

# Cannabis and psychosis: the Maltese contribution

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## Abstract

Three different Maltese scientists have contributed to research on the link between cannabis and psychosis. The object of this article is to review and chronicle the work that has been done by these three colleagues in this field. Work has helped to establish whether cannabis causes psychosis, whether the continued use of cannabis by patients with schizophrenia affects the course of the disease and its treatment, and whether or not it is possible to change the habit of cannabis use in patients who have a psychotic disorder.

## Introduction

The relationship between cannabis and psychosis has been the focus of much study in recent years. Fortuitously, much work in this area has been carried out by Maltese researchers, mostly working in the UK, but on occasion in Malta. This contribution outlines the Maltese contribution to medical knowledge in this field.

## Keywords

Cannabis, psychotic illness, schizophrenia

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## Does cannabis cause psychosis [schizophrenia]?

There has been much debate recently as to whether cannabis use increases the risk of developing chronic psychotic disorders such as schizophrenia. The first study to provide compelling evidence that cannabis use may cause schizophrenia was that of Andreasson & Allebeck,<sup>1</sup> who carried out a 15 year follow up of 50 465 Swedish Conscripts who had self reported on their cannabis use at age 18. They found that those who tried cannabis by age 18 years were 2.4 times more likely to develop schizophrenia than those who had not. The risk of developing schizophrenia was related in a dose-response way to the number of times cannabis had been used. Compared with those who had not used cannabis, the risk of developing schizophrenia was 1.3 times higher for individuals who had used cannabis 1 to 10 times, 3 times higher for individuals who had used cannabis between 1 and 50 times, and with a 6-fold increase in risk for those who had used cannabis more than 50 times. These risks were substantially reduced, but persisted nevertheless, after statistical adjustment for variables that could confound, or explain, this association, including having a psychiatric illness at age 18 years and having divorced parents. In the adjusted analysis, those who used cannabis 1 to 10 times were 1.5 times more likely, and those who used cannabis 10 times or more 2.3 times more likely to develop schizophrenia, compared with individuals who never used cannabis. Although Andreasson and others argued that these findings supported a causal relationship between cannabis and schizophrenia, a number of limitations were raised regarding this study. As a means to address these limitations, a follow-up study of this same cohort was conducted by Stanley Zammit,<sup>2</sup> a Maltese Doctor working in Cardiff, and others who reported risk of schizophrenia over a 27-year follow-up period that covered most of the risk period for the onset of psychotic disorders. This study improved on the original study in a number of ways. First, the psychiatric register provided more complete coverage of all individuals diagnosed with schizophrenia. Second, statistical control was improved and included a wider range of potentially important confounding variables, including other drug use, IQ, social integration and other established risk factors for schizophrenia. Third, to examine the possible role of a prodrome of schizophrenia leading to cannabis use at age 18 (the 'self-medication hypothesis'), the authors also examined cases that occurred more than 5 years after conscription, by which time any prodrome of schizophrenia would have been

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evident. Fourth, the authors also undertook separate analyses of individuals who only reported using cannabis at the initial assessment to try and tease out the effects of cannabis from those of other drugs. Zammit et al.<sup>3</sup> found that cannabis use at baseline predicted an increased risk of schizophrenia during the follow-up period in a dose–response manner. They demonstrated that the relation between cannabis use and schizophrenia persisted when they controlled for the effects of other drug use and other potential confounding factors, and that the association was very unlikely to have been due to self-medication. They estimated that, if the association was indeed causal, then about 13% of schizophrenia cases could be averted if all cannabis use was prevented.

Subsequently Zammit and others conducted a systematic review of cannabis use and risk of psychotic or affective mental health outcomes.<sup>9</sup> This was carried out to clarify whether cannabis can cause psychotic or affective symptoms that persist beyond transient intoxication. They systematically reviewed the evidence pertaining to cannabis use and occurrence of psychotic or affective mental health outcomes. Studies were included if longitudinal and population based. 35 studies from 4804 references were included. There was an increased risk of any psychotic outcome in individuals who had ever used cannabis (pooled adjusted odds ratio=1.41, 95% CI 1.20–1.65). Findings were consistent with a dose-response effect, with greater risk in people who used cannabis most frequently (2.09, 1.54–2.84). Results of analyses restricted to studies of more clinically relevant psychotic disorders were similar. Depression, suicidal thoughts, and anxiety outcomes were examined separately.

Findings for these outcomes were less consistent, and fewer attempts were made to address non-causal explanations than for psychosis, and the authors were less confident about a causal relationship between cannabis use and these outcomes than they were for psychosis. A substantial confounding effect was present for both psychotic and affective outcomes, but the authors nevertheless concluded that the evidence that cannabis use increased the risk of psychotic illnesses such as schizophrenia was strong enough that individuals using cannabis should be advised about this risk.

### **How does cannabis use impact on psychosis?**

Anton Grech, a Maltese Doctor working in both Malta and the Institute of Psychiatry, London, and others carried out a comparison between psychotic patients from two different cultural settings, South London and Malta.<sup>5</sup> Cannabis consumption and use of other substances was much more widespread in the former. In both centres, psychotic patients abused substances much more than controls. A particularly strong association between cannabis abuse and psychosis was shown by the fact that the odds ratio for cannabis abuse in patients over controls was greater in both centres than the odds ratio for substance abuse in general or for any other type of substance. This showed a fairly constant association between cannabis and psychosis.

Grech and others also have recently studied cannabis use and outcome of recent onset psychosis.<sup>6-8</sup> They wished to test the hypothesis that recent onset psychotic patients who use cannabis will have psychotic symptoms that are more severe and more persistent than those who do not use cannabis. They carried out a 4-year follow-up study of a cohort of 119 patients with recent onset of psychosis. The patients were divided into four groups according to duration of cannabis use, taking index admission and follow-up as reference points. Those subjects who persisted in the use of cannabis had more positive (but not negative) symptoms and a more continuous illness at follow-up. The main limitations of the study were: the relatively small sample size, and that the excess of male subjects and the presence of cannabis induced psychosis could have a confusing impact on the interpretation of the results. They concluded that it is possible that psychotic patients who use cannabis are at a greater risk of a more continuous illness with more positive symptoms than those who do not.

Zammit and colleagues also carried out another systematic review.<sup>4</sup> Investigating whether cannabis use affects the outcome of psychotic disorders as it is unclear if research findings support clinical opinion that cannabis use leads to worse outcomes in people with psychosis, or whether this impression is confounded by other factors.

They observed that cannabis use was consistently associated with increased relapse and non-adherence. However it was noted that few studies adjusted for baseline illness severity, and most made no adjustment for alcohol, or other potentially important confounders. When these confounders were taken into consideration, the results became less convincing. Therefore it was difficult to be confident that most of the associations reported were specifically due to cannabis. Despite clinical opinion, it remains important to carry out further research to establish whether cannabis is harmful, what outcomes are particularly affected by cannabis use, and how these effects occur. Furthermore, unlike determining whether or not cannabis use increases risk of rare disorders such as schizophrenia, studies that examine questions about the effects of cannabis on the outcome of people with psychosis are very feasible.

### **Can cannabis use be reduced by psycho-education in psychotic patients?**

Mark Agius, a Maltese doctor working in Luton, studied this issue in reporting on the outcomes of a service working for three years with patients who had suffered a first episode of psychosis. A group of patients in the early intervention (EI) service were compared to a group of patients who received 'treatment as usual in Community Mental health teams. More patients admitted to using illicit drugs at the beginning of the intervention in the EI group than in the CMHT group. Less patients in the EI group than in the CMHT group were using illicit drugs at the end of three years, indicating more patients stopped using illicit drugs in the EI group than in the CMHT group. This may be because of more effective psycho-education

in the EI group.<sup>10-11</sup> Clearly, given what has been shown by Grech and by Zammit,<sup>4,6-8</sup> that is, that cannabis makes psychotic illnesses worse, then interventions to reduce cannabis in this group are very important. The psych-education provided within the EI group is a relatively simple and cheap intervention, but could make a substantial difference to morbidity at a population level.

## Conclusion

Maltese doctors have made a significant contribution to the development of knowledge about the relationship between cannabis and psychosis. While they have mostly worked in the UK, at least on one occasion, they have carried out research in Malta itself. Our aim in this article has been to chronicle the contribution of Maltese medical scientists to this area of research.

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