*Epidemiology and Psychiatric Sciences*

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# Can we interrogate public databases to fill critical gaps in mental health epidemiology? Testing the association between cannabis and psychosis in the UK as an example

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**Abstract**

The psychoactive properties of cannabis have been known forever. Since 1987, several prospective studies have suggested an increased risk of psychosis among cannabis users, with alternative explanations failing to account for such an effect. A cause–effect relationship has thus been implied. Further evidence has indicated that there is a dose–response relationship, and high-potency cannabis varieties confer the greatest risk of psychosis. As cannabis use has become more common over the last decades, one would expect a related increase in the number of schizophrenia cases. However, evidence in this regard remains equivocal for several reasons, including relying on databases that are not primarily designed to address such question and the issue that solid information regarding the incidence of schizophrenia is a relatively recent acquisition. Recent years have seen the development of online web publications, such as Google Trends and "Our World in Data", where data are explorable and interactable for tracking and comparing trends over specific periods and world regions. By using such databases, we believe that the question whether changes in cannabis use are associated with changes in schizophrenia rates can be answered, at least partly. Therefore, we tested these tools by evaluating trends in cannabis use and both cases and prevalence of schizophrenia in the United Kingdom, one of the countries where the incident rates for psychotic disorder have been suggested to be particularly increased by cannabis consumption. Crossing data from these tools revealed that interest in cannabis has been growing at the country level for over 10 years, with a parallel overlapping raise in psychosis cases and prevalence. Following up on this example, let us think of how many public health opportunities these public resources may offer. The question now is whether public health interventions for the benefit of the general population will follow suit.

## Editorial

**Cite this article:** Di Gennaro G, Colizzi M (2023). Can we interrogate public databases to fill critical gaps in mental health epidemiology? Testing the association between cannabis and psychosis in the UK as an example. *Epidemiology and Psychiatric Sciences* **32**, e40, 1–4. https://doi.org/10.1017/S2045796023000537

Received: 13 April 2023
Revised: 1 May 2023
Accepted: 20 May 2023

**Keywords:**
epidemiology; health outcomes; schizophrenia; social environment; statistics

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The psychoactive properties of cannabis use have been orally handed down since 2700 BC (Brand and Zhao, 2017), first paid attention by the physician Iban Beitar (1197–1248 BC) (Dhunjibhoy, 1930) and much later brought to the limelight of modern medicine by the French psychiatrist Jacque-Joseph Moreau in 1845 (Moreau, 1845). The latter highlighted how hashish, the cannabis plant–derived resin, could precipitate acute psychotic reactions like those observed in psychosis patients, fuelling the debate up to the current century whether it may have a causal role in the pathophysiology of schizophrenia-spectrum disorders (Abel, 2005). Already in 1930, drug-induced psychosis was considered the most common type of psychosis in India after both affective and non-affective psychoses, with hemp, a cannabis variety, as the main drug suggested (Dhunjibhoy, 1930).

Over the last 20 years, the topic has been set on fire, with reviews suggesting a higher risk of any psychotic outcome in people who have ever used cannabis (Moore *et al.*, 2007), which increases depending on level of use (Marconi *et al.*, 2016), independently of the confounding effect of temporary intoxication (Moore *et al.*, 2007). A dose-dependent effect of cannabis use has been also implicated in psychosis relapse, with increased frequency of use and cannabis potency putting patients at higher risk (Schoeler *et al.*, 2016). Such evidence has raised public health concern, especially considering the increasing consumption of cannabis for recreational purposes over the years, with about 200 million users worldwide. Also, trends in decriminalizing or legalizing cannabis use in many countries are likely to have a further impact on the phenomenon of cannabis-induced psychosis (Colizzi and Murray, 2018).

To establish an association between cannabis use and psychosis, and possibly a cause–effect relationship, the topic has been studied in different lines of research, with converging results (Colizzi and Bhattacharyya, 2020). Several prospective studies have been carried out since 1987, with a follow-up of 1 to 35 years, supporting a twofold increased risk of psychosis as a function of cannabis use (Colizzi and Bhattacharyya, 2020). As alternative explanations, some studies



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have addressed the confounding effect of other substances (Arseneault *et al.*, 2002) and tobacco (Di Forti *et al.*, 2015), suggesting a specific effect of cannabis in increasing risk of psychosis. Other studies have attempted to control for the confounding effect of preexisting psychopathology in cannabis users, finding that it may reduce (Henquet *et al.*, 2005) or be irrelevant (Arseneault *et al.*, 2002) but not deny the risk of developing psychosis among cannabis users. Further, a self-medication hypothesis has never been established (Spalletta *et al.*, 2007), and although a bidirectional relationship between cannabis use and psychosis may exist (Ferdinand *et al.*, 2005), it is unlikely that there is a full reverse causality entirely accounting for the effect of cannabis on psychosis (Colizzi and Bhattacharyya, 2020). Finally, cannabis use and psychosis have been found to share common genetic susceptibility to a small extent, without per se excluding the possibility that cannabis had a causal role in the development of psychosis (Power *et al.*, 2014).

More specifically, looking at a cause–effect relationship, studies indicate a variation in the incidence of psychosis across Europe (Di Forti *et al.*, 2019), as well as a higher magnitude of the association as a function of cannabis consumption (Di Forti *et al.*, 2015). Consistency of findings also emerges in terms of poorer psychosis outcome (Colizzi *et al.*, 2016) and cognitive function (Colizzi and Bhattacharyya, 2017) in the context of cannabis use. Specificity (Niemi-Pynttari *et al.*, 2013) and temporal sequence (Murray *et al.*, 2017) of the association have been proven along with evidence for a biological gradient (i.e., dose–response association) (Marconi *et al.*, 2016) and coherence from experimental proof that exposure to cannabis main ingredient, delta-9-tetrahydrocannabinol, produces psychosis-related behavioural effects (Colizzi *et al.*, 2019b) that are biologically plausible (Colizzi *et al.*, 2019a).

Of the above, there is an issue around the evidence that cannabis use may play a role in increasing the risk of psychosis that perhaps has dominated the debate more than all other aspects combined. As cannabis use has become more common over the last decades, one would expect a related increase in the number of schizophrenia cases. A study exploring the incidence of schizophrenia in South London reported that it doubled between the sixties and the nineties, with a parallel increase in the rate of cannabis use in the year before symptom presentation for those presenting with schizophrenia (Boydell *et al.*, 2006). However, another study from the UK failed to provide evidence of an increase in the incidence of psychotic disorders because of an increase in cannabis consumption at the population level (Frisher *et al.*, 2009). Evidence in this regard remains equivocal for several reasons, including, but not limited to, relying on databases that are not primarily designed to address such questions as well as the issue that, until about 25 years ago, only a few studies had provided solid evidence regarding the incidence of schizophrenia. In 2004, a large systematic review of 158 studies from 33 countries found substantial variations in the incidence of schizophrenia because of several risk factors, such as gender, urbanicity, and immigration status (McGrath *et al.*, 2004). The fact is that the incidence of schizophrenia is higher in countries such as the UK where high-potency cannabis is very popular in the market compared with countries such as Italy where more traditional and less potent cannabis varieties are still consumed (Di Forti *et al.*, 2019). Anyhow, lacking high-quality, comprehensive studies looking at temporal trends in the incidence of psychosis, especially in the context of cannabis use, we are currently unable to either support or disregard the possibility that a population-level increase in cannabis use has led to an increase in the incidence of psychosis worldwide.

To understand the evolution of a public health phenomenon, recent years have seen the development of online web publications where data are explorable and interactable for tracking and comparing trends over specific periods and world regions (Mathieu *et al.*, 2021). By using such databases, we believe that the question whether changes in cannabis use are associated with changes in schizophrenia rates can be answered, at least partly. Therefore, we tested these tools by evaluating trends in cannabis use and both cases and prevalence of schizophrenia in the UK, one of the countries where the incident rates for psychotic disorder have been suggested to be particularly increased by cannabis consumption (Di Forti *et al.*, 2019). An estimate of the number of cases and prevalence of schizophrenia in the UK was obtained from the so-called "Global Burden of Disease", a research program that involves thousands of researchers across the globe and looks at mortality and disability related to disease, injury, and risk factors. The results of this project are freely available on the dedicated website (https://www.healthdata.org/gbd) as well as on other providers such as "Our World in Data" (https://ourworldindata.org). Then, the volume of web searches in the UK related to the topic "Marijuana" in the time period 2005–2019 was extracted from Google Trends (https://trends.google.com/), an open-source website that can be used to detect the number of searches that take place over a specific period of time (e.g. daily, weekly or monthly) and over a specific period of interest. It calculates the historical values as the Relative Search Volume (RSV), which is a standardized measure consisting in the percentage of the highest value in the series (Nuti *et al.*, 2014). Google Trends represents one of the most used tools in digital epidemiological studies, and over the past decade, Google searches of specific keywords have been used as indicators of the prevalence of a variety of diseases. Also, they have been used more generally as a tool to identify the level of people's interest in a health topic (Breyer *et al.*, 2011; Flanagan *et al.*, 2021; Johnson and Mehta, 2014; Schootman *et al.*, 2015; Vasconcellos-Silva *et al.*, 2017). It is clear that this tool is invaluable for both monitoring a population's behaviour or interests in the past, as well as for making future estimates in order to intervene appropriately through the necessary public health interventions (Dugas *et al.*, 2013; Prasanth *et al.*, 2021). Subsequently, the mean annual RSV of marijuana was calculated for comparison with the number of annual cases as well as the prevalence of schizophrenia over the same period. Finally, to facilitate the graphical comparison, data were represented on the $z$-scores scale. Data analysis supported a strong correlation of the annual mean RSV pattern of cannabis use, with the trajectory of both schizophrenia cases and prevalence in the UK (Figure 1A and B).

Governments and public health officials need to develop the most effective strategies to tackle the risk of cannabis-induced psychosis in a way that minimizes morbidity and healthcare costs from the potential development of the disorder. The results that we present here are an example of how crossing public datasets could support it. On the one hand, Google Trends tool allows analysts to track interest in cannabis over time in a specific country. Combined with epidemiological data, it serves as input for stakeholders to understand how such interest in cannabis translates in cases of psychosis, with the goal of prioritizing strategies at the country level. Communicating such evidence on the risk of cannabis use is in turn essential for building public trust and reducing the harmful potential of its use.

Establishing a cause–effect relationship between two observed trends is beyond the scope of these resources. Thus, the evidence provided here that interest into cannabis and psychosis rates have

https://doi.org/10.1017/S2045796023000537 Published online by Cambridge University Press

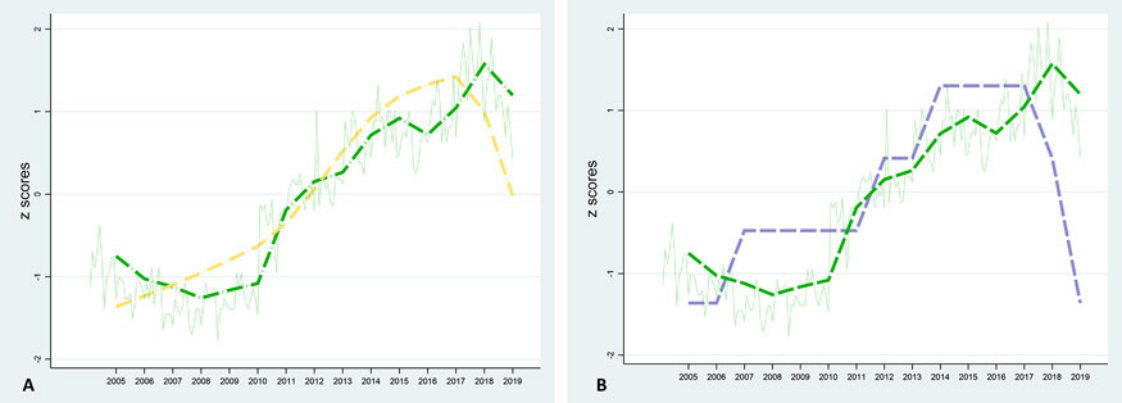


**Figure 1.** Correlation of the online search volume trajectory of the topic "Marijuana" (green dashed line) with number of cases (orange dashed line (A), Pearson's $r$ 0.87, $p < 0.001$) and prevalence (purple dashed line (B), Pearson's $r$ 0.60, $p = 0.019$) of schizophrenia. Data are expressed as $z$-scores to facilitate graphical comparison. Time span: 2015–2019.

increased in a very similar way is not sufficient per se to imply causation. Also, testing these tools revealed another reason for caution in data interpretation, that is the shortness of the time series that makes the presented statistical analysis highly exploratory. However, it is conceivable that such tools can be refined to offer a more systematic study of a specific phenomenon, that is, in the example provided here, a more frequent monitoring of schizophrenia cases and prevalence in order to bring out the volume of online interest in marijuana as a practical info-surveillance and forecasting tool. If we want to understand more about exposure to a risk factor, then we need to know how many people are affected by it. Coming back to our study example, knowing how many people interested in consuming cannabis are out there would allow having our ear to the ground in terms of policy responses or risk perceptions. This dataset fills this gap. It clearly shows that interest in cannabis has been growing at the country level for more than a decade. On parallel, an overlapping raise in psychosis cases and prevalence has been documented over the same period and region. Let us think of how many public health opportunities these public resources may offer. The question now is whether their global roll-out will produce evidence that is matched with public health interventions that can be administered quickly and equitably across the country, for the benefit of the general population.

**Availability of data and materials.** Data used in this Editorial are freely accessible on the dedicated websites (https://www.healthdata.org/gbd, https://ourworldindata.org and https://trends.google.com/).

**Acknowledgements.** We thank Professor Robin Murray for his comments on an early draft.

**Financial support.** This research received no specific grant from any funding agency, commercial, or not-for-profit sectors.

**Competing interests.** Outside this work, Marco Colizzi has been a consultant/advisor to GW Pharma Limited, GW Pharma Italy SRL and F. Hoffmann-La Roche Limited. Gianfranco Di Gennaro declares no conflict of interest.

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https://doi.org/10.1017/S2045796023000537 Published online by Cambridge University Press