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Cannabis matters? Treatment responses to increasing cannabis presentations in addiction services in England.

Abstract

Aims To conduct a pilot project exploring how treatment providers understood the increasing demand of people presenting to services with cannabis related problems and how they responded to the demand for this type of treatment in the absence of an up to date evidence-base.

Methods A knowledge exchange event involving treatment providers (n=30) from one region in the United Kingdom supplemented by qualitative interviews (n=8) and focus groups with drug treatment staff (n=5). A thematic analysis of this material was then conducted.

Findings Five distinct themes emerged. First, numerous routes were identified into services for problematic cannabis users. Second, access to treatment for some groups is an issue. Third, the type of treatment offered varies considerably within and across services. Fourth, cannabis use was viewed as benign by many staff and clients with noticeable variations of risk. Finally, there is an acknowledgment that there is an evolving connoisseurship associated with contemporary cannabis use whereby the client has increasing expertise in relation to contemporary cannabis consumption that has yet to fully filter through to the practice of treatment providers.

Conclusions There appears to be a gap between treatment demand and evidence based treatment for cannabis related problems, so that while the trend in treatment demand continues to rise the translation of the evidence base into practise for effective treatment strategies has not kept pace with this demand.

Cannabis matters? Treatment responses to increasing cannabis presentations in addiction services in England.

Introduction

Although cannabis use has recently declined in the United Kingdom (Home Office 2014), treatment presentations have risen quite dramatically from 2005 through to 2014 (Public Health England 2014, see Figure 1). Moreover it is likely that presentations to treatment services represent a fraction of those people who are actually in need of treatment (Degenhardt, et al., 2003 Hamilton et al. 2014a). Estimates suggest that as few as 1 in 10 dependent cannabis users seek treatment in any given year (Gates et al. 2012), pointing to a significant proportion of problematic cannabis users who do not present to treatment services.

Figure 1 here

Significant issues stem from this emerging cannabis treatment-seeking population, in terms of changing pathways to treatment, changes in treatment options and changes to the drug treatment population. With regard to the latter, the UK Government recently acknowledged in the most recent drug strategy that:

...groups of people who would not fit the stereotype of a dependent drug user are presenting for treatment in increasing numbers. These individuals are often younger and are more likely to be working and in stable housing. We need to ensure that provision for these individuals is tailored and responsive (HM Government, 2010:6)

There has been growing interest in the demographic changes in drug use, and the potential impact this will have on successful treatment outcomes (Badrakalimuthu et al 2010, Gowing et al 2015). The Royal College of Psychiatrists (2011) recently examined this issue making a number of recommendations including the need for the ‘examination of trends in the extent, nature and predictors of substance use problems in older people’. Similarly Drugscope (2014) have reported on the increasing visibility of older drug users presenting to services for cannabis related problems. This demographic change in people using cannabis and in those seeking treatment observed in the UK has also been observed in the USA where Burns et al (2013) found a particularly sharp rise in consumption of cannabis by those aged fifty and over.

Another important contextual factor in the United Kingdom is the change in cannabis type over recent years. Using seizures as a proxy for street availability, data suggest decreasing availability of cannabis resin with a corresponding increase in high potency herbal cannabis, often referred to as ‘skunk’ (Cascini et al 2012; Di Forti et al, 2015). There has also been the appearance of synthetic cannabinoids sold as ‘legal highs’, increasing numbers of which have been controlled under the Misuse of Drugs Act (1971). It is not known what effect, if any, these factors have had on the increasing numbers of people presenting to treatment services.

There is currently little definitive information on ways of refining and improving the efficacy of cannabis treatment. Studies in Australia of cannabis treatment-seeking clinics show that

these are a more attractive environment for those new to drug treatment and potentially retains drug users in treatment until treatment is completed, although this could be because cannabis only treatment in this context tends to be shorter than non-dedicated treatment provision (Copeland and Allsop, 2014). The use of cannabis withdrawal medication is restricted in the UK, the only licenced treatment being for the primary treatment of Multiple Sclerosis. Therefore, a prescriber who prescribes Sativex for cannabis withdrawal treatment would be doing so 'off licence'.

Relatively little research has been carried out on the topic of cannabis treatment, primarily because of what was considered to be the absence of a dependence mechanism, despite the fact that research has demonstrated that cannabis users readily respond to information identifying treatment as an option (Copeland, 2001). The last Cochrane review on the subject of cannabis treatment highlights numerous treatment options (Denis et al 2006). As of June 2013, the review was withdrawn from publication by the Cochrane Collaboration on the grounds that it is 'substantially out of date' (Cochrane 2013). It was noted at the time, however, that few of the interventions included in the review are well placed to deliver long-term abstinence. This is true of both face-to-face and remotely delivered interventions such as Computer and Internet based interventions (see Tait, et al. 2013). Some interventions are, however, successful in ameliorating the impacts of withdrawal or reducing the social impacts of cannabis use. Work published subsequently reveals a similar pattern (Danovitch and Gorelick, 2012; Copeland and Swift, 2009; Vandrey and Haney, 2009; Elkashef et al., (2008) Budney, et al., 2007; Nordstrom and Levin, 2007).

Existing NICE guidance on cannabis treatment recommends psychosocial interventions although it states that CBT and psychodynamic therapy should not be offered as a matter of routine (NICE, 2007). Recent systematic reviews have been undertaken. Marshall et al.'s review (2014) of evaluations of pharmacotherapies for cannabis dependence found pharmacotherapies to be largely ineffective, although again the evidence base was limited. Davis et al.'s (2014) report on a meta-analysis of ten RCTs of behavioural interventions (BT) for treatment-seeking cannabis users examined a range of options. All interventions included Cognitive Behavioural Therapy (CBT) plus contingency management, relapse prevention, motivational interviewing or a combination of these. BT was shown to significantly more effective in reducing severity and frequency of use than control conditions although, while BT outperformed waiting list controls, it did not outperform active control conditions (Davis et al., 2014, p.13). Qualified evidence exists, therefore, that combined CBT and behavioural therapies may be effective in reducing the severity and frequency of cannabis use. A recent review of by the European Monitoring Centre on Drugs and Drug Addiction concluded that there was no definitive evidence 'for the superiority of any specific treatment to others. Treatment context and the individual's choice in entering treatment are more important determinants of outcome than treatment modality' (EMCDDA, 2015, p 61).

There is, then, something of a knowledge vacuum. A patchwork of evidence exists on cannabis treatment, but the last systematic review of the topic was last completed nine years ago (Denis et al 2006) precisely at a point when the availability of cannabis type was in flux. The situation is compounded by the way that funds are allocated for drug treatment. Organisations have to negotiate challenging funding regimes and are often pitted in competition with one another to secure finances to deliver needed services. In such an environment, opportunities for knowledge exchange become limited. As it stands, there is a necessity for learning across the drug treatment sector as to effective interventions for people who present with primary problems associated with cannabis. Overall it is uncertain what types of interventions are being offered to this new treatment population or how treatment providers formulate evidence based services given the lack of available research in this area.

Ultimately, little is known about what works, for whom and in what circumstances (Pawson and Tilley, 1997) in relation to cannabis treatment.

Methodology

The research team carried out a pilot study into the changing patterns of cannabis treatment. Initially, this involved scoping the data for emerging trends in cannabis treatment (Hamilton, et al., 2014a), which formed the context to an information workshop and knowledge exchange event in April 2013. Participants included service user representatives, consultant psychiatrists, drugs workers from the statutory and third sector from adult and young people providers, mental health workers, from one region of the United Kingdom (n=30).

Alongside the workshop, follow up semi-structured interviews (n=8) and a focus group with 5 participants were undertaken drawn with representatives purposively drawn from the above sample. The focus group participants consisted of 2 male and 3 female drug workers in the statutory and third sector. The main criteria for selection was to engage the views of respondents who had been involved in delivering cannabis treatment interventions in the twelve months prior to the research commencing. All worked with adult cannabis users in the past, although one respondent was currently delivering interventions with younger users.

We carried out a thematic analysis of the interview and focus group data. The aim was to try and ascertain:

- a) In what way treatment providers were meeting the increasing demand of people presenting to services with cannabis related problems and;
- b) How they responded to the demand for this type of treatment.

The research was given approval by the University of Leeds ethics committee. For reasons of confidentiality and anonymity, respondents have been assigned a pseudonym and their place of work disguised.

Findings

Five distinct themes emerged. First, numerous routes were identified into services for problematic cannabis users. Second, the type of treatment offered varies considerably within and across services. Third, access to treatment for some groups is an issue. Fourth, cannabis use was viewed as benign by many staff and clients with noticeable variations of risk across. Finally there is an acknowledgment that the client has increasing expertise in relation to contemporary cannabis consumption that has yet to fully filter through to the practice of treatment providers.

Theme 1: Pathways into Treatment (Routes and Motivations)

It was apparent from our research that there was a diversity of formal routes into treatment, by which we mean the referral process and whether that was initiated by the users themselves or via a third party such as their GP, Mental Health Worker, Education System or Criminal Justice System. The disparate referral routes are matched by service providers' interpretation on the underlying reasons for why this was necessary. These consistently included: anger, anti-social behaviour, family arguments, sexual health issues and stress-related (mental-health) reasons. In addition, public information campaigns were thought to be a contributing factor. Although this was the case, it was also apparent that for several participants this was the tip of the iceberg and that problematic cannabis users were not accessing treatment due to referrer resistance.

There was some variety over the routes through which service users were entering treatment and this has a knock-on effect for the service provided. Interview respondent 1, a drugs worker for a national service provider highlights some of the complexities over routes into cannabis treatment:

I am seeing a young girl tomorrow who has come through from the mental health team. I got a call from the mental health team: a single mum who has tried to – she tried to take her own life last week, cannot stop smoking cannabis. Because of the nature of it, me and a female colleague are going to do a home visit because there is a child involved, tomorrow, and do an assessment and *see how we can help. We have got another referral...–* for a young man that has come from a doctor. So it is always changing. So when you close someone down, you have another one come along, you know.

(IR4) This respondent confirmed that referrals were instigated through contact with the criminal justice system, but were not triggered by drug testing, rather conversations with the arrest referral team:

..if somebody was flagged up as having a cannabis issue, then they would be signposted to services.

It is worth noting that the number of cannabis possession offences recorded by the police nearly doubled between 2004/5 and 2011/12, and that cannabis possession accounts for 70% of police recorded drug offences (Shiner 2015). With this level of police interest and activity it is a possible contributing factor for the increase in presentations to treatment services for cannabis. In short the net-widening of the police is matched by treatment services.

A recurring issue that was thought to trigger self-referral or one instigated by others was anger:

(IR2):

Anger, that seems to be the biggest one that I've come across.

(IR5):

Parents will constantly mention that they will get very angry very quickly over somewhat-you know, like the smallest request to do something. And that is what interests me in terms of – I think that would – for me, is an element of cannabis withdrawal that perhaps goes unrecognised.

(IR6):

Our service has seen a massive change in trends recently...especially young men being very aggressive very angry.

Anger, aggression and irritability are all recognised as components of cannabis withdrawal (Budney et al 2004). Withdrawal could account for the behaviour our respondents report, but it could be co-incidental and unrelated, however the frequency with which this issue was raised warrants further investigation.

Theme 2: Access to Treatment Services

As indicated at the outset, there has been growing concern about the demographic changes in drug use, and the potential impact this will have on treatment. Where cannabis is the primary issue, these issues seem to be magnified.

One of our respondents notably reframed the emphasis with regard to accessing treatment:

I do not like the phrase hard to reach when it comes to young people and substance users. *I don't think that's true. I think services are hard to access, not people being hard to reach. So we have to become flexible in the ways in which we work.*

More specific examples of barriers to treatment were expressed by one worker who highlighted that although child protection issues have become associated with female opiate users there was concern that these were now affecting female cannabis users (IR6):

There's a lot of stigma about female adult service users coming into treatment where there's childcare. A lot of stigma about that, a lot of fear, especially about how we're supposed to assess people in this day and age as well.I think there are more females coming through, but I don't think we get anywhere near the number or the amount... with the amount that are using.

Gender differences in access to treatment have been observed for some time however little attention has been given to the gender imbalance in relation to cannabis treatment (Hamilton et al 2015). Females may perceive treatment as male orientated and dominated (Montanari et al 2011). Another particular area of interest concerned use amongst BME groups. In one of the focus groups, a drug worker/service manager referred to a group of young BME men as being heavy end users who were not seeking treatment. It transpired too that there had been an emergence of young female Asian users in the same area which raised cultural issues about service provision and treatment. Others also suggested that some ethnic minority cannabis users do not access treatment services. Interview respondent 7 a senior manager in a regional service comments suggested that this is a general problem with health services:

I think there's a hidden population that don't access services. Whether it's drug treatment services, whether it's alcohol services, or like primary care or health generally, I think that is a problem, a bit of an iceberg and I can't tell you if any – at all, what type of support they are having because it is taboo to talk about these things within certain cultures...I think it's really hard because young people wouldn't make the referral themselves into the service. I think we miss a lot of them and I think we are missing a hell of a lot of them, especially in children's home and stuff (IR7).

Theme 3: Variations of Treatment Practice

In the UK context, particularly from the late 1990s onwards the treatment context shifted (Seddon, 2006). This was most noticeable with the roll-out of quasi-compulsory treatment for certain drug and alcohol users in the form of Drug Rehabilitation Requirements and Alcohol Treatment Requirements. In essence, there has emerged what we refer to as a clear 'treatment narrative', which foregrounds substitute treatment.

The sector faces challenges in developing a coherent programme of treatment for cannabis users in the absence of an established substitution prescribing programme as with opioid treatment. Interview respondent 8, a support worker for a recovery community in the region illustrates the point:

But with cannabis being a new thing, it's obviously presenting new challenges and how to deal with it...There's no substitute medication that people can go on...

Here we see some reflection on the lack of treatment narrative for cannabis. It is indicative of the lack of available knowledge at the disposal of treatment providers in the region. However there was evidence of a range of attempted treatment options provided in the region.

According to another respondent his service ‘prescribed treatment like anti-anxiety medication’ (IR7) but others used ‘a more proactive assertive outreach as well as reactive crisis intervention work’ (IR1).

if someone drops out of treatment for whatever reason, a referral comes through to me and I will... go try and find them...make sure they are all right, find out what is going on, why they may have dropped out of treatment, and try and facilitate them back in if they want that. But the prime, main reason is to make sure they are okay.

The focus group revealed other techniques, mainly revolving around ‘psychosocial interventions’:

We tend to use lots of drug diaries, lots of targets and ‘what kind of two or three things are you going to try to change or alter this week’ sort of thing

There was a sense also that the treatment offered was contingent on the needs of the particular client as for interview respondent 6 and her work with younger groups the diary approach was seen to be less useful:

because we’re not looking at someone that’s doing it every single day or four or five times a week...we can’t measure it because they’re doing it as a peer group... We tend to work with young people for three to six months doing one-to-one psychosocial interventions. So, the CBT, the motivational interview in terms of looking at motivation to change (IR6).

IR7 noted that ‘contingency management’ was at the fore of their service delivery:

We’d heard about this before... in addition to psychological interventions, like psychosocial interventions, combining contingency management which provides money or other incentives for attending appointments, or for producing drug negative urinalysis results. It [is supposed] to improve abstinence outcomes during and after treatment. However, it is unknown whether advantages of contingency management with motivation enhancement therapy or CBT outweigh the extra costs associated with contingency management. So it’s another option, but it’s just whether or not it’s as effective and there’s still a lot more research. But yeah that was an interesting one. So paying clients for attending appointments, paying clients to provide negative samples

There is some sense that service providers in the region are using therapies widely discussed in the literature, although their application to problematic cannabis users has yet to be evidenced. Others, meanwhile, seem to be employing service specific interventions.

Theme 4: Benign nature of cannabis

There has also been a long-standing tendency for policy-makers and practitioners to ignore or downplay problems with cannabis: a situation that Michael Dennis and colleagues have referred to as ‘benign neglect’ (Dennis et al., 2002). This is reinforced by the scant attention paid to problematic cannabis use in the 2010 drug strategy and subsequent annual reviews (HM Government, 2015). There was a sense that the benign neglect of cannabis had filtered down to the service level. Indeed, a common line of argument was the perception that cannabis was generally viewed by both the general population and by other key workers (including by other treatment workers) as being relatively harmless vis-à-vis heroin,

mirroring previous research in this area (e.g. Pinikahana et al, 2002). For example, prevailing attitudes of the benign nature of cannabis are clearly expressed by IR1:

I know there are people... who ...would be absolutely delighted if some of their clients stop using heroin, stop using crack cocaine, and the only drug they were using after that was cannabis. I think some would deem that as a success in that client's recovery programme.

This view of cannabis has to be understood within the historic emphasis of targeting and treating predominantly people who use opiates and the health and social problems associated with this type of treatment presentation.

If someone tested positive to cannabis it was dismissed, we were more intrigued about the class A drugs.

(IR4):

..if you're not injecting heroin or whatever or you're only using weed, and there is this kind of stereotype that weed, cannabis, is a much lesser drug, you know, "What do you mean you've got an issue with it?" sort of, kind of thing.

(IR5):

..I think, also, is this kind of mythology that cannabis is harmless.

(IR6)

there was a little bit of judgement – yes I think the service as a whole was quite judgemental in terms of well, working with crack and heroin users, *they've got such chaotic lives the cannabis users not so much.*

Most respondents had worked in drug treatment services for some time and as is apparent from the quotes recognised the shift in attitude that was required in relation to cannabis. Elsewhere a subtheme to emerge from our research was a definite sense of an intergenerational chasm in understandings of the perceived harms of cannabis. In this case the context is that of the family as it was widely suggested that cannabis initiation and subsequent use takes place in the family setting and that this in turn may be downplaying the seriousness of cannabis use for certain individuals. Interview respondent 6 explains:

there's a couple of lads that I'm working with now, Dad smokes and you know it's okay, Dad's always smoked, it's never been an issue. Therefore if they've got that perception then they tend to believe that and then when you come in and start talking about some of the risks, they don't believe what you're trying to say. So there's a lot of that going on in families.

The focus group covered similar terrain. In response to a question about different perceptions of cannabis use, our respondents noted:

FG1 you get some that are smoking a lot more and that's not perceived as a problem because my dad smokes weed, I smoke skunk so we're all - that's all right.

FG2 *I think in some families... it's perceived as the lesser of some of the evils.*

FG4 I think where you see the difference is the older generations are smoking cannabis not skunk. So it won't cause them quite the level of problems mentally and criminally, all that kind of stuff. However the children

are now reverting to strong cannabis and it becomes problematic, the whole lifestyle and behaviours are different to the parent.

The benign neglect of cannabis in policy circles seemed to translate into making cannabis a low priority for services over a number of years. This was reinforced by a sense that there were significant intergenerational differences in appreciations over the risks associated with cannabis use. As the levels of cannabis users seeking or entering treatment for cannabis problems has recently risen, there was a sense that the services and the personnel lack the knowledge and skills to accommodate this new clientele, typified by the variations in treatment practice discussed earlier. This is compounded, furthermore, by a systemic challenge for the sector whereby there is a lack of emphasis on the treatment of cannabis users and where knowledge of the drug and its effects lags behind that of the users.

Theme 5: Changing Nature of 'Expertise'

A significant recent development in the emerging drug markets has been the rise of twin markets in herbal and synthetic cannabis. As regards the former, there is a sense that 'home grown' cannabis relying on often sophisticated production techniques has entered the market place at significant levels (Potter et al 2014). Alongside this, synthetic cannabinoids, often produced and marketed as replacements for the 'real thing' (Winstock et al 2015) are similarly more widely available. For example, products such as 'Spice' have emerged which are supposed to recreate the effects of cannabis. In our research the former seemed to represent more of an issue than the latter as synthetic cannabinoid use was not perceived by our respondents to be a significant issue across this particular region:

I've not seen it much. I've really not seen it. I've seen – a couple of young people have said to me they're not interested in it because it's too different [in terms of]effects, that they've got no interest in it whatsoever. ... it doesn't seem to have hit off I don't think massively[FG3].

Interview respondent 3 a drugs worker from a large provider in one of the major cities stated:

...one thing I haven't actually seen so much here is the ascension of cannabinoids as well. Because in [town in North-West] that was a really big thing. Quite an emerging big thing really. And one of the things that you'd sort of notice with that is that the synthetic cannabinoid did seem to give much more of a negative experience on the whole than cannabis would give.

However, the increasingly sophistication of cannabis production techniques had led to increasing choice of cannabis products. In turn this has created a feeling that there is a sense of connoisseurship around the drug, creating a knowledge mismatch whereby the nature of cannabis is changing but the learning and skill set of service providers has remained fixed:

I mean I think certainly if you went back - the further you go back, certainly if you went as far back as the eighties or whatever when people were buying weed they'd just be buying what they could get sort of thing. Whereas, I've known... people will select particular kinds and they will - they won't smoke this and they will smoke that, but they prefer this. (IR2).

Some respondents vocalised their lack of knowledge in relation to cannabis, its effects and how to respond to those seeking help.

(IR1):

..workers aren't familiar with cannabis users and how to work with cannabis users, they're not confident in working with how to do it – "Oh, I don't want to, I don't know how to work with someone that's used cannabis. I don't know what to do." And these are qualified nurses that have been qualified for years and working in treatment services for years.

This contrast between the workers lack of knowledge with regard to cannabis and the expertise and knowledge of the client provides an interesting contrast. Furthermore, it suggests that growth in manufacturing of cannabis creates greater choice with specifications being refined around types and strains which sees the user situated as 'expert'. The service provider may find themselves in the position, then, of 'novice', not privy to this developing culture around usage with technological advances production underpins. Further to this, as technology facilitates and speeds supply it advances production and potency to the extent that progress may outpace the knowledge service providers have of the substances their clients are using.

Discussion

Overall, although more contact was being made with treatment services for cannabis problems, there was little consensus among service providers as to what was the most effective course of action. This is perhaps unsurprising given the lack of consensus from the literature in this regard. In effect, providers felt that for cannabis users there was not a treatment narrative in the same way that one had emerged for opiate users based around a substitution prescribing model, reflecting the relative absence of a pharmacotherapy solution specifically for cannabis. The main themes and messages that emerged were that there was an eclectic mix of interventions offered by providers which again is not surprising given the varied presenting needs of individuals. That said, it was also the case that services are hard to access for some groups and as a consequence cannabis treatment presentations may increase over time as services respond accordingly. Despite increasing presentations to treatment, some workers continue to view cannabis as benign and intergenerational use is a possible explanation for why this is so. Finally, an interesting juxtaposition has developed where cannabis users have become 'expert' while treatment providers are 'novice' in terms of their knowledge and ability to recognise and offer bespoke treatment to the cannabis connoisseur.

Based on our study, we would offer the following suggestions for future research into the emerging cannabis treatment population.

1. Our research suggested that more people were using strains of higher potency cannabis and less synthetic variants. Although this is probably localised, national studies should investigate the changing markets of cannabis and how consumers and users negotiate this
2. As the general problem drug user population has been in decline, it is possible that drug services are spreading their net wider and have been more willing to engage and accept people who use cannabis in a problematic way. Indeed, the recovery agenda could directly or unintentionally be encouraging workers and services to include and accept cannabis use as a contemporary and primary problem. Future research should consider in more detail the pathways into treatment for those experiencing problems with cannabis.
3. Although cannabis related problems span all ages and backgrounds, there is still a lack of knowledge about the profile and needs of users who experience such problems (Temple et al 2011). It is also the case that organisations are

grappling with the demands of new and often reduced funding structures including a hugely competitive tendering process for the delivery of services where more needs to be delivered for less. As it stands, there is a necessity for learning across the drug treatment sector as to effective interventions for people who present with primary problems associated with cannabis.

Conclusion

There appears to be a gulf between the demand and supply of evidence based treatment for cannabis related problems. While the trend in treatment demand continues to rise the translation of the evidence base into practise for effective treatment strategies has not kept pace with this demand. We have put forward five, somewhat tentative reasons for this. First, the routes into services for problematic cannabis users are unclear which has a knock-on effect for the kinds of provision offered. Second, access to treatment for problematic cannabis use reflects broader barriers experienced by other treatment seekers. The services are in effect hard to access for those from BME backgrounds and females. Third, the type of treatment offered varies considerably within and across services, with little understanding therefore of what works, for whom, in what circumstances and in what respects (Pawson and Tilley, 1997). Fourth, cannabis use was viewed as relatively harmless by many staff with noticeable variations of risk. This has been reflected in policy circles over recent years (Dennis, et al., 2002). Finally, there is an acknowledgment that the client has increasing expertise in relation to cannabis consumption stemming from a certain connoisseurship that has emerged in relation to contemporary cannabis choice. This knowledge base has yet to be matched by those responsible for providing treatment. Ultimately, there is a disjunction between evidence, policy and practice in the provision of cannabis treatment at a point in time when cannabis matters.

Declaration of Interest

The authors report no conflicts of interest

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