 per 100,000 person-years, though with imprecision around this estimate (95%CI: 10.6–37.5;  $I^2$ : 97.6%). Higher rates of most outcomes were observed in men. There was consistent evidence of raised rates in more deprived and fragmented social environments, but no clear pattern by rural-urban status.

**Conclusions:** Patterns of incidence of psychotic disorders in Ireland are broadly consistent with the wider literature from the Global North. Findings could help identify populations at higher risk of psychosis in Ireland.

Keywords: Systematic review; incidence; epidemiology; psychotic disorders; Ireland

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# Introduction

Psychotic disorders are associated with substantial psychiatric and physical morbidity (Firth et al., 2019), negative social outcomes and premature mortality (Hjorthøj et al., 2019; Laursen 2011), and require early intervention to reduce the risk of these deleterious outcomes. A substantial body of evidence suggests that the longer people go without treatment for psychosis (socalled 'duration of untreated psychosis' [DUP]) the worse these outcomes become (Csillag et al., 2018; Marshall et al., 2005). This has led to the development of Early Intervention in Psychosis [EIP] services (McGorry et al., 1996), which provide early, multidisciplinary care for people experiencing psychosis for the first time, founded upon evidence-based treatments (Csillag et al., 2018). Treatments offered in EIP services often include pharmacological intervention, cognitive behavioural therapy, physical health monitoring and physical health interventions, supported education/employment programmes, family therapy and carer support.

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Randomised controlled trials [RCTs] have demonstrated that EIP care over treatment as usual results in beneficial functional and social outcomes for people with psychosis (Kane et al., 2016; Nordentoft et al., 2014). EIP services have become a dominant model of care provision for young people experiencing psychosis in many countries including England, Australia, Denmark, Canada and the US (Csillag et al., 2018). In Ireland, EIP services have also recently been established in some areas, including Dublin (O'Donoghue et al., 2021), Cork, Sligo, and Cavan and Monaghan (Fayyaz et al., 2021). A recent health economic evaluation of EIP services in Ireland has suggested that they are associated with substantial potential incremental net benefits over the first year of treatment, in terms of both health sector and societal economic benefits (Behan et al., 2020). This economic impact is particularly important, given the high total economic cost of schizophrenia in Ireland, which was estimated to be €460.6 million as far back as 2006 (Behan et al., 2008), made up of substantial direct costs (€117.5 million) and indirect costs (€343 million) due to lost productivity faced by both patients and their informal caregivers.

The timely provision of evidence-based psychosis care must be predicated on an understanding of predicted local need to allocate resources in a just and proportional way to optimise service delivery. The incidence of psychotic disorders follows

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highly replicable and precisely delineated demographic and social distributions (Jongsma et al., 2019; Kirkbride et al., 2012; Kirkbride et al., 2017), which has been used in other jurisdictions, most notably England, to develop models to predict future need for services based on a local understanding of the determinants of psychosis risk in different populations (McDonald et al., 2021). Thus, in planning psychosis care in the Irish context, it is crucial to understand the epidemiological landscape through which the incidence of psychotic disorders manifests in the population. Although several reviews have investigated the incidence of psychotic disorders in the UK (Kirkbride et al., 2012) and worldwide (Jongsma et al., 2019; McGrath et al., 2004), a dedicated synthesis of the evidence base for the incidence of psychotic disorders in the Republic of Ireland has not previously been conducted, despite a long history of methodologically robust studies in this space (see, for example, publications from the CAMFEPS study in Cavan and Monaghan (Scully et al., 2002; Nkire et al., 2021), and publications from recent data from the DETECT Early Intervention in Psychosis [EIP] service in South Dublin and Wicklow (O'Donoghue et al., 2021; O'Donoghue et al., 2016).

The aim of this systematic review is to summarise and assess the current evidence on the incidence of psychotic disorders in the Republic of Ireland, and examine how this varied by sociodemographic variables (age, sex, ethnicity, religion, etc.) and neighbourhood characteristics (social deprivation, social fragmentation, population density, etc.).

# **Methods**

In this systematic review, we sought to synthesise evidence on the incidence of psychotic disorders in the Republic of Ireland from the published literature between 1950 and 2021, and investigate how rates varied by reported sociodemographic and socioenvironmental factors. Our review was prospectively registered on the PROSPERO systematic review protocol database: CRD42021245891. We followed guidelines for the conduct and reporting of systematic reviews from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [PRISMA] statement (Supplemental Table 1) (Moher et al., 2009).

# Eligibility criteria

We sought to identify all studies:

- Published between 1 January 1950 and 31 August 2021
- Reporting the incidence of psychotic disorders in any study, wholly or partially conducted in Ireland, or which provided sufficient information to derive incidence rates
- Including participants from the general adult population aged 16–64 years old
- Including any non-organic psychotic disorder according to a validated classification system (i.e. Diagnostic and Statistical Manual [DSM] (American Psychiatric Association 2013) or International Statistical Classification of Diseases and Related Health Problems [ICD] (World Health Organization 2004).)
- Published in English

Studies were excluded if they focused solely on:

- Organic psychotic disorders, or those with clear evidence of an intellectual disability
- Non-population-based samples or specialist groups (e.g. perinatal mental health, prison, military or other specialist populations)

#### Information sources and search strategy

We searched four electronic databases: OVID Medline, Embase, PsycInfo and Web of Science. We also screened citation lists of included publications, and contacted authors of relevant papers to identify potentially missed studies or omitted data relevant to our review.

We developed our search strategy (see Supplemental Methods) in conjunction with a UCL librarian, adapted from a previously validated search strategy for incidence studies (Jongsma et al., 2019). Our search strategy included terms for (i) psychotic disorders, (ii) incidence / first episode psychosis [FEP], and (iii) a location-based term for studies restricted to the Republic of Ireland. Our initial search was conducted between March 2021 and August 2021 by one researcher (RPJ).

#### Study selection

After excluding duplicates, citation titles were screened independently by two authors (RPJ, JBK). Citations were rated as either excluded, insufficient information or included; discrepancies were resolved by consensus, with only citations flagged as included or as insufficient information progressing to abstract review. The same process was repeated at abstract review stage. One author (RPJ) reviewed the full text of remaining citations for eligibility, with uncertainties resolved by consensus with the senior author (JBK).

#### Data extraction

Data extraction was conducted by a single author (RPJ) into a prespecified spreadsheet, with uncertainties discussed and resolved with the senior author (JBK), who also reviewed the spreadsheet for accuracy. We extracted citation-level (e.g. setting, publication year, diagnostic outcomes, study quality), rate-level (e.g. number of cases, denominator data, rates and standard errors), individuallevel (e.g. age, sex, ethnicity or socioeconomic status) and arealevel (e.g. deprivation) data, as provided in each citation (see Supplemental Methods; Supplemental Table 2). Data were extracted from each citation according to the original metric reported in each study (i.e. the age groups reported in each study, or quintiles of deprivation).

# Diagnostic outcomes

We extracted rate-level data from all identified citations according to the diagnostic codes used in each original citation. We then used algorithms previously developed for use in other national and international systematic reviews of psychotic disorders (Jongsma et al., 2019; Kirkbride et al., 2012) to create broad diagnostic outcomes of interest (Supplemental Table 3) following the International Classification of Diseases, 10<sup>th</sup> edition [ICD-10]. We included the following outcomes: all psychotic disorders (ICD-10 F10-33), non-affective psychotic disorders (F20-29), schizophrenia (F20), affective psychotic disorders (F30.2, 31.2, 32.3, 33.3), bipolar disorder (F30.2, 31.2), depression with psychotic features (F32.3, 33.3) and substance-induced psychoses (F1x.5). We did not distinguish between different types of rates in our study (i.e. 'first contact', 'first episode', 'first admission' etc) because they typically estimate a similar latent construct of 'treated' incidence, with nomenclature reflecting the mode of care delivery at the time (for example, studies of 'first admission' tend to be older, based on case ascertainment when treatment was almost exclusively based on inpatient care). Exceptions exist, including the CAMFEPS epidemiological study, which employed population-based case finding, such that rates may be closer to the true incidence in the population, which we captured as part of our assessment of methodological quality.

#### Methodological quality and risk of bias of included studies

To assess risk of bias, we identified seven relevant epidemiological criteria (Supplemental Table 4, a-g) indicative of study quality for estimating incidence rates in psychiatric epidemiology, based on previous reviews (Jongsma et al., 2019; Kirkbride et al., 2012). These items included reporting of a defined catchment area, accurate denominator estimation, population-based case finding, standardised research diagnoses, defined inclusion criteria, and conduct of a 'leakage' study to identify cases potentially missed during the initial ascertainment period (see Supplemental Table 4 for more details). We also included two additional criteria (h-i) regarding the reporting of sufficient data to derive both incidence rates and associated statistical uncertainty (h), and whether crude and standardised rates were reported (i). In a small deviation from our protocol, we retrospectively dropped criterion (e) because our review did not identify any study that reported incidence by ethnicity or country-of-birth, the primary purpose for which this criterion has been used previously (Kirkbride et al., 2006). Thus, each citation was scored on our risk of bias assessment from 0 to 8 ('a-i', except 'e').

# Data synthesis

We adopted a narrative synthesis to describe variance in incidence of psychotic disorders in Ireland for each diagnostic group (see 'Diagnostic outcomes', above), where possible assessing variance by sociodemographic and socioenvironmental characteristics. In instances where several citations provided overlapping data from the same setting (for example, for a series of studies in the Cavan-Monaghan region), we reported data from the most relevant (i.e. principal) citation(s) for a given outcome. Incidence rates were reported per 100,000 person-years as our measure of effect.

Where at least five incidence rates (with corresponding standard errors) were available for a given analysis, we also conducted a random effects meta-analysis to formally pool the data, and estimated between-study heterogeneity in reported rates. Heterogeneity was estimated using the Q-test, and quantified using the I<sup>2</sup>-statistic (Higgins and Thompson 2002). Where possible, we also conducted meta-regression to inspect whether reported rates varied by risk of bias (study quality). We also assessed identified citations for the presence of small study effects, the most common of which is publication bias, via visual inspection of funnel plots and a formal Egger's test of publication bias where we had sufficient data to pool estimates. All analyses were conducted in Stata, version 17.

# Results

#### Study selection

After removing duplicate records, our initial search identified 1,975 citations (Fig. 1) of which 21 met our inclusion criteria (Scully et al., 2002; Nkire et al., 2021; O'Donoghue et al., 2016; Keatinge 1986; Baldwin et al., 2005; Morgan et al., 2001; Omer et al., 2012; Keatinge 1987; Daly et al., 1995; Baldwin et al., 2002; Waddington et al., 2004; Kingston et al., 2011; Baldwin et al., 2003; Owoeye et al., 2013; Lyne et al., 2014; Keatinge 1988; Browne et al., 2005; Ninuallain et al., 1987; Kelly et al., 2010;

Jablensky et al., 1992; Omer et al., 2014). Via author contacting, we identified a further two citations which met inclusion criteria (O'Donoghue et al., 2021; Fayyaz et al., 2021). Of the 23 citations included in this review (Table 1), only six unique citations contained poolable incidence rate data for metaanalyses (see below) as the remainder of citations did not provide a corresponding estimate of standard error alongside reported rates.

#### Study characteristics

Citations were published between 1986 (Keatinge 1986) and 2021 (O'Donoghue et al., 2021; Fayyaz et al., 2021; Nkire et al., 2021) and contained incidence data on psychotic disorders collected between 1974 (Ninuallain et al., 1987) and 2016 (Fayyaz et al., 2021). Sample sizes ranged from just 30 new cases of bipolar disorder or mania with psychotic features in Dublin South Central (Daly et al., 1995) between 1975 and 1981, to 593 new cases of any FEP in the Dublin East Treatment and Early Care Team [DETECT] EIP service in South Dublin and Wicklow between 2006 and 2014 (O'Donoghue et al., 2021).

Twelve citations (52.2%) reported incidence rates of psychotic disorders in the Cavan-Monaghan First Episode Psychosis Study [CAMFEPS] (Scully et al., 2002; Nkire et al., 2021; Baldwin et al., 2005; Morgan et al., 2001; Omer et al., 2012; Baldwin et al., 2002; Waddington et al., 2004; Kingston et al., 2011; Baldwin et al., 2003; Owoeye et al., 2013; Browne et al., 2005; Omer et al., 2014), with a further citation reporting inception rates of FEP in the COPE EIP service in the same catchment area following the end of the CAMFEPS study in 2011 (Fayyaz et al., 2021). Six citations provided incidence data from studies partially set in Dublin (O'Donoghue et al., 2021; O'Donoghue et al., 2016; Daly et al., 1995; Lyne et al., 2014; Kelly et al., 2010; Jablensky et al., 1992), including the World Health Organization [WHO] Ten-country study (Jablensky et al., 1992) and three citations from the DETECT EIP service (O'Donoghue et al., 2021; O'Donoghue et al., 2016; Lyne et al., 2014). Other locations included Clare and Wexford (O'Donoghue et al., 2016; Keatinge 1986; Keatinge 1987; Lyne et al., 2014), Waterford (Keatinge 1988) and Carlow, Westmeath and Roscommon (Ninuallain et al., 1987), as part of the 'The Three-County Study'.

All included citations used either DSM-IV (n = 17; 73.9%)or ICD criteria (n = 6; 26.1%). The most common method of diagnostic assessment reported was the Structured Clinical Interview for DSM Disorders [SCID] (n = 10; 43.5%). The most common diagnostic outcomes were 'all FEP disorders' (n = 18; 77.3%) and 'affective psychotic disorders' (n = 18; 78.3%), followed by 'non-affective psychotic disorders' (n = 12; 52.2%) and 'bipolar disorder with psychotic features' (n = 12; 52.2%) (Table 1; Supplemental Figure 1). Most citations included in this review adopted an age range from 15 years and older (Table 1) with no upper cut-off (Scully et al., 2002; Nkire et al., 2021; Keatinge 1986; Baldwin et al., 2005; Morgan et al., 2001; Keatinge 1987; Daly et al., 1995; Baldwin et al., 2002; Waddington et al., 2004; Kingston et al., 2011; Baldwin et al., 2003; Owoeye et al., 2013; Keatinge1988; Browne et al., 2005; Omer et al., 2014). Four citations (O'Donoghue et al., 2021; O'Donoghue et al., 2016; Lyne et al., 2014; Ninuallain et al., 1987) specified an upper cut-off of 64 or 65 years old, while the WHO 10-Country study was restricted to 15-54 years (Jablensky et al., 1992). One citation did not report an age range (Kelly et al., 2010).

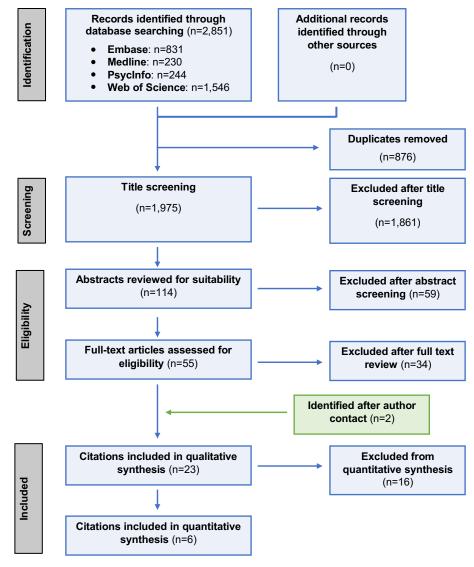


Figure 1. PRISMA flow diagram of search strategy.

# Risk of bias within studies

Study quality varied from one (Baldwin et al., 2003) to seven (Scully et al., 2002; O'Donoghue et al., 2016; Baldwin et al., 2005; Jablensky et al., 1992) out of eight, with a median of five (interquartile range [IQR]: 4–6; see Supplemental Table 5). Only one criterion was met by all studies: 'a. Defined catchment area', while the criterion met least often (N = 6; 26.1%) was 'i. reporting crude and standardised rates'.

# Variation in incidence rates by individual characteristics

#### All first episode psychotic disorders

We identified fifteen citations which estimated the overall crude incidence of all first episode psychotic disorders in Ireland (O'Donoghue et al., 2021; Fayyaz et al., 2021; Scully et al., 2002; Nkire et al., 2021; O'Donoghue et al., 2016; Baldwin et al., 2005; Morgan et al., 2001; Baldwin et al., 2002; Waddington et al., 2004; Kingston et al., 2011; Baldwin et al., 2003; Owoeye et al., 2013; Lyne et al., 2014; Browne et al., 2005; Jablensky et al., 1992; Omer et al., 2014), conducted between 1978 (Jablensky et al., 1992) and 2016 (Fayyaz et al., 2021), and published between 1992 (Jablensky et al., 1992) and 2021 (O'Donoghue et al., 2021; Fayyaz et al., 2021; Nkire et al., 2021). Of these, 11 citations (Scully et al., 2002; O'Donoghue et al., 2016; Baldwin et al., 2005; Morgan et al., 2001; Baldwin et al., 2002; Kingston et al., 2011; Baldwin et al., 2003; Owoeye et al., 2013; Lyne et al., 2014; Browne et al., 2005; Omer et al., 2014) provided overlapping data with four principal citations (O'Donoghue et al., 2021; Fayyaz et al., 2021; Nkire et al., 2021; Jablensky et al., 1992); nine (Scully et al., 2002; O'Donoghue et al., 2016; Baldwin et al., 2005; Morgan et al., 2001; Baldwin et al., 2002; Kingston et al., 2011; Baldwin et al., 2003; Owoeye et al., 2013; Browne et al., 2005; Omer et al., 2014) contained overlapping data from the CAMFEPS study (Nkire et al., 2021), and two (O'Donoghue et al., 2016; Lyne et al., 2014) provided overlapping data from the DETECT EIP service (O'Donoghue et al., 2021). The four principal citations (O'Donoghue et al., 2021; Fayyaz et al., 2021; Nkire et al., 2021; Jablensky et al., 1992) provided unique information on incidence rates from 1187 FEP cases in total; crude incidence rates were similar across three studies (O'Donoghue et al., 2021; Fayyaz et al., 2021; Jablensky et al., 1992), varying from 22.0 (Jablensky et al., 1992) (95%CI: 17.3-28.0) to 25.6 (O'Donoghue et al., 2021) cases per 100,000 person-years (95%

							Diagnostic outcomes included										
Citation (First author, pub. date, citation)	Location	Study	Period	Age range	Diagnostic confirmation method	Diagnostic classification system	FEP	NAP	AP	SZ	BD/ M	PD	SIP	0	N (cases)	Pop. at- risk	Study quality
Baldwin et al., 2002	C-M	CAMFEPS	1995-2000	15+	SCID / Clinical	DSM-IV	Х		х		Х	х		Х	69	73,638	5
Baldwin et al., 2003 <sup>#</sup>	C-M	CAMFEPS	1995-2002	15+	NR	DSM-IV	Х	Х	Х	Х	Х	Х		Х	146	NR	1
Baldwin et al., 2005	C-M	CAMFEPS	1995-2003	15+	SCID / Clinical	DSM-IV	Х	Х	Х	Х	Х	Х		Х	194	76,670	7
Browne et al., 2005 <sup>#</sup>	C-M	CAMFEPS	1995-2004	15+	NR	DSM-IV*	Х	Х	Х	Х	Х	Х		Х	223	NR	2
Daly et al., 1995	DSC	-	1975–1981	15+	Case notes / PSE	ICD-9					Х				30	NR	5
Fayyaz et al., 2021	C-M	COPE	2012-2016	16+	SCID	DSM-IV	Х			Х	Х	Х	Х	Х	115	NR	6
Jablensky et al., 1992	D	WHO	1978	15-54	PSE, PPHS	CATEGO / ICD-9	Х	Х	Х						67	149879	7
Keatinge 1986	C&W	K-T	1978–1981	15+	NR	ICD-9			Х						166	NR	5
Keatinge 1987	C&W	K-T	1978–1981	15+	NR	ICD-9			Х						166	NR	5
Keatinge 1988	M&W*	K-0	1978-1980	15+	NR	ICD-9			Х						93	~ 19,366	4
Kelly et al., 2010	SD&C-M	-	1995-2001	NR	SCID	DSM-IV	Х		Х	Х					324	NR	5
Kingston et al., 2011	C-M	CAMFEPS	1995-2008	15+	NR	DSM-IV	Х		Х		Х	Х	Х	Х	372	~ 79,317	4
Lyne et al., 2014 <sup>#</sup>	SD&W*	DETECT	2007-2011	16-65	SCID	DSM-IV	Х	Х	Х						NR	NR	4
Morgan et al., 2001 <sup>#</sup>	C-M	CAMFEPS	1995-2000	15+	NR	DSM-IV	Х	Х	Х	Х	Х			Х	69	~ 61,497	2
Ninuallain et al., 1987	CWR	3CS	1974–1976	15-64	PSE, SCL, AS	CATEGO / ICD-8		Х	Х						34	NR	4
Nkire et al., 2021	C-M	CAMFEPS	1995-2010	15+	SCID	DSM-IV	Х		Х		Х	Х	Х	Х	432	~ 84,457	6
O'Donoghue et al., 2016	SD&W	DETECT	2006-2011	16-65	SCID	DSM-IV	Х								292	266212	7
O'Donoghue et al., 2021	SD&W	DETECT	2006-2014	18-65	SCID	DSM-IV	Х	Х	Х						593	NR	6
Omer et al., 2012	C-M	CAMFEPS	1995–2007	15+	NR	DSM-IV*	Х	Х		Х					NR	NR	2
Omer et al., 2014	C-M	CAMFEPS	1995–2007	16+	NR	DSM-IV	Х	Х		Х					255	NR	6
Owoeye et al., 2013	C-M	CAMFEPS	1995–2008	15+	SCID	DSM-IV	Х		х		Х	Х	х	Х	370	~ 84,959	6
Scully et al., 2002	C-M	CAMFEPS	1995-2000	15+	SCID	DSM-IV	Х	Х	Х	Х	Х	Х		Х	69	73,638	7
Waddington et al., 2004 <sup>#</sup>	C-M	CAMFEPS	1995-2002	15+	NR	DSM-IV	Х	Х			Х	Х		Х	153	76,691	2
						Total:	18	12	17	9	12	10	4	11			

Legend: N: number of cases; NR: Not reported; ~derived; Pop.: population.

Location: C-M: Cavan-Monaghan; DSC: Dublin South Central; D: Dublin; C&W: Clare & Wexford; M&W: Monaghan & Waterford; SD&C-M: South Dublin & Cavan-Monaghan, SD&W: South Dublin & Wicklow; CWR: Carlow, Westmeath, Roscommon. Study: CAMFEPS: Cavan-Monaghan First Episode Psychosis Study; COPE: Carepath for Overcoming Psychosis Early; WHO: World Health Organization 10-country / DOSMED study; K-T: Keatinge thesis; K-O: Keatinge other; DETECT: Dublin East Treatment and Early Care Team; 3CS: Three-county Study.

Diagnostic confirmation method: SCID: Structured Clinical Interview for DSM Disorders; Clinical: Clinical idagnosis; PSE: Present State Examination; PPHS: Personal & Psychiatric History Schedule; SCL: Syndrome Check List; AS: Aetiology Schedule. Diagnostic outcomes included: FEP: All first episode psychotic disorders; NAP: Non-affective psychosis; AP: Affective psychosis; SZ: Schizophrenia; BD/M: Bipolar disorder/Mania; PD: Psychotic Depression; SIP: Substance-induced psychotic disorders; O: Other psychotic disorders.

#Conference abstract.

\*likely, but not reported. Based on other citations from same group/setting, or other deduction.

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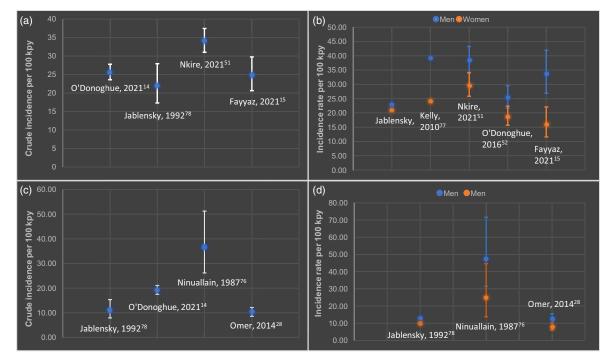


Figure 2. Crude incidence rate per 100,000 person-years of selected psychotic outcomes in the Republic of Ireland, overall and by sex. Legend: 100 kpy: 100,000 person-years. (A) All psychotic disorders; (B) All psychotic disorders, by sex; (C) Non-affective psychotic disorders; (D) Non-affective psychotic disorders, by sex.

CI: 23.6–27.8), but was higher (34.1 per 100,000 person-years; 95% CI: 31.0–37.5) in one study from Cavan and Monaghan (Fig. 2a) (Nkire et al., 2021). Study quality was high (rated 6 or 7 out of 8; Table 1).

Five principal citations (Fayyaz et al., 2021; Nkire et al., 2021; O'Donoghue et al., 2016; Kelly et al., 2010; Jablensky et al., 1992) provided FEP incidence data separately for men and women, with evidence of higher rates for men than women (Fig. 2b). For example, Nkire et al. (2021) reported the incidence rate ratio [IRR] for all clinically relevant psychotic disorders to be 1.3 times higher in men than women (95%CI: 1.1–1.6), while Fayyaz et al. (2021) reported a greater crude IRR of 2.1 (95%CI: 1.4–3.1). Study quality was high (at least 6 out of 8; Table 1).

We failed to identify any citation which had published incidence rates by age group, although Omer et al. (2014) reported incidence rate ratios by age group in Cavan and Monaghan, with highest rates for men aged 15–34, although no statistically significantly differences by age for women were observed. Further data on median age-at-onset in these studies is given in the Supplemental Results section.

One citation reported FEP incidence rates by migrant status and region-of-birth (O'Donoghue et al., 2021), from the DETECT EIP service in South Dublin and Wicklow. Although no overall difference in FEP incidence was observed between migrant and Irish-born groups (IRR: 1.02; 95%CI: 0.83–1.24), subgroup analyses found rates were 1.83 (95%CI: 1.11–3.02) times higher for people born in Africa than Ireland.

#### Non-affective psychotic disorders

Eleven citations provided data on the overall incidence of nonaffective psychotic disorders in Ireland (O'Donoghue et al., 2021; Scully et al., 2002; O'Donoghue et al., 2016; Baldwin et al., 2005; Morgan et al., 2001; Waddington et al., 2004; Baldwin et al., 2003; Lyne et al., 2014; Browne et al., 2005; Ninuallain et al., 1987; Jablensky et al., 1992; Omer et al., 2014), of which four principal citations provided the most relevant data (O'Donoghue et al., 2021; Ninuallain et al., 1987; Jablensky et al., 1992; Omer et al., 2014). These studies were conducted in Dublin (O'Donoghue et al., 2021; Jablensky et al., 1992), Wicklow (O'Donoghue et al., 2021), Cavan and Monaghan (Omer et al., 2014) and Carlow, Westmeath and Roscommon (Ninuallain et al., 1987). We observed heterogeneity in rates (Fig. 2c), from around 10-11 new cases per 100,000 person-years in two good quality studies (6 (Nkire et al., 2021) or 7 (Jablensky et al., 1992) out of 8) in Dublin (N = 35 cases, 15–54 years (Jablensky et al., 1992)) and Cavan-Monaghan (N = 132 cases, 15 + years) (Nkire et al., 2021) to 36.6 per 100,000 person-years in the 3-county study (quality: 4 of 7, N = 34 cases, 15–64 years) (Ninuallain et al., 1987). Finally, in the most recent and largest (N = 443) study identified, we derived the incidence of non-affective psychotic disorders from the DETECT EIP service in South Dublin and Wicklow (O'Donoghue et al., 2021) as 19.2 (95%CI: 17.4-21.1) per 100,000 person-years (quality: 6 of 8, 16-64 years).

Three principal citations (Ninuallain et al., 1987; Jablensky et al., 1992; Omer et al., 2014) reported higher point estimates of rates in men than women (Fig. 2d), albeit with overlapping confidence intervals, where provided (Ninuallain et al., 1987; Omer et al., 2014). Only one citation (Ninuallain et al., 1987) (the Three-County study) reported rates by age, finding no evidence of differences in this small study (Supplemental Figure 2a).

One citation provided rates by migrant status and region-ofbirth (O'Donoghue et al., 2021). As described above, no overall differences by migrant status were observed, but rates were higher for migrants born in Africa compared with Ireland (IRR: 1.78; 95% CI: 1.00–3.18; p = 0.049).

#### Schizophrenia

We identified 16 citations (Fayyaz et al., 2021; Scully et al., 2002; O'Donoghue et al., 2016; Nkire et al., 2021; Keatinge 1986; Baldwin

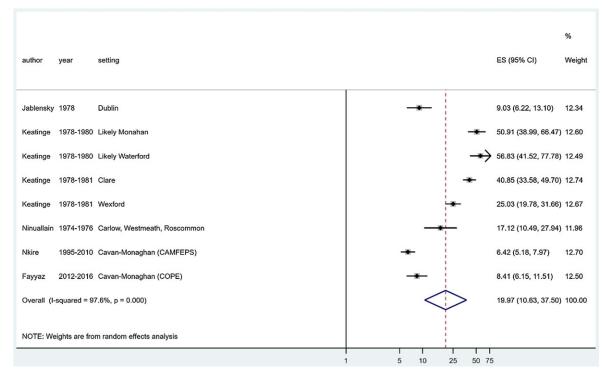


Figure 3. Forest plot of the incidence of schizophrenia in the Republic of Ireland, 1974–2016. Legend: 100 kpy: 100,000 person-years. The citation from Keatinge which reported data from 'Likely Monaghan' and 'Likely Waterford' is included despite the author not explicitly reporting the catchment areas of this study, only that the study took place in two Irish counties. However in that publication, the author does acknowledge the two hospitals involved in the data collection for this study, which can be traced back to the counties of Monaghan and Waterford, respectively.

et al., 2005; Morgan et al., 2001; Keatinge 1987; Baldwin et al., 2002; Kingston et al., 2011; Baldwin et al., 2003; Owoeye et al., 2013; Lyne et al., 2014; Keatinge 1988l; Browne et al., 2005; Ninuallain et al., 1987; Jablensky et al., 1992), including seven principal citations (Fayyaz et al., 2021; Nkire et al., 2021; Keatinge 1986; Lyne et al., 2014; Keatinge 1988; Ninuallain et al., 1987; Jablensky et al., 1992) on the overall incidence of schizophrenia. We rated study quality as high (Fayyaz et al., 2021; Nkire et al., 2021; Jablensky et al., 1992) or medium (Keatinge 1986; Lyne et al., 2014; Keatinge 1988; Ninuallain et al., 1987). These seven citations provided nine overall incidence rates of schizophrenia (with data from the Monaghan and Waterford (Keatinge 1988), and Clare and Wexford (Keatinge 1986) citations disaggregated by county). Incidence rates ranged from 6.4 (95%CI: 5.2-8.0) in Cavan-Monaghan (Nkire et al., 2021) to 57.0 (95%CI: 41.5-77.8) per 100,000 person-years in Waterford (Keatinge 1988), representing an almost 9-fold variation.

We estimated the pooled incidence of schizophrenia as 20.0 per 100,000 person-years (95%CI: 10.6–37.5; Fig. 3), despite very high heterogeneity between estimates (I<sup>2</sup>: 97.6%), from eight estimates of incidence provided by six of the seven citations identified here (Nkire et al., 2021; Keatinge 1986; Keatinge 1988; Ninuallain et al., 1987; Jablensky et al., 1992); one citation could not be included as no standard error was derivable (Lyne et al., 2014). In a random effects meta-regression, higher study quality was associated with lower incidence of schizophrenia (p < 0.001; Fig. 4). We found no evidence of 'small study effects' (Supplemental Figure 3; Egger's test p = 0.77).

Five principal citations reported incidence rates of schizophrenia separately for men and women (Fayyaz et al., 2021; Nkire et al., 2021; Ninuallain et al., 1987; Kelly et al., 2010; Jablensky et al., 1992), with higher point estimates consistently found for men (Supplemental Figure 4); two recent citations from separate samples in Cavan and Monaghan, including the CAMFEPS study (Nkire et al., 2021) (IRR: 3.1; 95%CI: 1.9–5.2) and COPE EIP service (IRR: 3.3; 95%CI: 1.6–7.0) reported rates that were three times higher for men than women.

Although three principal citations reported the number of new cases of schizophrenia by age group (Keatinge 1986; Keatinge 1988; Ninuallain et al., 1987), only one provided accompanying estimates of incidence (Ninuallain et al., 1987), and this was underpowered to detect trends by age (Supplemental Figure 2b).

#### Affective psychotic disorders

We identified two principal citations (and five further nonprincipal citations from the same studies (Scully et al., 2004; O'Donoghue et al., 2016; Baldwin et al., 2005; Morgan et al., 2001; Baldwin et al., 2003; Browne et al., 2005)) which provided data to derive incidence rates of affective psychotic disorders (O'Donoghue et al., 2021; Omer et al., 2014). In recent data from the DETECT EIP service in South Dublin and Wicklow (O'Donoghue et al., 2021), we derived the crude incidence as 6.4 cases per 100,000 person-years (95%CI: 5.5–7.6), using data ascertained between 2006 and 2014. From the principal Cavan-Monaghan citation (Omer et al., 2014), using data ascertained between 1995-2007, we derived a slightly higher crude incidence of 9.5 cases per 100,000 person-years (95%CI: 8.0–11.3) in people aged 16 and older (Omer et al., 2014).

Two unique citations provided rates separately for men and women (Omer et al., 2014). Derived rates from the CAMFEPS were similar for men (9.2; 95%CI: 7.2–11.8) and women (9.8; 95%CI: 7.6–12.6), as well as in published data from a separate study conducted in South Dublin and the Cavan-Monaghan region (Kelly et al., 2010).

We did not identify any study which had published rates of affective psychotic disorders by age. One citation provided rates by migrant status and region-of-birth (O'Donoghue et al., 2021), but found no differences in a small sample of cases (N = 33).

#### Bipolar disorders with psychotic features

Three unique citations (Fayyaz et al., 2021; Nkire et al., 2021; Daly et al., 1995) from 11 reports containing overlapping data (Fayyaz et al., 2021; Nkire et al., 2021; Baldwin et al., 2005; Morgan et al., 2001; Daly et al., 1995; Baldwin et al., 2002; Waddington et al., 2004; Kingston et al., 2011; Baldwin et al., 2003; Owoeye et al., 2013; Browne et al., 2005) provided incidence rates on bipolar disorders or mania separately. First admission rates of mania in Dublin South Central between 1975 and 1981 for people aged 18-60 years old were reported as 8.2 per 100,000 person-years (95%CI: 5.6-11.9), although a lower figure was reported for people aged 15 years and older (4.5; 95%CI: 3.1-6.5) (Daly et al., 1995). In Cavan and Monaghan, the incidence of Bipolar I Disorders between 1995 and 2010 was estimated as 6.9 per 100,000 person-years (95%CI: 5.6-8.5) for people aged 15 years and older (Nkire et al., 2021). A more recent estimate of the incepted rate of Bipolar I Disorders from the COPE EIP service in this area (2012-2016) reported a lower estimate of 2.8 cases per 100,000 person-years (95%CI: 1.6-4.8) (Fayyaz et al., 2021). All citations reported similar rates for men and women.

One study (Daly et al., 1995) reported first admission rates of mania by age group, with higher rates in younger age groups (18–19, 20-29 years). This study also reported gradients by social class, with higher point estimates of incidence in people from lower social classes (groups V and VI: 8.2 per 100,000 person-years; 95% CI: 4.5–14.8) compared with social class groups I and II (4.7; 95% CI: 2.4–9.0) and III and IV (4.5; 95%CI: 2.4–8.4), though the small sample sizes precluded any conclusions being drawn.

#### Depression with psychotic features

We identified two unique citations (Fayyaz et al., 2021; Nkire et al., 2021) from nine overlapping reports (Fayyaz et al., 2021; Nkire et al., 2021; Baldwin et al., 2005; Baldwin et al., 2002; Waddington et al., 2004; Kingston et al., 2011; Baldwin et al., 2003; Owoeye et al., 2013; Browne et al., 2005) which provided data on the incidence of depression with psychotic features. Both were conducted in the Cavan-Monaghan region, in either the CAMFEPS epidemiological study (1995–2010) (Nkire et al., 2021) or the COPE EIP service (2012–2016) (Fayyaz et al., 2021). Both studies estimated similar incidence/incepted rates of depression with psychotic features (CAMFEPS, 15 years and older: 7.3 per 100,000 person-years; 95% CI: 6.0–8.9. COPE EIP service, 16 years and older: 5.6; 95%CI:3.8–8.2). Neither study found statistically significant difference in rates for men and women.

# Substance-induced psychotic disorders

The same two citations (Fayyaz et al., 2021; Nkire et al., 2021) provided unique data on the incidence of substance-induced psychotic disorders, from four overlapping citations (Fayyaz et al., 2021; Nkire et al., 2021; Kingston et al., 2011; Owoeye et al., 2013). In CAMFEPS, incidence was estimated as 2.0 per 100,000 personyears (95%CI: 1.4–3.0) (Nkire et al., 2021), with a similar rate reported in the COPE EIP service (Fayyaz et al., 2021) (3.2; 95%CI: 1.9–5.3). Both studies reported substantially higher rates for men than women (IRR<sub>CAMFEPS</sub>: 7.0; 95%CI: 2.1–23.4, IRR<sub>COPE</sub>: 13.9; 95%CI: 1.8–105.7), albeit with imprecision around these estimates. Other psychotic outcomes

See Supplemental Results.

# Variation in incidence rates by area-level characteristics

We identified four principal citations (O'Donoghue et al., 2016; Keatinge 1988; Kelly et al., 2010; Omer et al., 2014) and one overlapping citation (Omer et al., 2012) which reported the incidence of any psychotic disorder outcome by area-level characteristics, including socioeconomic deprivation (O'Donoghue et al., 2016; Omer et al., 2014), social fragmentation (O'Donoghue et al., 2016; Omer et al., 2014), population density (O'Donoghue et al., 2016), or rural-urban classification (Keatinge 1988; Kelly et al., 2010; Omer et al., 2014). Three of the four studies, all rated as high quality (6 or 7 out of 8) were published since 2010 (O'Donoghue et al., 2016; Kelly et al., 2010; Omer et al., 2014), with one older, lower quality (4 out of 8) study published in 1988 (Keatinge 1988); this study reported overlapping first admission rates of schizophrenia in rural Monaghan (51.0 per 100,000 person-years; 95%CI: 39.1-66.6) and more urban Waterford (57.0; 95%CI: 41.7-78.0).

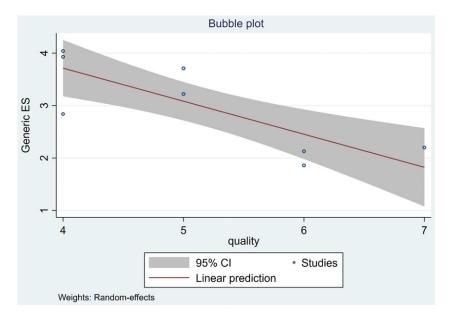
Kelly et al. (2010) reported first admission rates of various psychotic outcomes between 1995 and 2001 in a rural setting (Cavan-Monaghan) and an urban setting (South Dublin), and found higher crude rates of schizophrenia in men (IRR: 1.92; 95% CI: 1.52–2.44) and women (IRR: 1.34; 95%CI: 1.00–1.80) living in urban areas. By contrast, crude rates of affective psychotic disorders appeared lower in the urban setting (IRR<sub>men</sub>: 0.48; 95% CI: 0.34–0.67) and women (IRR<sub>women</sub>: 0.60; 95%CI: 0.43–0.83).

In Cavan and Monaghan, Omer et al. (2014) found sex-specific effects of place on the incidence of all psychotic disorders, such that women living in the most urban (IRR: 1.34; 95%CI: 1.03-1.73) and most social fragmented (IRR: 1.72; 95%CI: 1.33-2.24) parts of the region had higher rates. By contrast, these effects were not observed for men, but their rates were higher in the most deprived part of the region (IRR: 1.58; 95%CI: 1.25-2.01). Following multivariable adjustment only material deprivation remained associated with increased rates of psychotic disorder (IRR per standard deviation increase in deprivation: 1.13; 95%CI: 1.03-1.24) in this sample. This finding accords with further evidence from the DETECT service, which reported that age-standardised incidence rates of FEP were 3.43 times higher in the most-versus-least deprived quartile (95%CI: 1.24-7.75). Partial evidence (third vs first quartile) of increased rates in more socially fragmented areas was also observed (IRR: 2.40; 95%CI: 1.05-5.51) (O'Donoghue et al., 2016). No statistically significant variation by population density or social capital was observed, although we noted a trendlevel association in incidence between quartiles with the highest and lowest levels of social capital (IRR: 1.43; 95%CI: 0.99-2.06). Similarly to Omer et al. (2014), findings from DETECT indicated a stronger effect for deprivation on FEP rates in men, and a stronger effect for social capital on FEP rates in women.

# Discussion

# Principal findings

We identified 23 citations which met criteria for our systematic review of the incidence of psychotic disorders in Ireland, published between 1950 and 2021. Although our review highlights heterogeneity in estimates of various psychotic disorders in Ireland, some consistent trends emerged. For example, three out of four principal citations reported the overall incidence of psychotic



**Figure 4.** Correlation between study quality and (log) incidence of schizophrenia in the Republic of Ireland, 1974–2016. Legend: 100 kpy: 100,000 person-years. The figure indicates strong, statistically significant (*p* = 0.04) negative correlation between (higher) study quality (*x*-axis) and (lower) (log) incidence of schizophrenia.

disorders to be between 22 and 25 per 100,000 person-years in working age adults up to 65 years old, including in two recent studies based on incepted rates via EIP services in rural and more urban parts of Ireland (O'Donoghue et al., 2021). Only one study, based on a population-based case finding approach over a 15-year period in people aged 15 years and older, reported higher rates in the rural Cavan-Monaghan region of 34.1 per 100,000 personyears (Nkire et al., 2021). Nonetheless, this apparent variation falls within internationally reported estimates. For example, the lower estimates are consistent with pooled rates reported in the most recent systematic review of the international literature since 2002 (26.6 per 100,000 person-years) (Jongsma et al., 2019). Meanwhile, the upper figure from Cavan and Monaghan is consistent with pooled estimates in England for working aged adults (16-64 years old; 31.7 per 100,000 person-years) (Kirkbride et al., 2012; O'Donoghue et al., 2016).

In our review, we identified sufficient data to pool the overall incidence of schizophrenia in Ireland, estimated as 20.0 per 100,000 person-years (95%CI: 10.6–37.5; N = 8 settings). This is similar to the latest available estimate reported in the international systematic review (18.6; 95%CI: 15.1–22.9) (Jongsma et al., 2019; O'Donoghue et al., 2016; Nkire et al., 2021). Fewer studies in Ireland had published rates of affective psychotic disorders, but available data placed rates between 6-10 per 100,000 person-years. This range falls between a slightly lower figure reported in the latest international review (4.6; 95%CI: 3.1–6.8) (Jongsma et al., 2019; O'Donoghue et al., 2016; Nkire et al., 2021) and a higher figure reported from a review of English studies (12.4; 95%CI:9.0–17.1) (Kirkbride et al., 2012; O'Donoghue et al., 2016). Data on the incidence of substance-induced psychoses in Ireland were sparse, but where available, were very low.

We found consistent evidence of higher rates of most psychotic outcomes in men versus women, although affective psychotic disorders occurred more equally, again consistent with the wider literature (Jongsma et al., 2019; O'Donoghue et al., 2016; Nkire et al., 2021; Kirkbride et al., 2012). Very few studies in our review published incidence data by age, and no studies reported incidence by ethnicity, with only one recent study (O'Donoghue et al., 2021) reporting rates by migrant status and region- and country-of-birth. Finally, limited available evidence in Ireland (O'Donoghue et al., 2016; Keatinge 1988; Kelly et al., 2010; Omer et al., 2014) found support for an association between higher levels of deprivation and social fragmentation and greater psychosis rates, in studies which included both rural (Omer et al., 2014) and more urban (O'Donoghue et al., 2016) catchment areas. There was no clear evidence that population density or urban-rural status was associated with incidence.

#### Meaning of the findings

Our systematic review is drawn from a longstanding tradition of high quality epidemiological studies of the incidence of psychotic disorders in Ireland since the late 1970s. Notably, over half of the identified citations are based on the population of Cavan and Monaghan, providing a rich characterisation of the incidence (and in other reports, prevalence (Youssef et al., 1991; Scully et al., 2004)) of psychotic disorders in one rural part of Ireland. One possible reason for the higher incidence rates observed in this region than elsewhere could be that the CAMFEPS study used epidemiological principles and true community case finding to ascertain cases all cases occurring in the population, regardless of help-seeking. A further 26% of works were conducted in parts of Dublin, providing evidence from a contrasting, urban setting. These data have the potential to inform planning need for care in EIP services in Ireland, particularly with the availability of recent data on the incepted rate of psychotic disorders published from the COPE (Fayyaz et al., 2021) and DETECT (O'Donoghue et al., 2021; O'Donoghue et al., 2016) EIP services operating in these catchments, respectively. Similar initiatives have provided evidence-based predictions of future need for EIP care in England (McDonald et al., 2021; Kirkbride et al., 2013), which are currently incorporated in official guidelines from the National Institute of Health and Clinical Excellence [NICE] to inform service planning and commissioning (NHS England, 2016; NHS England 2020).

Despite this, we observed less evidence about the incidence in other parts of Ireland, for some diagnostic outcomes including affective psychotic disorders and substance use disorders, and by some important characteristics (including age, ethnicity and migrant status). Future studies could address these gaps to build a more complete epidemiological understanding of psychosis in Ireland.

We identified only one study, published in 2021, which presented data on the incidence of psychotic disorders in different groups by migrant status and region-of-birth (O'Donoghue et al., 2021). While there was no overall evidence that migrants had elevated rates of FEP (including non-affective and affective psychotic disorders separately), there was some evidence of heterogeneity by country-of-birth, with the most robust finding that rates were approximately doubled in people born in Africa compared with the Irish-born population. This effect size is somewhat lower than reported for people of Black African or Black Caribbean heritage consistently reported in studies in England (Kirkbride et al., 2012; O'Donoghue et al., 2016), including in rural populations (Kirkbride et al., 2017), where rates are typically reported to be between 4-6 times greater than the White or White British comparison group. Although several explanations for this discrepancy are possible, it is worth noting that the findings in Ireland (by region-of-birth) may not be directly comparable with findings elsewhere based on ethnicity. As the Irish population becomes increasingly ethnically diverse, it will be important to precisely delineate psychosis risk by ethnicity in the future, and data from the 2022 Census will provide information about the extent of ethnic diversity in the country (the proportion of the population identifying as White Irish has decreased from 87.6% in the 2006 Census (Central Statistics Office, 2006) to 82.2% in 2016 (Central Statistics Office 2021)). This important issue emphasises the need to understand the intersectional roles of ethnicity, migrancy and region-of-origin in the aetiopathology of psychotic disorders.

To some extent the findings of our review accord with the international literature on the incidence of psychotic disorders and socioenvironmental factors in Global North contexts. Both deprivation (Croudace et al., 2000; Richardson et al., 2018; Lewis et al., 2020; Kirkbride et al., 2014) and social fragmentation (Allardyce et al., 2005) have been consistently associated with the incidence of (at least) non-affective psychotic disorders. Interestingly, the non-linear association between deprivation and psychosis risk observed in the DETECT catchment by O'Donoghue et al. (2021) (with elevated risk confined to the most deprived group only) has been reported frequently elsewhere (Croudace et al., 2000; Richardson et al., 2018). This suggests that a threshold of deprivation may exist, after which presentations for new onset cases of psychosis begin to increase in rate. While population density has also been longitudinally and cross-sectionally associated with the incidence of psychotic disorders in some (Richardson et al., 2018; Lewis et al., 2020; Kirkbride et al., 2014), but not all (Kirkbride et al., 2007) studies outside of the Republic of Ireland, no consistent gradient emerged in the limited data identified on this issue in this review.

# Limitations

To our knowledge this was the first systematic review to examine the incidence of psychotic disorders in the Republic of Ireland. We prospectively registered our systematic review methodology and conformed to the PRISMA guidelines. Nonetheless, we acknowledge some limitations of our review. We restricted data and papers to published material identified via four major scientific databases, which may have omitted grey or unpublished data. Nonetheless, we identified rare works including PhD theses on this topic (Keatinge 1986). Together with the absence of evidence of small study effects, this suggests that the number of omitted citations from this review was small. We also contacted authors of some included works, which led to the identification and inclusion of two recently published papers not identified during our original search (O'Donoghue et al., 2021; Fayyaz et al., 2021). We recommend caution in interpreting rates from the recent COPE EIP service (Fayyaz et al., 2021) alongside other rates reported in this study; findings from COPE are reported as 'incepted' rather than 'incidence' rates, given that (unlike the earlier CAMFEPS study in the same region) rates were based on the number of new cases taken on by the EIP team, which may not be the same as the total number of new cases arising in this population.

One major limitation of our review was the marked heterogeneity and low number of studies generally available for any single outcome reported here. Moreover, we note that higher quality studies tended to report lower incidence rates of schizophrenia. Thus, the heterogeneity identified in this review may be explained by several factors, including differing age ranges of the studies, differences in case finding procedures, or stochastic variation. To mitigate against these issues, we relied on a narrative synthesis rather than meta-analysis.

We also note that 19 of the 23 citations included in this review were based on studies which collected data prior to (and including) 2010. Only four citations have provided more recent data on the incidence of psychotic disorder in Ireland, with the latest based on data up until 2016 (Fayyaz et al., 2021). We also noted that better study quality was strongly correlated with reporting of lower rates of schizophrenia (Fig. 4). While we found no formal evidence of small study effects (including publication bias), the Egger's test may be underpowered when few data points (N = 8)are available. Together, these findings call for ongoing, high quality epidemiological studies of the incidence of psychotic disorder in Ireland. Importantly, these studies should collect a core set of minimum data aligned to age, sex/gender, ethnicity, migration and deprivation/urbanisation to allow precise characterisation of need for care for psychosis across the country. Although our review focussed on the adult age range, 16-64 years old, the lowest age range for any study included in our review was 15 years old (Scully et al., 2004; O'Donoghue et al., 2016; Nkire et al., 2021; Keatinge 1986; Baldwin et al., 2005; Morgan et al., 2001; Omer et al., 2012; Keatinge 1987; Daly et al., 1995; Baldwin et al., 2002; Waddington et al., 2004; Kingston et al., 2011; Baldwin et al., 2003; Owoeye et al., 2013; Keatinge 1988; Browne et al., 2005; Ninuallain et al., 1987; Jablensky et al., 1992), highlighting the paucity of evidence on psychosis incidence during childhood and early adolescence. Finally, our quality criteria were designed by the authors, adapted from previously published systematic reviews (Kirkbride et al., 2012; O'Donoghue et al., 2016). They may not necessarily reflect all criteria that other stakeholders in the field consider vital or relevant, and future work could explore this issue.

#### Conclusion

The epidemiological data identified here is broadly consistent with the wider international literature in understanding variation in the incidence of psychotic disorders. Rates were broadly higher for men, younger people – and in the one published study in Ireland on the topic to date (O'Donoghue et al., 2021) - certain migrant groups, most notably those born in Africa. Rates were also increased in more deprived and socially fragmented communities. These findings have implications for public mental health in Ireland, since they can potentially facilitate and inform accurate resource allocation for the delivery of EIP services, as well as other primary and secondary healthcare services involved in care for those experiencing psychosis. Future efforts to continually monitor changes in the incidence of psychotic disorders in Ireland will help inform accurate, effective and timely public health responses. The continued rollout of EIP services in Ireland is providing new data and information about the epidemiology of psychotic disorders, as evidenced by recent publications from the DETECT service in South Dublin and County Wicklow (O'Donoghue et al., 2021; O'Donoghue et al., 2016; Lyne et al., 2014). Combining these evidence-based services with rigorous epidemiological intelligence available in Ireland (Nkire et al., 2021), will lead to actionable insights to inform the delivery of effective, early intervention for psychosis services in local communities according to population need.

**Supplementary material.** The supplemental material for this article can be found at https://doi.org/10.1017/ipm.2023.35.

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**Competing interests.** TD, GB, JBK received consultancy fees from the Health Services Executive, Ireland, to conduct this systematic review, as part of a wider project to predict the incidence of psychotic disorders in Ireland using statistical modelling. HSE were not involved in the design, conduct, drafting or final decision to approve this work for peer-reviewed academic publication. The views contained in this publication are not the views of HSE. No other conflicts of interest are declared.

**Ethical standard.** The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. No specific ethical approval was required due to the secondary nature of this work.

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**Preprint information.** A preprint version of this manuscript, supplemental materials, data extraction template, detailed screening decision-making, and extracted data can be found on PsyArXiv at: 10.31234/osf.io/dhfys

# References

- Allardyce J, Gilmour H, Atkinson J, Rapson T, Bishop J, McCreadie RG (2005). Social fragmentation, deprivation and urbanicity: relation to firstadmission rates for psychoses. *British Journal of Psychiatry [Internet]*, 401– 406, Available from: http://bjp.rcpsych.org/cgi/content/abstract/187/5/401
- American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Disorders. American Psychiatric Association.
- Baldwin P, Scully P, Quinn J, Morgan M, Kinsella A, O'Callaghan E, et al. (2002). First episode bipolar disorder: systematic comparison of incidence with other affective and non-affective psychoses among an epidemiologically complete, rural population. *Bipolar Disorder [Internet]* 4, 39–40, Available from: https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N& PAGE=fulltext&D=psyc4&AN=2002-04233-007

- Baldwin PA, Scully PJ, Quinn JF, Morgan MG, Kinsella A, Owens JM, O'Callaghan E, Waddington JL (2003). Reduced rural incidence of schizophrenia is primarily a female phenomenon: the Cavan-Monaghan first episode study at seven years. *Schizophrenia Research* **60**, 33.
- Baldwin P, Browne D, Scully PJ, Quinn JF, Morgan MG, Kinsella A, Owens JM, Russell V, O'Callaghan E, Waddington JL (2005). Epidemiology of first-episode psychosis: illustrating the challenges across diagnostic boundaries through the Cavan-Monaghan study at 8 years. *Schizophrenia Bulletin [Internet]* **31**, 624–638, Available from: https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed9&AN= 41253315
- Behan C, Kennelly B, O'Callaghan E (2008). The economic cost of schizophrenia in Ireland: a cost of illness study. *Irish Journal of Psychological Medicine [Internet]* 25, 80–87, Available from: https:// pubmed.ncbi.nlm.nih.gov/30282214/
- Behan C, Kennelly B, Roche E, Renwick L, Masterson S, Lyne J, O'Donoghue
  B, Waddington J, McDonough C, McCrone P, Clarke M (2020). Early intervention in psychosis: health economic evaluation using the net benefit approach in a real-world setting. *The British Journal of Psychiatry [Internet]* 217, 484–490, Available from: https://pubmed.ncbi.nlm.nih.gov/31339083/
- Browne DJ, Scully PJ, Quinn JF, Morgan MM, Baldwin PA, Kinsella A, Owens JM, O'Callaghan E, Waddington JL (2005). Comparative incidence and characteristics of psychosis in major depressive disorder among an epidemiologically complete population: the Cavan-Monaghan first episode study at 9 years. *Schizophrenia Bulletin* **31**, 217.
- **Central Statistics Office** (2021). Census 2006: Principal Demographic Results [Internet]. https://www.cso.ie/en/census/census2006reports/census 2006principaldemographicresults/
- Central Statistics Office (2021). Census of population 2016 Profile 8 Irish Travellers. *Ethnicity and Religion [Internet]*, https://www.cso.ie/en/ releasesandpublications/ep/p-cp8iter/p8iter/p8e/
- Croudace TJ, Kayne R, Jones PB, Harrison GL (2000). Non-linear relationship between an index of social deprivation, psychiatric admission prevalence and the incidence of psychosis. *Psychological Medicine [Internet]* **30**, 177–185, Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd= Retrieve
- Csillag C, Nordentoft M, Mizuno M, McDaid D, Arango C, Smith J, Lora A, Verma S, Di Fiandra T, Jones PB (2018). Early intervention in psychosis: from clinical intervention to health system implementation. *Early Intervention in Psychiatry*. 12, 757–764.
- Daly I, Webb M, Kaliszer M (1995). First admission incidence study of mania, 1975-1981. *British Journal of Psychiatry*. **167**, 463–468.
- Fayyaz S, Nkire N, Nwosu B, Amjad N, Kinsella A, Gill M, McDonough C, Russell V, Waddington JL (2021). Carepath for overcoming psychosis early (COPE): first 5 years of clinical operation and prospective research in the Cavan-Monaghan early intervention service. *Irish Journal of Psychological Medicine [Internet]*, 1–14, [cited 2022 Jan 14]; Available from: https:// pubmed.ncbi.nlm.nih.gov/34353408/
- Firth J, Siddiqi N, Koyanagi A, Siskind D, Rosenbaum S, Galletly C, *et al.* (2019). The Lancet Psychiatry Commission: a blueprint for protecting physical health in people with mental illness. *The Lancet Psychiatry.* **6**, 675–712.
- Higgins JPT, Thompson SG (2002). Quantifying heterogeneity in a metaanalysis. *Statistics in Medicine [Internet]* 21, 1539–1558, Available from: https://onlinelibrary.wiley.com/doi/10.1002/sim.1186
- Hjorthøj C, Stürup AE, McGrath JJ, Nordentoft M (2017). Years of potential life lost and life expectancy in schizophrenia: a systematic review and metaanalysis. *The Lancet Psychiatry [Internet]* **4**, 295–301, Available from: http:// www.ncbi.nlm.nih.gov/pubmed/28237639
- Jablensky A, Sartorius N, Ernberg G, Anker M, Korten A, Cooper JE, et al. (1992). Schizophrenia: manifestations, incidence and course in different cultures A World Health Organization Ten-Country Study [Internet], Psychological Medicine. Monograph Supplement. England, 20, 1, Available from: http://www.journals.cambridge.org/abstract\_S0264180 100000904
- Jongsma HE, Turner C, Kirkbride JB, Jones PB (2019. International incidence of psychotic disorders, 2002-17: a systematic review and meta-analysis.

Lancet Public Health [Internet] 4, e229–e244, Available from: https://pubmed.ncbi.nlm.nih.gov/31054641/

- Kane JM, Robinson DG, Schooler NR, Mueser KT, Penn DL, Rosenheck RA, et al. (2016). Comprehensive versus usual community care for first-episode psychosis: 2-year outcomes from the NIMH RAISE early treatment program. *American Journal of Psychiatry* 173, 362–372.
- Keatinge CM (1986). Schizophrenia in rural Ireland: a community comparison of tolerance of mental illness, level of social support and attitudes towards psychiatric facilities. *Dissertation Abstracts International [Internet]* 46, 3220, Available from: https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y& NEWS=N&PAGE=fulltext&D=psyc2&AN=1986-55003-001
- Keatinge C (1987). Schizophrenia in rural Ireland: a case of service overutilisation. International Journal of Social Psychiatry [Internet] 33, 186–194, Available from: https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC= Y&NEWS=N&PAGE=fulltext&D=emed3&AN=18673405
- Keatinge C (1988). Psychiatric admissions for alcoholism, neuroses and schizophrenia in rural and urban Ireland. *International Journal of Social Psychiatry [Internet]* 34, 58–69, Available from: https://ovidsp.ovid.com/ ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed4&AN= 18133561
- Kelly BD, O'Callaghan E, Waddington JL, Feeney L, Browne S, Scully PJ, Clarke M, Quinn JF, McTigue O, Morgan MG, Kinsella A, Larkin C (2010). Schizophrenia and the city: a review of literature and prospective study of psychosis and urbanicity in Ireland. *Schizophrenia Research* [*Internet*] 116, 75–89, Available from: http://www.sciencedirect.com/ science/article/B6TC2-4XMTFKC-2/2/ee3e482ccb8effd5b56cc212610aa62b
- Kirkbride JB, Fearon P, Morgan C, Dazzan P, Morgan K, Tarrant J, Lloyd T, Holloway J, Hutchinson G, Leff JP, Mallett RM, Harrison GL, Murray RM, Jones PB (2006). Heterogeneity in incidence rates of schizophrenia and other psychotic syndromes: findings from the 3-center AeSOP study. *Archives of General Psychiatry [Internet]* 63, 250–258, https://jamanetwork. com/journals/jamapsychiatry/fullarticle/209393
- Kirkbride JB, Morgan C, Fearon P, Dazzan P, Murray RM, Jones PB (2007). Neighbourhood-level effects on psychoses: re-examining the role of context. *Psychological Medicine [Internet]* 37, 1413–1425, Available from: http:// www.ncbi.nlm.nih.gov/pubmed/17472758
- Kirkbride JB, Errazuriz A, Croudace TJ, Morgan C, Jackson D, Boydell J, Murray RM, Jones PB (2012). Incidence of schizophrenia and other psychoses in England, 1950-2009: a systematic review and meta-analyses. *PLoS One [Internet]* 7, e31660, http://www.ncbi.nlm.nih.gov/pubmed/ 22457710
- Kirkbride JB, Jackson D, Perez J, Fowler D, Winton F, Coid JW, Murray RM, Jones PB (2013). A population-level prediction tool for the incidence of first-episode psychosis: translational epidemiology based on cross-sectional data. *BMJ Open [Internet]* 3, 1–14, http://www.pubmedcentral.nih.gov/ articlerender.fcgi?artid=3585967&tool=pmcentrez&rendertype=abstract
- Kirkbride JB, Jones PB, Ullrich S, Coid JW (2014). Social deprivation, inequality, and the neighborhood-level incidence of psychotic syndromes in East London. *Schizophrenia Bulletin [Internet]* 40, 169–180, Available from: https://www.ncbi.nlm.nih.gov/pubmed/23236081
- Kirkbride JB, Hameed Y, Ioannidis K, Ankireddypalli G, Crane CM, Nasir M, et al. (2017). Ethnic minority status, age-at-immigration and psychosis risk in rural environments: evidence from the SEPEA Study. Schizophrenia Bulletin [Internet] 43, 1251–1261, Available from: https:// academic.oup.com/schizophreniabulletin/article/43/6/1251/3829518
- Kirkbride JB, Hameed Y, Ankireddypalli G, Ioannidis K, Crane CM, Nasir M, Kabacs N, Metastasio A, Jenkins O, Espandian A, Spyridi S, Ralevic D, Siddabattuni S, Walden B, Adeoye A, Perez J, Jones PB (2017). The epidemiology of first-episode psychosis in early intervention in psychosis services: findings from the social epidemiology of psychoses in East Anglia [SEPEA] Study. *American Journal of Psychiatry [Internet]* 174, 143–153, http://ajp.psychiatryonline.org/doi/10.1176/appi.ajp.2016. 16010103
- Kingston T, Owoeye O, Kinsella A, Russell V, O'Callaghan E, Waddington JL (2011). Schizophrenia spectrum disorders in relation to the totality of psychosis: from first episode to long-term outcome. In Handbook of Schizophrenia Spectrum Disorders, Vol II: Phenotypic and Endophenotypic Presentations (ed. MS Ritsner), pp. 269–279.

- Laursen TM (2011). Life expectancy among persons with schizophrenia or bipolar affective disorder. Schizophrenia Research 131, 101–104.
- Lewis G, Dykxhoorn J, Karlsson H, Khandaker GM, Lewis G, Dalman C, Kirkbride JB (2020). Assessment of the role of IQ in associations between population density and deprivation and nonaffective psychosis. JAMA Psychiatry [Internet] 77, 729–736, https://jamanetwork.com/journals/ jamapsychiatry/fullarticle/2762528
- Lyne JP, Renwick L, O'Donoghue B, Madigan K, Kinsella A, Turner N, et al. (2014). Incidence, illness characteristics and early outcome in an Irish first episode psychosis service. Schizophrenia Bulletin [Internet] 153, S233, Available from: https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y& NEWS=N&PAGE=fulltext&D=emed15&AN=71728937
- Marshall M, Lewis S, Lockwood A, Drake R, Jones P, Croudace T (2005). Association between duration of untreated psychosis and outcome in cohorts of first-episode patients: a systematic review. *Archives of General Psychiatry*. 62, 975–983.
- McDonald K, Ding T, Ker H, Dliwayo TR, Osborn DPJ, Wohland P, Coid JW, French P, Jones PB, Baio G, Kirkbride JB (2021). Using epidemiological evidence to forecast population need for early treatment programmes in mental health: a generalisable Bayesian prediction methodology applied to and validated for first-episode psychosis in England. The British Journal of Psychiatry [Internet] 219, 383–391. doi: 10.1192/bjp.2021.18 [cited 2021 Mar 8].
- McGrath J, Saha S, Welham J, El Saadi O, MacCauley C, Chant D (2004). A systematic review of the incidence of schizophrenia: the distribution of rates and the influence of sex, urbanicity, migrant status and methodology. BMC Medicine 2, 1–22.
- McGorry PD, Edwards J, Mihalopoulos C, Harrigan SM, Jackson HJ (1996). EPPIC: an evolving system of early detection and optimal management. *Schizophrenia Research.* **22**, 305–326.
- Moher D, Liberati A, Tetzlaff J, Altman DG (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Medicine [Internet]* 6, e1000097, Available from: http://www.ncbi.nlm.nih. gov/entrez/query.fcgi?cmd=Retrieve
- Morgan MG, Scully PJ, Quinn JF, Kinsella A, Owens J, Waddington JL (2001). Schizophrenia and bipolar disorder as low incidence, selective male afflictions, in an epidemiologically complete rural population: the Cavan-Monaghan first episode study at 5 years. *Schizophrenia Research* 49, 40.
- NHS England, the National Collaborating Centre for Mental Health, National Institute for Health and Care Excellence (2016). Implementing the Early Intervention in Psychosis Access and Waiting Time Standard: Guidance [Internet]. Wakefield, https://www.england.nhs.uk/mentalhealth/ wp-content/uploads/sites/29/2016/04/eip-guidance.pdf
- NHS England (2020). Implementing the Early Intervention in Psychosis Access and Waiting Time Standard - Updated Commissioning Guidance,
- Ninuallain M, O'Hare A, Walsh D (1987). Incidence of schizophrenia in Ireland. *Psychological Medicine [Internet]* 17, 943–948.
- Nkire N, Scully PJ, Browne DJ, Baldwin PA, Kingston T, Owoeye O, Kinsella A, O'Callaghan E, Russell V, Waddington JL (2021). Systematic epidemiological and clinical comparisons across all 12 DSM-IV psychotic diagnoses in the Cavan-Monaghan First Episode Psychosis Study (CAMFEPS). Psychological Medicine [Internet] 51, 607–616, https://www. cambridge.org/core/journals/psychological-medicine/article/systematicepidemiological-and-clinical-comparisons-across-all-12-dsmiv-psychoticdiagnoses-in-the-cavanmonaghan-first-episode-psychosis-study-camfeps/ AADCF9A2341B4E245468CE3A158248F7
- Nordentoft M, Rasmussen JO, Melau M, Hjorthoj CR, Thorup AA (2014). How successful are first episode programs? A review of the evidence for specialized assertive early intervention. *Current Opinion in Psychiatry*. 27, 167–172.
- O'Donoghue B, Lyne JP, Renwick L, Lane A, Madigan K, Staines A, O'Callaghan E, Clarke M (2016). Neighbourhood characteristics and the incidence of first-episode psychosis and duration of untreated psychosis. *Psychological Medicine [Internet]* 46, 1367–1378, Available from: http:// journals.cambridge.org/abstract\_S003329171500286X
- O'Donoghue B, Lyne J, Roche E, Mifsud N, Renwick L, Behan C, Clarke M (2021). Risk of first-episode psychosis in migrants to the Republic of Ireland. *Psychological Medicine [Internet]*, 1–8, [cited 2021 Jun 24]. Available from:,

https://www.cambridge.org/core/product/identifier/S003329172100177X/type/journal\_article

- Omer S, Kirkbride JB, Pringle DG, Russell V, O'Callaghan E, Waddington JL (2012). Neighbourhood-level socio-environmental factors and incidence of first episode psychosis by place at onset in rural Ireland [Conference Abstract]. Schizophrenia Research 136, S221.
- Omer S, Kirkbride JB, Pringle DG, Russell V, O'Callaghan E, Waddington JL (2014). Neighbourhood-level socio-environmental factors and incidence of first episode psychosis by place at onset in rural Ireland: the Cavan-Monaghan First Episode Psychosis Study [CAMFEPS]. *Schizophrenia Research [Internet]* **152**, 152–157, Available from: http://www.ncbi.nlm. nih.gov/pubmed/24342585
- Owoeye O, Kingston T, Scully PJ, Baldwin P, Browne D, Kinsella A, Russell V, O'Callaghan E, Waddington JL (2013). Epidemiological and clinical characterization following a first psychotic episode in major depressive disorder: comparisons with schizophrenia and bipolar I disorder in the Cavan-Monaghan First Episode Psychosis Study (CAMFEPS). *Schizophrenia Bulletin [Internet]* 39, 756–765, https://ovidsp.ovid.com/ ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med10&AN= 23716714
- Richardson L, Hameed Y, Perez J, Jones PB, Kirkbride JB (2018). Association of environment with the risk of developing psychotic disorders in rural populations: findings from the Social Epidemiology of Psychoses in East Anglia study. *JAMA Psychiatry [Internet]* 1];75, 75–83, Available from: https://jamanetwork.com/journals/jamapsychiatry/ fullarticle/2664261

- Scully PJ, Quinn JF, Morgan MG, Kinsella A, O'Callaghan E, Owens JM, Waddington JL (2002). First-episode schizophrenia, bipolar disorder and other psychoses in a rural Irish catchment area: incidence and gender in the Cavan-Monaghan study at 5 years. *British Journal of Psychiatry [Internet]* 181, s3–9, https://www.cambridge.org/core/journals/the-british-journal-ofpsychiatry/all-issues
- Scully PJ, Owens JM, Kinsella A, Waddington JL (2004). Schizophrenia, schizoaffective and bipolar disorder within an epidemiologically complete, homogeneous population in rural Ireland: small area variation in rate. Schizophrenia Research [Internet] 67, 143–155, Available from: http://www.sciencedirect.com/science/article/B6TC2-49WN0TH-2/2/ 5f2c5574a990059a4a0d6301e164b4a3
- Waddington J, Baldwin P, Morgan M, Quinn J, Scully P, Kinsella A, *et al.* (2004). Incidence and demographics of first episode psychosis in major depressive disorder among an epidemiologically complete population: the Cavan-Monaghan first episode study at 7 years. *Schizophrenia Research* **70**, 30.
- World Health Organization. (2004). International Classification of Diseases (ICD) [Internet]. [cited 2021 Oct 14]. Available from: https://www.who.int/standards/classifications/classification-of-diseases
- Youssef HA, Kinsella A, Waddington JL (1991). Evidence for geographical variations in the prevalence of schizophrenia in rural Ireland. *Archives of General Psychiatry [Internet]* **48**, 254–258, Available from: http://www.ncbi. nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve