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Environmental risk factors for schizophrenia spectrum disorders around the globe: a mapping review of the literature

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Abstract

Aims. There is a substantial body of literature on environmental risk associated with schizophrenia. Most research has largely been conducted in Europe and North America, with little representation of the rest of the world; hence generalisability of findings is questionable. For this reason, we performed a mapping review of studies on environmental risk for schizophrenia spectrum disorders, recording the country where they were conducted, and we linked our findings with publicly available data to identify correlates with the uneven global distribution. Our aim was to evaluate how universal is the 'common knowledge' of environmental risk for psychosis collating the availability of evidence across different countries and to generate suggestions for future research identifying gaps in evidence.

Methods. We performed a systematic search and mapping of studies in the PubMed and PsycINFO electronic databases reporting on exposure to environmental risk for schizophrenia including obstetric complications, paternal age, migration, urbanicity, childhood trauma, and cannabis use and subsequent onset of schizophrenia spectrum disorders. This search focused on articles published from the date of the first available publication until 31 May 2023. We recorded the country where they were conducted. We downloaded publicly available data on population size, measures of wealth, medical provisions, research investment, and of quality research outputs per country and performed regression analyses of each predictor with the number of studies and recruited cases in each country.

Results. We identified 308 publications that included a sample size of 445,000 patients with schizophrenia spectrum disorders. The majority were conducted in northern Europe and North America, with large parts of the world totally unrepresented. In the associations between the number of environmental risk studies for schizophrenia with potential predictors, we found that neither population nor wealth or research investment were strong predictors of research outputs in the field. Interestingly, the stronger correlations were found for number of researchers per population and for indicators of top-end scientific achievements, such as number of Nobel laureates per country.

Conclusions. Our results demonstrate a gap of knowledge due to the underrepresentation of studies on environmental risk of schizophrenia spectrum disorders in large parts of the world. This has implications not only in the generalisability of any findings from research conducted in the Northern hemisphere but also in our ability to progress in efforts to make causal inferences about biological pathways to schizophrenia. These findings reinforce the need to focus research on populations that are underrepresented in research and underserved in health care.

Introduction

Schizophrenia is a severe mental disorder characterised by several psychopathological dimensions (i.e. positive, negative, cognitive, and affective symptoms), which encompass characteristic distortions of thinking and perception, interpersonal relating, cognitive impairments, affective flattening and restricted emotional resonance (Owen *et al.*, 2016). These abnormalities lead to impaired quality of life (Bobes *et al.*, 2022), reduced life expectancy (Hjorthøj *et al.*, 2017) and high disability-adjusted life-years (DALYs) (GBD 2018; He *et al.*, 2020).

Research has identified several risk factors, both genetic and environmental, associated with schizophrenia specifically or with psychotic disorders in general (Prata *et al.*, 2019; Radua *et al.*, 2018). A comprehensive umbrella review found strong evidence linking migration and ethnic minority status to psychotic disorders, while factors like childhood trauma and urbanicity showed suggestive evidence and advanced parental age showed weak or no association with psychotic disorders (Radua *et al.*, 2018). Other evidence points out that the most replicated

environmental risk factors associated with schizophrenia include advanced paternal age, obstetric complications, urbanicity, childhood adversities, migration or ethnic minority status and cannabis use (Vassos *et al.*, 2020).

Studies on the association between environmental risk factors and prevalence of schizophrenia are common and widely distributed as they are usually cross-sectional and easier to conduct. However, they are suffering from limitations when trying to explore causal inferences, as they cannot exclude the possibility of reverse causality, i.e. that the onset of the disorder may affect the environmental exposure and explain the observed association. For this reason, incidence studies, where the environmental exposure is measured before the onset of the disease are considered more pertinent and interpretable both for risk estimation and hypothesis formation of potential causation (Grimes and Schulz, 2002; Schulz and Grimes, 2002).

Moreover, a well-known limitation of research is whether findings from a study can be extrapolated to other populations and generalisability is always challenging. For this reason, it is important to conduct studies in different populations, to see if the measured effects are replicated and more important to examine if they hold a 'global truth', with significant importance in our understanding of the disorder.

Bearing this in mind, we performed a mapping review (Campbell *et al.*, 2023; Christou *et al.*, 2024) of studies examining the association between specific environmental risk factor measured before the onset of psychosis (paternal age, obstetric complications, urbanicity, childhood adversities, ethnic minority status, cannabis use) and schizophrenia or schizophrenia-related disorders, assigning the country where they were conducted and the total number of participants they included. Our aim was to evaluate how universal is the 'common knowledge' of environmental risk for psychosis collating the availability of evidence across different countries and to generate suggestions for future research identifying gaps in evidence. Using publicly available data, we explored the role of country characteristics in the geographical distribution of the conducted studies.

Methods

Relevant studies were identified by searching Pubmed directly and PsycINFO electronic database via OVID, from the date of the first available article up to 31 May 2023.

The following search term were used: (schizophrenia OR psychosis OR psychotic) AND (cohort OR incidence OR prospective OR longitudinal). These search terms were combined with specific terms for each environmental risk factors of interest: (1) for paternal age: paternal age; (2) for obstetric complications: Pregnancy Complications OR Obstetric Complications OR Infectious; (3) for urbanicity: urban rural difference OR urban OR urbanisation OR urbanicity; (4) for childhood adversities: child* AND (abuse OR trauma OR neglect OR incest OR loss OR adversity OR bullying); (5) for migration: migration OR ethnic minority OR immigrants OR migrants OR refugee); (6) for cannabis use: cannabis OR cannabis abuse. For a detailed search strategy for both electronic databases, see Supplementary Table 1.

Cross-references from the articles identified as well as an additional screening of the references of recent reviews or meta-analyses on environmental factors was made. Unpublished studies, conference abstracts or grey literature', not undergoing peer-review process, were not included. No language or age restriction was applied. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) has been proposed for use in mapping reviews and its recommendations were followed (Tricco *et al.*, 2018; Supplementary Table 2).

Inclusion and exclusion criteria

We included any cohort, incidence, prospective and longitudinal studies with evidence that the measured environmental factor predates the psychosis outcome, including schizophrenia (SZ, ICD-10 diagnostic code F20.x) and/or schizophrenia spectrum disorder (SSD, ICD-10 diagnostic code F22-29) and/or non-affective psychosis (NAP, ICD-10 diagnostic codes F20.x, F22-29) and/or first episode psychosis (FEP, ICD-10 diagnostic code F23). Further inclusion criteria were: diagnoses of psychosis using standardised structured interview, hospital records, or administrative registers; including a comparison group of healthy controls or population controls. Case-control, cross-sectional studies and any kind of studies where the exposure was collected retrospectively were included only if the exposure was dated before the onset of the outcome measure. In studies that had a mixed sample of affective and non-affective psychosis, if authors analysed affective and non-affective psychosis separately, we included the study and its results. However, if the study combined affective and non-affective psychosis in the same analysis, without a clear distinction, we excluded it.

Screening and data extraction

Articles were identified and assessed for eligibility independently by at least two of the investigators (S.T., S.S., F.M.C.M.). The final search results were imported into EndNote (version 20.6), where duplicates were removed. The records were then screened based on their titles, abstracts and full texts. The titles and the abstracts of all studies identified through the search strategy were examined, and studies that clearly did not pertain to the topic of interest were excluded. The full-text articles of the remaining studies were retained, and after duplicates removed, data extraction was conducted.

The following key information from eligible studies were extracted in duplicate: environmental risk factor investigated, name of first author, year, country and region; timeframe; indication of whether the studies had overlapping samples; diagnosis received (SZ, SSD, NAP, FEP); total sample size with number of cases; if association measures were reported; details regarding the risk factors.

To ensure accuracy and consistency in our analysis of the number of studies and participants by country and risk factors, we followed several rules. When multiple papers were published on the same cohort or included overlapping samples, we listed all papers when counting the number of studies per country. However, for participant counts, we either included the largest sample from these studies or summed the smaller, non-overlapping samples if their total exceeded that of the largest sample. When a study examined multiple environmental risk factors, we counted the number of subjects for each risk factor separately. Nonetheless, when counting the number of papers per country, each study was counted only once. When a study had more than one outcome (narrow schizophrenia or broader psychosis) the larger number of subjects was counted. In the case of papers reporting samples recruited in several countries we have listed the paper several times, allocating the corresponding number of subjects studied in each country. Any

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disagreement at either screening or extraction stage was resolved through consensus in meetings between the authors.

Determinants of geographical differences

To explore possible determinants of geographical differences in published research, we tested associations of the number of papers and number of cases with country characteristics from publicly available resources. These included population, total and per capita gross domestic product (GDP), both nominal and purchasing power parity (PPP) (Stepovic, 2019), number of doctors (total and per 10k inhabitants), research and development (R&D) spending (in PPP and as % of GDP), number of researchers per 1 million inhabitants, number of Nobel prizes in physics, chemistry, physiology or medicine and economics, as an index of top quality researchers across sciences, and number of publications per country indexed in Pubmed in the decade 2010–2019 (see Supplementary methods for details and Supplementary Table 3 for the extracted data). The number of cases in each study represents the number of patients with SSD within the study sample (see Supplementary Table 4 for details).

Statistical analysis

We performed bivariate correlations of each of these country indices with the number of papers published and the number of cases, first including only countries with at least 1 paper (28 countries) and second with all countries with a population over 4 M (131 countries), to include the smallest country with relevant publications in our list. To reduce multicollinearity, among highly correlated or conceptually similar predictors (e.g. the four variables measuring GDP, overall or per capita) we retained only the one which was mostly correlated with the number of papers and cases. Since we included countries' population among the independent variables, among similar predictors we preferred the one which was giving an index per capita rather than a total number.

For countries with at least one publication, we performed a series of simple regressions of each of the retained country characteristics with the total number of published papers and number of cases per country as dependent variables. Given the fact that the included predictors were still partially correlated, we performed multiple regressions to isolate the effect of each independent variable while controlling for the influence of all the others. For countries with population over 4 million, we performed Tobit regressions, which allows for censored data, as the majority of countries had zero papers and cases. All analyses were performed in R version 4.4.2 using the packages Hmisc, jtools, broom, ggstance, and plots were generated with corrplot, ggplot2, sf, rnaturalearth, rnaturalearthdata, rgeos.

Results

Included studies and characteristic of the analysed samples

The search yielded a total of 11,354 records potentially relevant for this systematic review. After excluding studies that based on titles and abstracts were clearly not related to our topic of interest ($n = 10{,}795$), the full text of the remaining studies ($n = 559$) was screened for inclusion. Once the duplicated and non-pertinent articles were removed, and after including studies from cross-references as well as from additional screening of the references from recent reviews or meta-analyses on environmental factors, 308 papers were included. Figure 1 summarises the flow chart of the study selection.

The identified 308 papers from the mapping review (see Supplementary Table 4 for details) reported 357 associations as some publications included more than one environmental factor: 43 studies investigated paternal age, 126 obstetric complications, 23 urbanicity at birth, 48 childhood adversities, 95 migration/ethnic minorities, 22 cannabis use (see Supplementary Table 5 for the geographical distribution of number of studies and cases per risk factor).

Number of studies and of cases with psychotic disorders published per country

The majority of the studies reporting associations between environmental risk and psychosis were performed in the UK ($n = 53$), Sweden ($n = 50$), Denmark ($n = 47$) and the US ($n = 34$). The geographical distribution of the studies per country ($n = 342$, as studies reporting multiple cohorts were counted for each participating country) is presented in Figure. 2. We did not identify any studies meeting our inclusion criteria in most of Africa, Central and South America and large parts of Asia, with few exceptions. The number of cases were highly correlated with the number of studies published in each country ($r = 0.89$). The countries with most included cases with schizophrenia and schizophrenia spectrum disorders were Sweden (82016), Denmark (64855), USA (54636), and the UK (50012) (see Supplementary Fig. 1).

Determinants of geographical differences

In order to select among highly correlated or conceptually similar predictors the ones to use in the multiple regression models, we first examined bivariate correlations of number of papers and cases with all the predictors in the 28 countries with at least one publication and in 131 countries with population over 4 M people. Country population was not correlated with any of the two outcomes. Among the four measures of wealth, GDP per capita nominal was mostly correlations with papers and cases. Among the two measures of medical resources (medical practitioners total N or per 10,000 population) the latter was mostly correlated with papers and cases. From the two measures of R&D spending (total or % of GDP) the latter was mostly correlated with papers and cases (Supplementary Table 6 and 7). Correlation plots of the retained variables are presented in Supplementary Fig. 2 and 3.

In simple regressions of country characteristics with numbers of papers published or cases included, the only significant associations at alpha < 0.05 were: (i) the number of researchers per 1 M population with papers and cases ($P = 0.023$ and 0.009, respectively), (ii) the number of Nobel prizes in sciences ($P = 0.036$ and 0.046 respectively) and (iii) R&D spending % of GDP with number of cases ($P = 0.033$). In the multiple regression model with each predictor adjusted for the others, the only nominally significant association ($P = 0.049$) was between the number of researchers per 1 M and number of cases (Table 1).

Among the full list of countries and regions, we selected the 131 countries with population over 4 M people, to include the smallest country with at least one publication. Bivariate correlations between numbers of papers and cases with the predictors were very similar with the previous analyses in the 28 countries with at least one publication (Supplementary Table 7, Supplementary Figure 3). In univariate Tobit models, with the exception of country population, all other predictors were strongly associated with

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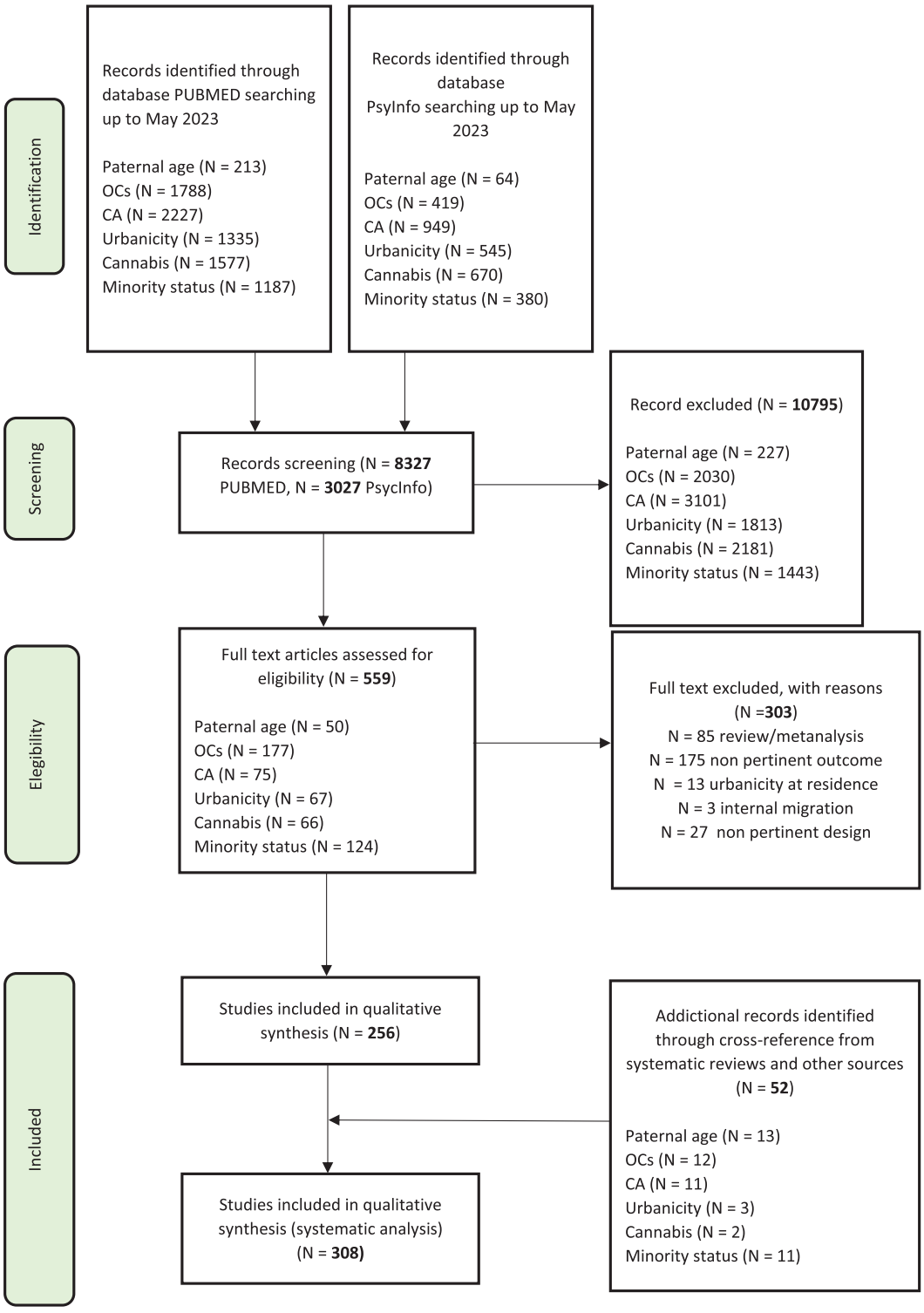

Figure 1. Flowchart of the studies' selection.

the number of papers published (all P-values $<$ 5e-05). In the multiple Tobit regression, with all the selected predictors adjusted for each other, only the association of the number of researchers per 1 M population with the number of papers and the number of cases remained significant ($P = 0.029$ and 0.009, respectively; Table 2).

Discussion

To the best of our knowledge, this is the first mapping review evaluating the geographical distribution of studies examining the association between the most replicated environmental risk factors for psychosis (paternal age, obstetric complications, urbanicity,

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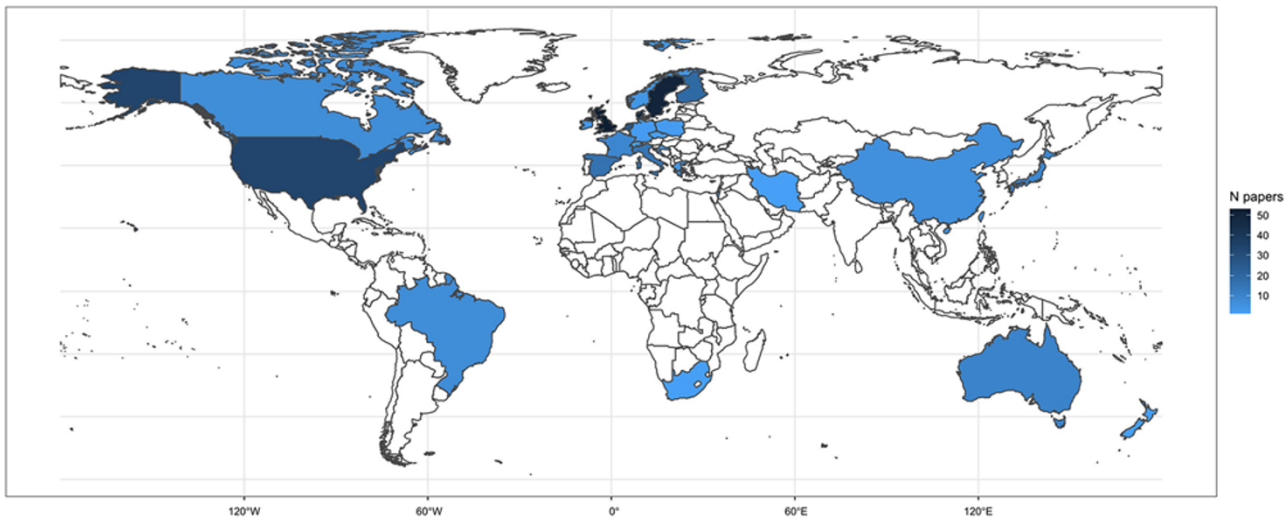

Figure 2. Geographical distribution of number of published papers per country.

Table 1. Univariable and multivariable linear regression results in 28 countries with at least one publication

		Studies per country			Cases per country		
		Est.	t	p	Est.	t	p
Univariable	Population	−0.46	−0.151	0.881	65	0.014	0.989
	GDP_percap_nom	3.76	1.269	0.216	6640	1.498	0.146
	Medical_per10k	4.50	1.487	0.150	7030	1.57	0.129
	R.D_perGDP	5.08	1.698	0.102	9649	2.255	**0.033**
	Researchers_per1M	7.13	2.422	**0.023**	12042	2.858	**0.009**
	Nobels	6.18	2.206	**0.036**	8813	2.093	**0.046**
	Publications	3.13	1.048	0.304	5036	1.134	0.267
Multivariable	Population	6.91	1.149	0.266	11165	1.313	0.206
	GDP_percap_nom	−6.57	−1.396	0.18	−8957	−1.348	0.194
	Medical_per10k	3.09	0.948	0.356	4550	0.987	0.337
	R.D_perGDP	−0.71	−0.141	0.889	−2598	−0.363	0.721
	Researchers_per1M	11.372	1.729	0.101	19661	2.116	**0.0499**
	Nobels	14.049	2.022	0.058	18664	1.901	0.073
	Publications	−9.89	−1.041	0.312	−11818	−0.881	0.39

childhood adversities, migration or ethnic minorities, cannabis use) and incident psychotic disorders.

The first main finding is that the identified studies have been conducted mostly in the Western world with large areas totally unrepresented. Notably, our review shows that out of the 357 cohorts investigating the association between risk environmental factors and psychosis, more than 50% were recruited in just four countries (UK, Sweden, Denmark, US) and most of them in high-income countries. There is a paucity of data on some continents such as Africa, South America and most parts of Asia. Psychological sciences have been criticised for relying on studies conducted in Western, Educated, Industrialised, Rich and Democratic (WEIRD) populations (Burkhard *et al.*, 2021; Rad *et al.*, 2018), which represented the minor part of the world population. Therefore, the risk is of transporting some theories and norms of human behaviour in contexts that differ in terms of ethnicity, cultural and social background, and economic resources compared to those in which they were generated.

The scarcity of evidence on the risk of psychosis in large parts of the world is aggravated by the shortage of genetic studies, the other significant contributor to the causation of psychosis, in non-European populations (Polderman *et al.*, 2016; Tosato and Lasalvia, 2009). Starting with genetic epidemiology research, the most comprehensive meta-analysis (Polderman *et al.*, 2015) demonstrated that the heritability of human traits has been estimated by twin studies from 39 different countries, with a large proportion of studies (34%) conducted in USA, with South America, Africa and Asia heavily underrepresented. Molecular genetic studies are similarly biased, as a disproportionate majority of participants in published

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Table 2. Univariable and multivariable tobit regression results in 131 countries with population > 4 million

		Studies per country			Cases per country		
		Est.	z	p	Est.	z	p
Univariable	Population	2.598	1.039	0.299	3856	1.109	0.267
	GDP_percap_nom	14.719	6.025	**<0.0011**	20790	6.088	**<0.0011**
	Medical_per10k	15.067	4.547	**<0.001**	20640	4.538	**<0.0011**
	R.D_perGDP	14.640	5.408	**<0.001**	20490	5.633	**<0.0011**
	Researchers_per1M	15.609	5.795	**<0.001**	21710	5.958	**<0.0011**
	Nobels	7.972	4.070	**<0.001**	11123	4.042	**<0.0011**
	Publications	9.725	4.505	**<0.001**	13666	4.542	**<0.0011**
Multivariable	Population	0.456	0.158	0.875	1581	0.429	0.668
	GDP_percap_nom	0.736	0.203	0.839	230.3	0.048	0.962
	Medical_per10k	3.785	1.154	0.248	4874	1.106	0.269
	R.D_perGDP	−4.744	−0.922	0.357	−8152	−1.2	0.230
	Researchers_per1M	14.176	2.187	**0.029**	22420	2.616	**0.009**
	Nobels	1.132	0.388	0.698	1900	0.501	0.616
	Publications	4.474	1.070	0.284	5907	1.092	0.275

genome-wide association studies (GWASs) are of European descent (Peterson *et al.*, 2019) with slow or questionable progress towards diversification the recent years (Fatumo *et al.*, 2022). As a result, potential benefits of genomic research in understanding disease aetiology and improving prediction and clinical care would lead to greater health inequality between different populations and parts of the world. For example, polygenic scores, which have been proved valuable tools for capturing genetic liability to disease, have poor transferability between populations (Martin *et al.*, 2019). Relevant to this review, polygenic prediction of schizophrenia is much higher in European (liability R2 of 7.3%) than in African ancestry cohorts (R2 of 1.7%), demonstrating that any potential clinical implementation is arguably closer in the former compared to the later population (Lewis and Vassos, 2022).

Considering the specific risk factors we included, one of the most extensively studied is obstetric complications (OCs) (Cannon *et al.*, 2002; Davies *et al.*, 2020) due to its central role to the neurodevelopmental model of psychosis (Murray and Lewis, 1988). Studying the role of obstetric complications in different environments is important for two reasons: firstly, the prevalence of OCs differs among world regions; for example, preterm birth is associated with 5–18% of pregnancies, with the highest rates occurring in Africa and North America (Romero *et al.*, 2014). The prevalence of obstetric haemorrhage is higher in Africa (27.7%) compared to North America (13.1%) and Europe (12.7%) (Nathan, 2019), but studies to verify the long-term outcome of both preterm birth and haemorrhage in Africa are lacking. Secondly, the unequal distribution of OCs worldwide is based on the essential maternal healthcare services that are universally used in high-income countries, but overwhelming disparities exist in many countries across Asia and Africa (Yaya and Ghose, 2019). This calls for action to ensure a better perinatal health, especially in low-income countries and raises the question of whether the high prevalence of OCs in countries with reduced childbirth assistance can lead to an increase in the incidence of adverse long-term outcomes, including psychosis.

Most evidence for the association of paternal age with psychosis comes from Scandinavian countries (McGrath *et al.*, 2014; Petersen *et al.*, 2011). In industrialised countries, the age in which one has children is postponed, prioritising educational and career goals. The decision to plan to have children also depends on policies implemented to support parenting and maternal work and the availability of economic benefits or kindergartens. Considering the global increase in education and life expectancy, a trend for delaying parenthood is expected; therefore, it is important to evaluate if late paternal age has a worldwide association with risk of psychosis in children.

Childhood adversities is a complex and heterogeneous phenomenon which has unequivocally been associated with increased risk for mental health problems including psychosis (Baldwin *et al.*, 2023; Varese *et al.*, 2012). According to the World Health Organisation, 36% of children have been psychologically abused, 23% physically abused, 16% neglected, 18% of the girls and 8% of the boys sexually abused worldwide (WHO, 2014). A recent systematic review (Moody *et al.*, 2018) found differences in self-reported lifetime prevalence for different types of childhood maltreatment not only between boys and girls but also among continents. For example, the prevalence of physical abuse is 12% for girls and 27% for boys in Europe, and reportedly higher in Africa (60% and 51% in boys and girls respectively); however, it is difficult to know whether the same criteria have been used to define childhood adversities and to evaluate their psychological impact in different social and cultural environments. The inclusion of low-income countries in psychosis research would allow us to accurately estimate the strength of the association and also identify resilience factors, potentially mitigating the effect of the trauma.

The evidence of association of urbanicity at birth and early development with psychosis comes almost exclusively from Northern Europe (Vassos *et al.*, 2012), where the presence of registers makes possible to link the person's place of birth to the number of inhabitants in the area. This association has been challenged in

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low- and middle-income countries where urbanicity at residence was not associated with the prevalence of psychosis (DeVylder *et al.*, 2018). However, incidence studies are missing in large parts of the world. Given that urbanicity is a proxy indicator for exposures that have not yet been identified, examining the geographical distribution of this effect can give us useful insights on the potentially causal underlying risk factors. As nowadays low-middle income countries are undergoing a profound social transformation, with large numbers of people moving into the cities, it is projected that they will soon contain the largest urban agglomerations of population (Kii, 2021). Therefore, there is an urgent need to research if this will come with an increased incidence of psychotic disorders.

There is a robust association between migration or ethnic minority status with psychosis (Cantor-Graae and Selten, 2005; Selten *et al.*, 2020). However, most evidence comes from migration to Europe, usually from similar or lower-income to high-income countries, with very limited data on the opposite direction or on internal migration. The raised rates in second-generation migrants suggest that schizophrenia is unlikely to predispose people to migrate because there is no evidence of an increased incidence in the countries of origin (Bhugra *et al.*, 1996). It can be argued that migration is a proxy risk since other factors as ethnic density in neighbourhoods of the host countries (Boydell *et al.*, 2001) or indicators of social disadvantage (Stilo *et al.*, 2017) have been associated to increased rates of psychosis, as proposed by the socio-developmental pathway to psychosis (Morgan *et al.*, 2010). Thus, if the odds of psychosis in migrants are associated with social vulnerability or the social adjustment/integration in the host country (Tarricone *et al.*, 2021), it is pertinent to test this hypothesis in different regions with different social structures.

Finally, the strong association between cannabis use and psychosis (Marconi *et al.*, 2016; Tosato *et al.*, 2013) is based on more diverse evidence from studies conducted in countries with very different drug-legislation and compounds available (Di Forti *et al.*, 2019). Cannabis remains by far the world's most-used drug, (UNODC, 2023), and the prevalence of use ranges from 16.6% of the population in the USA to 9.7% in West and Central Africa (UNODC, 2023), while cannabis use is less prevalent in East and Southeast Asia (1.2%) (Kalayasiri and Boonthae, 2023). It should be noted that in the last decade there is a long-term trend of increased THC content (almost by 50%) in seized cannabis herb in Western and Central Europe and the USA (UNODC, 2023), and high-potency cannabis increase the risk of dependence and psychotic disorders (Connor *et al.*, 2021). Similar to other environmental risk factors, expanding research on cannabis and psychosis in areas of the world with different habitual use and THC concentrations would be very valuable.

From our exploratory analysis of the association of the number of papers and recruited cases per country with a variety of potential predictors, the number of researchers per population stands out as the only variable associated with research output when adjusting for all other predictors. The only other predictors nominally associated with research output in 28 countries with at least one publication were the number of Nobel laureates in science and the percentage of GDP invested in research and development. These findings suggest that a country's focus on research both at baseline (number of researchers employed, R&D spending) and at the higher end (number of Nobel laureates) are among the strongest predictors of published research outputs in the field of environmental risk for incidence of psychosis.

It is remarkable that the total population had no effect on the number of publications. Similarly, the wealth of countries measured as GDP total and per capita, the number of medical practitioners or the number of publications in PubMed during the last decade before covid were not significantly associated with research output in the joint model adjusting for all the predictors. When examining bivariate correlations in the analysis of countries with population over 4 M, it was observed that out of the measures of wealth, GDP per capita rather than total GDP was mostly correlated with the number of relevant publications. Similarly, doctors per population unit rather than total number of doctors and R&D % of GDP rather than total R&D expenditure are mostly correlated with the number of cases. These findings indicate that rather than the total resources of countries, it is the density of researchers or the prioritisation of public spending in research and development mostly associated with research output in this field.

The findings should be interpreted in the context of various strengths and limitations. The scale of this review, examining six well-established environmental factors, which identified 308 studies meeting inclusion criteria allowed us to examine the distribution of published research at a global level and to analyse country characteristics as predictors of the volume of research outputs. We acknowledge that this is a non-exhaustive list but includes some of the most replicated and validated environmental risk factors for psychosis (Vassos *et al.*, 2020). Our mapping review was conducted without linguistic limitations, so the likelihood of missing papers published in non-English-language journals is minimal. It should be noted that the electronic databases we used for our search (PubMed and PsycINFO) are dominated by papers in English language and it is possible that studies from researchers objecting to the globalisation of science may be underrepresented. The heterogeneity between studies in the diagnosis of inclusion did not allow us to draw conclusions regarding schizophrenia specifically, but to study the association between environmental factors and a broader spectrum of psychotic disorders. Finally, a certain heterogeneity in the quality of the extracted data was found because in some papers it was not possible to extract either the timeframe, or the region of recruitment. This lack of information may not have allowed us to correctly identify all the overlapping cohorts, but since this limitation is relevant to a small number of papers, we do not believe that this has affected the bigger picture of our findings.

It is interesting to note that the strongest evidence of association between environmental factors and psychosis comes from Scandinavian countries, such as Sweden and Denmark, which have long-standing comprehensive national and health registers. These countries have a public health system, easily accessible, usually free of charge, where diagnostic and treatment pathways of care are standardised and systematically recorded. In addition, preventative measures and early intervention services potentially influence the incidence and outcome of first episode psychosis. This type of health organisation is not available in a large part of the world, which further highlights the need for a global representation of research on risk for psychosis.

Conclusions

In summary, our mapping review provides evidence that almost the totality of research on environmental risk for psychosis has been conducted in high-income countries, mostly including non-ethnically diverse populations from North America and Western Europe. Our findings reinforce the need to focus research on populations that are underrepresented and underserved in health care

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by enabling local investment or funding training and recruitment of researchers in low-income countries.

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