So near yet so far: why won’t the UK prescribe medical cannabis?

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ABSTRACT
Although cannabis-based products for medicinal use are now legal in the UK, it is still challenging for patients to gain access, and only very few National Health Service prescriptions have been written to date. This paper attempts to make sense of why the UK lags behind so many other countries which also have legalised medical cannabis. From consulting with parents and patients, prescribers, pharmacists and decision-makers it seems that there are a series of distinct barriers to prescribing that need to be overcome in order to improve patient access to medical cannabis in the UK. These include concerns about the perceived lack of scientific evidence. To alleviate these concerns, we highlight the importance of patient-centred approaches including patient-reported outcomes, pharmacoepidemiology and n=1 trials, which can contribute to the development of the evidence base for medical cannabis. We hope that this paper will help policymakers and prescribers understand the challenges to prescribing and so help them develop approaches to overcome the current situation which is detrimental to patients.

INTRODUCTION
In November 2018 when the UK made cannabis-based products for medicinal use (CBPMs) legal most people assumed these would immediately be made available to patients, but they were wrong. In the year since almost no National Health Service (NHS) prescriptions have been issued1 and less than a hundred have been made available from private providers at a cost of at least £1000 a month.2 For these reasons, some parents of children with severe epilepsy continue to go overseas to get their children access to the only treatment which has proven to be effective for their condition, that is, a cannabinoid medication. Moreover, the vast majority of the estimated 1.4 million medical cannabis users3 source from the black market with its problems of illegality, unknown quality, content and provenance. Given the substantial evidence of utility of CBPMs in many disorders as identified in the US National Academy of Sciences review in 20174 this failure of delivery in the UK seems odd and, to many, inexcusable.

CONCERNS ABOUT PERCEIVED LACK OF EVIDENCE
Statements such as ‘insufficient evidence of efficacy’ or ‘it is too dangerous’ are common and used even in the face of strong personal evidence from patients that CBPMs work and, in many cases, can be life-changing and well tolerated. Many doctors fail to include the evidence of the patient’s lived experience and cite the lack of placebo-controlled trials in every possible indication for their hesitation to prescribe. While tens of thousands of individual patient reports of the therapeutic value of CBPMs as in the Canadian and Minnesota databases5 6 do not equate to the so-called gold-standard double-blind randomised controlled trial (RCT) level of proof, they are highly suggestive of a pattern of evidence which should be taken seriously rather than summarily dismissed. These large-scale databases could be further interrogated and systematically analysed to collate patient-reported outcomes (PROs) and other existing evidence for peer-reviewed publications. In the UK, Drug Science recently launched Project TWENTY21, the largest national medical cannabis registry in Europe, with the aim to create a structured body of


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ABSTRACT

Strengths and limitations of this study

- There are a series of distinct barriers to prescribing medical cannabis that need to be overcome in order to improve patient access in the UK.
- Concerns about the perceived lack of randomised controlled trial evidence are misplaced as many patient-centred approaches including patient-reported outcomes, pharmacoepidemiology and n=1 trials can be applied.
- Thousands of UK patients self-medicating with illicit cannabis-based products for medicinal use and the international database evidence suggest this new class of drugs offers a significant advance in treatment for many in whom current medicines are either ineffective or poorly tolerated.
- We hope that this paper will help policymakers and prescribers understand the challenges to prescribing and so help them develop approaches to overcome the current unsatisfactory situation.

INTRODUCTION

In November 2018 when the UK made cannabis-based products for medicinal use (CBPMs) legal most people assumed these would immediately be made available to patients, but they were wrong. In the year since almost no National Health Service (NHS) prescriptions have been issued1 and less than a hundred have been made available from private providers at a cost of at least £1000 a month.2 For these reasons, some parents of children with severe epilepsy continue to go overseas to get their children access to the only treatment which has proven to be effective for their condition, that is, a cannabinoid medication. Moreover, the vast majority of the estimated 1.4 million medical cannabis users3 source from the black market with its problems of illegality, unknown quality, content and provenance. Given the substantial evidence of utility of CBPMs in many disorders as identified in the US National Academy of Sciences review in 20174 this failure of delivery in the UK seems odd and, to many, inexcusable.

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evidence for the effectiveness and tolerability of medical cannabis for a broad range of conditions (https://drug-science.org.uk/project-twenty21/). Moreover, Drug Science is also currently working on audits using existing data of patients with epilepsy prescribed medical cannabis, showing, for example, a clear reduction of seizures after medical cannabis use.

The major criticism of the lack of placebo-controlled trials is misplaced. Prescribers often mistakenly state that without these they cannot prescribe. However, there are over 50 medicines or indications that have been licensed by Food and Drug Administration and/or European Medicines Agency between 1999 and 2014 without RCT data.

Moreover, the ex-head of National Institute for Health and Care Excellence (NICE) and the Medicines and Healthcare products Regulatory Agency, Sir Michael Rawlins, challenged this RCT preconception in the 2008 Harvean Oration, highlighting that:

Randomised controlled trials (RCTs), long regarded at the ‘gold standard’ of evidence, have been put on an undeserved pedestal. Their appearance at the top of ‘hierarchies’ of evidence is inappropriate; and hierarchies, themselves, are illusory tools for assessing evidence. They should be replaced by a diversity of approaches that involve analysing the totality of the evidence-base.

Placebo-controlled double-blind trials are clearly a very important element of medicine where their primary role is to provide evidence for companies to get a marketing authorisation. Such trials are done in tightly selected patient groups that are not representative of the average patient who often has many different medical comorbidities. Therefore, even when such trials are positive, they are only suggestive of efficacy in the wider patient groups and other approaches such as effectiveness trials or clinical audits are required to properly estimate real-world value to individual patients.

Of these new approaches, PROs are probably the most significant development. These have received immense investment from the US National Institutes of Health (NIH) and many new scales have been developed for this purpose. PRO measures are now required as elements of outcome measures for clinical trials funded by the NIH in the USA (https://commonfund.nih.gov/promis/index). PROs put more emphasis on the patient’s life and well-being and have been shown to be more sensitive to the effects of medical cannabis than traditional symptom-based measures. For example, a large recent naturalistic German study on pain syndromes using PROs found adding a CBPM very significantly improved outcomes in patients with neuropathic pain. Other recent papers showing real-world benefits from CBPMs using patient reports have been reported in Parkinson’s disease and autism. NICE has developed a cadre of expert patients to advise them of the patients’ perspective (https://www.scie-socialcareonline.org.uk/the-expert-patients-rogramme/).

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any prescriber resist similar claims in their patients, particularly if they had seen their own previously prescribed treatments fail? In such cases to deny a patient a CBPM simply because they are using an ‘illegally’ sourced preparation is illogical and could be construed as being unethical. Germany took this view when deciding to make medical cannabis available. The General Medical Council (GMC) guidance on good medical practice makes it clear that all registered doctors must take into account and respect patients’ views and experience.

Scientific support for ABA trials is well established in educational, behavioural and psychological assessment but less so in medical research. An ABA(B) trial design is well suited for determining whether medical cannabis is efficacious. Bayesian analysis can also combine separate ABA(B) results from different populations of patients, such as cannabis and non-cannabis users, stratified as suggested by experts whose experience has identified possible confounding variables. This approach is known as multilevel regression and poststratification.

WHAT ARE THE REASONS FOR THIS RESISTANCE?

One source of this resistance is that because CBPMs are patient driven, to welcome them would be an admission that the patients are more knowledgeable than the doctor. Despite over a decade of demands by the Department of Health and Social Care (DHSC) for patients to have a say in medical practice in the UK, there has been little progress. In this debate it is usually forgotten that cannabis was a licensed medicine in the UK before 1971. So why does the government not just reissue the license that applied then? Phenergan and chloral hydrate have continued to be available in the UK since that time despite no double-blind clinical trial data and chloral is sometimes used as an antiepilepsy treatment in the children with epilepsy who are denied CBPMs!

Another factor is the ‘not invented here’ syndrome. UK prescribers often say they only trust data collected here; an attitude justified by our high-quality health technology assessment processes especially NICE. However, to ignore data from other countries in a field as complicated as medical cannabis likely distorts the truth. Medical cannabis has been available for over a decade in many states in the USA and there are nearly 20,000 patients on the Minnesota database, providing detailed data on various conditions and PROs since 2015. These data should be interrogated and formally published as a way to accelerate clinically relevant information to potential prescribers as the Health Secretary Matt Hancock stated in July 2019.

This statement calls into question the current DHSC rule that medical cannabis must be considered a ‘Special’. The challenges of Specials to prescribers are not trivial and include:

1. Organisational bureaucracy and the subsequent delay of prescribing, approval and supply.
2. Transferring a patient between one sector and another, especially where, for example, primary care will not continue prescribing of a superficially expensive special or unlicensed product.
3. Local secondary and primary care services having different rules and guidance, particularly about prescribing unlicensed medicines.
4. Responsibility for prescribing—a licensed product’s manufacturer is accountable for any untold harm if the product is used within the license, but with an unlicensed product or Special the prescriber assumes responsibility for any harm that occurs, unless it can be directly attributed to a defect in the actual product.

These complexities do give some support to doctors’ perception of prescribing as too difficult. Moreover, the DHSC has made cannabis a special ‘special’ as prescribing requires a special pink pad that has to be ordered. Why such constraints are required is unclear given the established safety of cannabis medicines, but they are problematic for the prescriber and likely deter use.

Most UK doctors have no experience of medical cannabis and comments like ‘I don’t know what to prescribe’ are often heard. Though understandable they reflect poorly on a profession which generally welcomes engaging with new therapeutics; until medical cannabis came along prescribers were rarely fearful of new therapeutics. Moreover, new is not really a credible term given the decade of CBPMs in USA, Canada and the Netherlands, and its subsequent publications on the practical considerations in medical cannabis administration and dosing. The 1998 House of Lords report on medical cannabis provided clear evidence on efficacy and value of medical cannabis. Both delta-9-tetrahydrocannabinol (THC) (eg, as nabilone) and a mixture of delta-9-THC and cannabidiol (as Sativex, made from whole plant extracts) have been licensed medicines in the UK for over a decade. The decision to move cannabis to Schedule 2 was made on the basis that there were adequate data that it was a medicine. While there is little in the way of teaching on medical cannabis in the undergrad or postgrad medical curricula, the past couple of years have seen an increasing amount of medical cannabis educational programmes of varying standards. Especially for clinicians it is essential to be able to find non-biased educational programmes, highlighting the need for accredited training to be made available. Drug Science is currently offering free online teaching courses on medical cannabis and is also working on the development of accredited courses together with the Society for the Study of Addiction.

Perhaps one reason for resistance to CBPMs is that for nearly 50 years the medical profession focused on the risks of cannabis with extreme claims of harms, including male sterility, lung cancer and schizophrenia. Though these have now been largely debunked and were generally the result of recreational rather than prescribed medical use, many practitioners may not know this. Even if they do, there can be significant concern in prescribing...
In order to clarify cost implications of prescribing CBPMs, it is essential to conduct a full health economic analysis. Quality cost savings analyses are lacking at present and will be important for governments to enable active changes.

CONCLUSIONS

The many thousands of UK patients self-medicating with non-regulated CBPMs and the international database evidence suggest these new medical products offer a significant advance in treatment for many in whom current medicines are either ineffective or poorly tolerated. They also offer the potential of significant cost savings to the NHS in terms of reduced hospital stays and less prescribing of other medicines particularly opioids for chronic pain. The failure of the medical and pharmacy professions to embrace CBPMs despite their being made ‘legal’ over 18 months ago is a great worry to patients and will already likely have led to preventable deaths from conditions such as epilepsy. We hope that this paper will help policymakers and prescribers understand the challenges to prescribing and so help them develop approaches to overcome the current highly unsatisfactory situation.

Correction notice This article has been corrected since it was published. The competing interests statement has been updated.

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REFERENCES

23 Boehnke KF, Litinas E, Clauw DJ. Medical cannabis use is associated with decreased opiate medication use in a retrospective cross-sectional survey of patients with chronic pain. J Pain 2016;17:739–44.
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This article was previously published with an error.

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It is time to embrace cannabis for medicinal use, say experts

20 months after cannabis-based products for medicinal use were legalised in the UK, attitudes towards using them are still highly sceptical, say researchers

Attitudes towards cannabis products for medicinal use need to change with much greater appropriate use of such products to help alleviate patients’ pain, suggests research published in the journal *BMJ Open*.

Researchers found that hundreds of thousands of UK patients were self-medicating with illegal cannabis-based products for medicinal use due to the fact that much of the medical and pharmacy professions have so far not embraced and prescribed legal cannabis-based products for their patients.

In November 2018 when the UK made cannabis-based products for medicinal use (CBPMs) legal, most people assumed these would immediately be made available to patients, but this has not happened.

In the year since then, almost no NHS prescriptions have been issued and less than a hundred have been made available from private providers at a cost of at least £1,000 a month.

Consequently, some parents of children with severe epilepsy continue to go overseas to get their children access to the only treatment which has proven to be effective for their condition – cannabinoid medication.

In addition, it is estimated that the vast majority of the estimated 1.4 million medical cannabis users source from the black market with its problems of illegality, unknown quality, content and provenance.

This is despite that fact that there is existing substantial evidence of effectiveness with cannabis products for medicinal use in many disorders as identified in the US National Academy of Sciences review in 2017.

Researchers from Imperial College London, London School of Economics and Drug Science (formerly known as the Independent Scientific Committee on Drugs), therefore, set out to understand why the UK was lagging behind so many other countries which also have legalised medical cannabis.

They consulted with parents and patients, prescribers, pharmacists and decision makers.

They found that there appeared to be a series of distinct barriers to prescribing that needed to be overcome in order to improve patient access to medical cannabis in the UK.

These include concerns about a perceived lack of scientific evidence but the researchers said these concerns were misplaced because many patient-centred approaches including patient reported outcomes, pharmacoepidemiology (study of the uses and effects of drugs) and trials involving a single patient could be applied.
International database evidence suggested this new class of drug offered a significant advance in treatment for many in whom current medicines were either ineffective or poorly tolerated.

Various reasons to explain why there was resistance to use of these drugs were given, such as the fact the use of medicinal cannabis products were something being driven by patients and not doctors, which the latter group might resent.

In addition, the current government insistence that medical cannabis be considered as a “special” product, meant challenges for prescribers.

For example, they faced additional organisational bureaucracy and the prescriber had to hold responsibility for any untold harm caused unlike any other product for which responsibility lay with the manufacturer.

Another reason for the resistance to prescribing of these products was that for almost 50 years, the medical profession focused on the risks of cannabis with claims of harms, including male sterility, lung cancer and schizophrenia. Though these have now been largely debunked and were generally the result of recreational rather than prescribed medical use, many practitioners may not know this.

The researchers say that the many thousands of UK patients self-medicating with non-regulated cannabis products for medicinal use and the international evidence suggested these new medical products offered an advance in treatment for many people.

They also offered the potential of cost savings to the NHS in terms of reduced hospital stays and less prescribing of other medicines particularly opioids for chronic pain, they argued.

They conclude: “The failure of the medical and pharmacy professions to embrace CBPMs despite their being made ‘legal’ over 18 months ago is a great worry to patients” and may, they say, have led to preventable deaths from conditions such as epilepsy.

“We hope that this paper will help policymakers and prescribers understand the challenges to prescribing and so help them develop approaches to overcome the current highly unsatisfactory situation.”