



## FEATURE

## ESSAY

# Why medical cannabis is still out of patients' reach—an essay by David Nutt

Cannabis has been used as a medicine for millennia, writes **David Nutt**, who charts its relatively recent prohibition, the effect on patients such as Billy Caldwell, and the failure of legal reform to make much difference

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Cannabis is arguably the world's oldest medicine, with evidence of such use from 3000 year old tombs in Egypt and Siberia. It had a place in Indian and Chinese medical writing from nearly as long ago. It didn't enter the UK until the late 1600s, but by the 1800s it was widely used, sold over the counter as an alcoholic tincture for problems such as tetanus and seizures. Its efficacy more broadly became apparent, and the definitive overview was published in the *Lancet* in 1890 by John Russell Reynolds.<sup>1</sup> Because he was the Queen's physician it is believed that Queen Victoria used cannabis medicines, particularly for period and childbirth pains.

The demise of cannabis as a medicine began rather surprisingly when in 1933 the US Senate voted to rescind the law on alcohol prohibition. This left the threat that 35 000 officers of alcohol prohibition enforcement (now the Drug Enforcement Administration) would lose their jobs, along with their director, Harry Anslinger.<sup>2</sup> So Anslinger created a new drug scare in alcohol's place: cannabis.

He used its Mexican name, marijuana, to associate its use with unofficial immigrants. Then, working with the less scrupulous media, he created scare stories about the damage wrought by cannabis: that its use would destroy Americans' lives and result in white women being raped by drug crazed foreigners, and so on. Though fanciful and dishonest, these stories created the intended public moral panic.

## Public enemy number one

Cannabis became public enemy number one among drug threats, and the DEA was saved.<sup>2</sup> To further vilify cannabis, and to prevent its cultivation for medical use, cannabis was removed from the US pharmacopoeia in 1934. The rest of the world was encouraged to support the ban: in its 1934 report the League of Nations' health committee agreed with the US that cannabis medicines had no value.

This report was relied on to control cannabis under the 1961 United Nations Single Convention on Narcotic Drugs and amazingly persisted as the international medical guidance on cannabis until 2018, being used as the justification by the World Health Organization for keeping cannabis a schedule 1 controlled drug till then. Even more absurdly, the 1934 report has been lost, so we can't explore its evidential base or reasoning.<sup>3</sup>

At first the UK held out against this outrageous denial of the value of medical cannabis, just as it did when the US similarly attempted to eliminate heroin as a medical treatment. Cannabis continued being used as a medicine in the UK until the 1971 Misuse of Drugs Act, when it was relegated to schedule 1, for harmful drugs with no unique medical value.

## Pressure from the US

The driver for this ban was continued pressure from the US, which still cherished the illusion that, by disallowing medicinal use, recreational use could be restricted. The ban's pretext was misuse of cannabis medicines by two GPs in Ladbroke Grove in London who were prescribing tincture of cannabis to patients. Rather than just having the GPs struck off the medical register, the government decided to accede to decades of US pressure.

Subsequently, many states in the US and now 20 countries have reinstated cannabis medicines, but UK governments, Conservative and Labour, resisted this trend, despite the remarkable 1998 House of Lords report that recommended that cannabis again be made a medicine.<sup>4</sup>

At first Tony Blair's Labour government was supportive. Then, for reasons still unclear but probably in response to pressure from certain newspapers, it made a sharp U turn. Cannabis possession offences were made a target for the police. Hundreds of thousands of people—mostly black or other ethnic minority young men—were convicted in the decade of the 2000s.<sup>5</sup>

## Significant political benefit

A common justification for ignoring the Lords' recommendations was that, because WHO hadn't changed the status of cannabis, for the UK to do so would breach international protocol. There was also significant political benefit in keeping cannabis illegal. Medical cannabis was sucked into this policy on the grounds that it might leak into the black market and that its use could be seen as a route to legalisation.

Attacks on medical cannabis were relentless, and thousands of self medicating patients were prosecuted. Worse, when patients started to justify their use of cannabis through the common law defence of necessity, this was abolished by Labour under Gordon Brown.<sup>6</sup> Magistrates hated this decision because it removed any latitude in their decision making: everyone brought to court was guilty. It also gave enormous power to the police: they could guarantee a conviction simply by making an arrest.

To justify keeping cannabis illegal, claims of harms, such as from use while driving, were publicised, and the danger of its causing schizophrenia was repeatedly raised. Sanctions for possession and selling were cranked up and efforts made to stop imports from abroad. Supplies began to dry up, but this had the disastrous perverse result of cannabis use becoming more harmful.

## Paradox of prohibition

This paradoxical effect of zealous prohibition increasing harms is not a new phenomenon. For more than a century attempts to prohibit drugs have led to the development and use of more harmful alternatives. So, when in the early 1900s smoking opium was banned, users switched to injecting morphine and heroin. Alcohol prohibition in the US led to hooch and methanol substitution.

History repeated itself with cannabis. When customs agencies cracked down on importation, suppliers started growing their own in the UK. But to maximise their investment they grew a new form known colloquially as skunk. This contains much higher amounts of  $\Delta$ -9-tetrahydrocannabinol (d9THC), typically over 10%, and the plant is depleted of the other major bioactive ingredient, cannabidiol (CBD). CBD acts as a functional antagonist to the most problematic effects of d9THC, and especially it can attenuate the psychotomimetic and cognition impairing effects of d9THC.<sup>7,8</sup> For this reason, recently, CBD has been used successfully as an adjunctive treatment for schizophrenia.<sup>9</sup>

The double whammy of losing CBD and increasing d9THC content in skunk was the worst possible outcome, as it engendered more psychotic-like experiences and more dependence. A recent analysis by researchers at King's College London found that traditional herbal or resin cannabis, with its balance of d9THC and CBD, doesn't cause schizophrenia—but that skunk might.<sup>10</sup>

## The harshest penalties

The absurdity of the prohibition of medical cannabis was clearly exposed by data on cannabis use. When medical cannabis was banned in 1971 fewer than half a million UK adults had used cannabis, yet by 2005 this number had risen 20-fold to over 10 million.<sup>11</sup> The UK had some of the highest rates of cannabis use in the world despite some of the harshest penalties. The ban on medical cannabis certainly hadn't reduced recreational use but had almost totally denied access for patients.

Two exceptions were nabilone, a synthetic form of d9THC, which is licensed for nausea and vomiting induced by chemotherapy and for cachexia, and later nabiximols (marketed as Sativex), containing equal amounts of d9THC and CBD, licensed for pain and spasticity in multiple sclerosis. However, neither was much used, partly because of their controlled drugs status and, in the case of Sativex, the high cost. These preparations also lack the many other components of the cannabis plant, such as the cannabinoid tetrahydrocannabinavarin, which preclinical studies indicated could be a potent anti-epilepsy agent<sup>12</sup> and which was predicted to boost the therapeutic effects of d9THC and CBD.

Although most of the world fell in line with the 1961 UN convention banning medical cannabis, the Netherlands decided to allow medical and recreational use despite US pressure not to do so. More recently, 30 US states have now allowed use of medical cannabis. By 2018 more than 200 million US citizens had access to medical cannabis—but not a single UK resident. In 2017 German authorities allowed medical cannabis for 57 different indications.

## Case of Billy Caldwell

The UK government resisted any softening of approach until 2018, when the case of the boy Billy Caldwell became public. Caldwell has a rare form of childhood epilepsy, Dravet syndrome, which results in thousands of seizures a month that are unresponsive to conventional anticonvulsant drugs.

His mother tried to obtain medical cannabis in the UK but was denied, so she took him to the US and Canada to seek treatment. This was remarkably successful. With CBD Billy's seizures reduced hugely, and with the addition of full extract cannabis oil they disappeared completely, probably because the oil contained some d9THC and tetrahydrocannabinavarin. He was able to stop his other medications, and his cognitive and motor abilities markedly improved.

When his mother returned home to Northern Ireland Billy's GP was so impressed by the transformation that he agreed to prescribe the cannabis oil. But when local medical authorities found out they threatened the GP with a charge of gross medical misconduct if he continued to prescribe an "illegal" drug, so he stopped.

To prevent Billy's condition deteriorating, his mother took him back to Canada for more supplies and tried to import them into the UK, declaring them at Heathrow airport customs. The drugs were confiscated, and Caldwell's condition rapidly worsened. His seizures returned, and he went into status epilepticus that required his admission to the intensive care unit at St Thomas' Hospital, London, where he was sedated and ventilated.

The public outcry to this cruel denial of a proved therapy, coupled with the possibility of Billy experiencing more brain damage or even dying, was profound. It persuaded the home secretary to give Billy a special licence to use cannabis oil, so his supplies were returned and his seizures stopped.

## Clearly a medicine

The chief medical officer for England then reviewed the schedule 1 status of medical cannabis. She stated that cannabis was clearly a medicine, so on 1 November 2018 cannabis products were moved into schedule 2 of the Misuse of Drugs Act, but limiting prescription to specialists, or a GP acting under the instructions of one. There are no specified medical indications for medical cannabis in the UK: as long as the specialist has evidence of efficacy—from published reports or

personal patient testimony—a prescription as a “special” can be offered.

However, the roll out of medical cannabis has been much slower than patients and parents had hoped. Still only a tiny number of children with severe juvenile epilepsies are being treated, and many others continue to have multiple seizures because neurologists will not prescribe.

There are several likely reasons for this. One is ignorance of the value of cannabis medicines, because few doctors have any training or experience in this area and are fearful of prescribing them off licence. Another reason for resistance could be that parents and patients lead this initiative rather than the medical profession. Some doctors fear that medical cannabis will lead to severe adverse effects such as psychosis, and others that it will lead to more recreational use, which seems unlikely given the current wide use and availability of black market cannabis. Additionally, some pharmacists and clinical commissioning groups are refusing to pay. Another substantial challenge is obtaining supplies, because currently all medical cannabis has to be sourced from foreign producers in the Netherlands and Canada.

## Cancer research model

We must hope the situation will soon improve. One way forward would be to use the cancer research model, where small expert groups aligned to a specific indication, such as Tourette's syndrome or adult epilepsy, are set up. These could conduct open effectiveness studies in this indication all using the same form and strength of medical cannabis and all collecting data on outcomes and adverse effects in the same way.

Something similar has already been developed for ketamine for depression.<sup>13</sup> Because such studies would come under the ambit of clinical audit rather than be a formal clinical trial they would be much easier to start and much less expensive than traditional trials. Any practitioners interested in joining such groups should email me.

One final point: about 70 years ago another natural medicine came into the medical arena. This was welcomed enthusiastically by UK doctors even though there had been no placebo controlled trials of its efficacy because it was seen to fulfil a major clinical need. That drug was penicillin. If today's medical profession could embrace cannabis in the same way as it did penicillin then the true value of this plant medicine should rapidly be realised.

## Biography

David Nutt is the Edmond J Safra professor of neuropsychopharmacology and a psychiatrist at Imperial College London. He trained in the UK at Cambridge, Guy's Hospital, London, and Oxford University, and at the US National Institutes of Health. His research focuses on the use of positron emission tomography and functional magnetic resonance imaging to understand how drugs work in the brain and the mechanism underpinning psychiatric disorders, particularly addiction, depression, and anxiety disorders. In 2008-09 he chaired the government's independent Advisory Council on the Misuse of Drugs. This essay is based on his 2019 Royal College of Psychiatrists president's lecture, available to view at <https://www.rcpsych.ac.uk/members/presidents-lectures>

Competing interests: I have read and understood the BMJ policy on declaration of interests and declare the following interests: I sit on the advisory boards of several research and pharmaceutical companies, which have no connection to medical cannabis. I have been paid to speak by several pharmaceutical companies that do not produce medical cannabis products. I founded and chair the charity DrugScience, which is funded by individual donations, a grant from Open Society Foundations, and book sales.

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