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Medical cannabis and road safety

**A research report for the
Department for Transport**

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Executive summary

1.1 Background

In 2018 the 2001 Misuse of Drugs Regulations were amended to legalise “cannabis-based products for medicinal use in humans” (CBPMs) (Misuse of Drugs (Amendments) Regulations, 2018), when prescribed by a doctor on the specialist register and where other treatments have failed. In this report, we use the term “medical cannabis” for CBPMs and licensed cannabis-based medicines. Medical cannabis products can be prescribed through the NHS although CBPMs are largely prescribed in private sector clinics.

There are signs that the number of medical cannabis users in the UK might increase in the future. In this context, the Department for Transport (DfT) is interested in the extent of the challenges medical cannabis use poses to road safety.

The relationship of cannabis to road safety largely concerns the impact of the psychoactive effects of delta-9-tetrahydrocannabinol (THC) on people’s ability to drive safely. The Road Traffic Act 1988 makes it an offence to drive while unfit through drink or drugs, and regulations which came into force in 2015 brought in a threshold-based offence of driving with blood concentrations of 2 micrograms of THC per litre, regardless of fitness.

DfT commissioned NatCen Social Research (NatCen) to carry out research to identify and report on evidence across the following three areas:

- the prescribing landscape and profile of users;
- the impact of medical cannabis on driving ability and road safety; and
- knowledge and understanding of how medical cannabis impacts on driving ability and behaviours of prescribers and users.

1.2 Methods

The research involved two components; interviews with key informants and a Rapid Evidence Assessment (REA) of academic and grey literature.

NatCen interviewed nine key informants identified through desk-based research and discussions with DfT. Participants held informed views relevant to the study and represented a range of stakeholder organisations and groups.

Interviews were conducted in March 2021 and audio recorded with participants’ permission.

For the REA, we developed a search strategy and inclusion criteria to identify relevant literature from four academic databases within the timeframe for the project. We complimented this by conducting a search of key websites. Papers published from 2011 onwards, in English, that addressed one of several themes related to the research questions were included. We prioritised reviews and those that were published more recently.

1.3 Key findings

1.3.1 Prescribing landscape

The current number of users who are prescribed medical cannabis through the NHS is in the low hundreds. There is a lack of data on how many patients are currently prescribed medical cannabis (mostly unlicensed CBPMs) in the private sector, but interview participants estimated that the number was likely to be in the low thousands.

Medical cannabis prescriptions vary by level of THC and cannabidiol (CBD), by THC:CBD ratio, and by mode of administration (for example, ingestion of oils or vaping of dried flowers), depending on the type and severity of the condition being treated.

Mode of administration is important for impairment. Vaporised (and smoked) cannabis has much higher maximum blood concentrations of THC, with much faster onset of the maximum concentration. In contrast, with oral administration such as cannabis oils, concentrations remain elevated for longer, at much lower maximum levels.

There is little published information on the characteristics of medical cannabis users in the UK. However, data from various countries shows that compared to recreational users, medical cannabis users are older, usually have poorer physical and mental health, and mainly use cannabis to alleviate symptoms of their health condition(s). They are less interested in psychoactive effects; take lower, controlled doses; and are less likely to have a substance use disorder.

Interview data indicated that medical cannabis users are around 60% male, aged from around 25 at the youngest to over 80, with a tendency toward middle age, and have varied work and activity profiles. They often have multiple health conditions which affect their quality of life.

In terms of the driving profile of medical cannabis users, interview participants presented a mixed picture. For example, one participant thought that hardly any of their patients were drivers, while another from a network of private clinics estimated that four out of ten of their patients drive. The health conditions of users emerged as one of the main challenges to driving.

1.3.2 Medical cannabis and driving impairment

Interview participants stressed the wide range of possible effects of cannabis and the subjective nature of individual responses to the drug. Effects that may impact on driving safety included drowsiness and sedation, impaired judgement, slower reaction time, poorer control of motor skills, lack of concentration, confusion and blurred vision.

The evidence reviewed indicated that the usual duration of neurocognitive impairment associated with use of medical cannabis containing THC is generally four hours or less (the evidence reviewed did not include comparable estimates for recreational cannabis use). Chronic recreational use of cannabis is linked to a mild to moderate loss in areas such as cognition and to impaired driving performance even without acute intoxication. However, understanding levels and durations of THC concentrations in medical users would be needed to assess how relevant this is for the medical cannabis user population.

Interview participants explained that higher THC levels might impact on the nature and level of impairment, but CBD was not regarded as a concern for road safety. Studies found similar results, although some reported that CBD may worsen THC-based impairment in some cases.

As well as impairment from taking THC, driving may also be impaired by users' health conditions or by non-cannabis medication. Reflecting this, some studies show improvements in driving capabilities as a result of taking medical cannabis for specific

health conditions such as spasticity in multiple sclerosis, and chronic pain, a finding echoed by some interview participants.

1.3.3 Cannabis use and road safety risks

Literature on cannabis use and risks to road safety (which mostly relates to recreational use) generally suggests a low-to-moderate increase in crash risk compared to driving sober. Increased risk may vary by type of collision, with lower additional risk for fatal crashes and more additional risk for less serious collisions as cannabis use may be more likely to cause crashes due to inattention than to aggressive driving. The evidence base has some limitations in how consistently studies measure the frequency and quantity of cannabis used and how cannabis use is isolated from use of alcohol. Culpability studies suggest a small fraction of total crashes would be avoided by eliminating cannabis-impaired driving. The impact of cannabis-impaired driving is minor relative to that of alcohol-impaired driving, although this is likely to be due in part to cannabis-impaired driving being less common. Within cannabis-impaired driving it is likely that medical cannabis users pose less of a risk than recreational users.

Evidence from the USA where states have different legal regimes around cannabis legalisation suggests differences in risk according to legal and policy frameworks (and how these are interpreted and implemented). This suggests that increased population-level risk from medical legalisation may be much lower than for decriminalisation or general legalisation.

1.3.4 Driving guidance for patients using medical cannabis

UK law requires that drivers tell the Driver and Vehicle Licensing Agency (DVLA) about any medical condition that could potentially affect their driving. For certain conditions that are deemed to pose an inherent threat to safe driving, including epilepsy (for which medical cannabis can be prescribed), DVLA must be informed. DVLA produces guidance for medical professionals on assessing fitness to drive to help them advise patients on whether to notify the DVLA of a medical condition. The guidelines give an outline of the elements required for safe driving (such as attention and concentration, good reaction time, and coordination) but apart from conditions where there are clearly laid down criteria for driving eligibility based on clinical history, such as epilepsy, it is down to the individual driver to judge whether their ability to drive safely is impaired.

In line with DVLA guidance, prescribers should give patients advice on driving while using medical cannabis, as they would with any other medication. This advice covers the main point that the patient should not drive if they feel impaired, and sometimes includes more specific guidance to support safe consumption. Prescribers should also consider the interaction of medical cannabis with other medications and monitor patients' responses to their medication, including those likely to impair driving.

Prescribers interviewed expressed little concern that patients would not adhere to the guidelines and did not see compliance with medical cannabis as being inherently different to compliance with other prescription medicines. Literature on adherence to safe driving guidelines mostly relates to recreational cannabis use, but suggests that adherence may be higher among users with a medical need as their main aim is to alleviate symptoms rather than to get high.

1.3.5 Possible changes in the future

The number of potential medical cannabis patients is large; some sources report that over one million people in the UK use illicit cannabis with medical intent. Sustained increase in the number of patients registered with private clinics seems likely, though the speed and scale of such growth are uncertain. Medical cannabis patient numbers in

the NHS are likely to grow much more slowly due to the use of a higher evidence threshold for recommending prescription. It is possible an accumulation of less robust “real-world” evidence will eventually encourage a policy change by NHS regulators to move NHS prescribing closer to the approach used in private clinics. Decreasing costs, greater awareness and a move away from opioid painkillers may all increase numbers.

The impact on road safety of increased numbers of prescriptions for medical cannabis is not clear. Medical cannabis may make people safer drivers by reducing impairments from illnesses which medical cannabis is treating, including pain, stiffness and mental distraction due to anxiety and ADHD. On the other hand, the psychoactive effects of THC clearly increase impairment through drowsiness and other cognitive impacts. The direct impact of such impairment on road safety is not clear, as patients will receive medical advice to only drive if they do not feel impaired.

In some cases people may become willing to drive if there is an improvement in their symptoms but still be somewhat impaired; some patients also report that their driving improves when using medical cannabis, which implies that they were driving previously. This suggests that in practice there are different degrees of impairment among drivers, even though legal rules and medical guidance are that patients should not drive if their driving “is impaired”. Participants criticised the idea of considering impairment as a binary phenomenon, with some preference for understanding impairment by degrees.

In short, increased use of medical cannabis may improve road safety through its positive effects on other sources of impairment. However it may decrease road safety through having people driving under the influence of THC, or enabling people to drive who previously felt unable. We cannot easily estimate the net effect of these factors for road safety.

1.4 Future research

Based on the findings from this study and gaps in the evidence base we identified several possible areas for further research, including:

- Investigation of the effectiveness of safe driving communications among medical cannabis users, taking account that they may be differently susceptible to communications compared to either other users of prescription medicines or recreational cannabis users.
- Evidence on impairment without acute intoxication in long-term users of doses typically associated with medical rather than recreational use, to determine whether permanently elevated THC levels occur and whether these pose a risk to driving ability.
- It may be possible to explore data collected by the various registries that currently exist in parallel, and to explore routine inclusion of driving-related indicators in these.

Some issues that arose relate to road safety and impairment more broadly rather than just to medical cannabis use:

- Evidence on the consistency of drivers’, doctors’ and regulators’ understandings of what constitutes impairment.
- Exploring data on the number of arrests or prosecutions of people for driving-related offences (either infringing threshold limits or driving while unfit), and the

outcomes of such cases including the functioning of the statutory medical defence.

2 Introduction

2.1 Background to the research

2.1.1 Rationale

Cannabis offers a range of medical benefits, but its psychoactive effects can pose a risk to a user's ability to drive safely. Cannabis is a controlled substance whose use is criminalised and until 2018 it sat outside of any regulatory framework. In 2018, cannabis-based products for medicinal use were made legal in the UK (details of this are covered in section 2). Availability of these products on the NHS is limited, but there is greater availability through clinics in the private sector.

If advocacy efforts to encourage greater prescription of cannabis by NHS doctors are successful, or if there is sustained growth in private prescribing, there could be an increase in the number of people using cannabis for medical purposes. In this context, the Department for Transport (DfT) is interested in the extent of the challenges medical cannabis use poses to road safety.

2.1.2 Terminology in this report

As described more extensively in section 2.1, three cannabis-based products are specifically scheduled under the 2001 Misuse of Drugs Regulations. In this report these products are called "licensed cannabis-based medicines" or "licensed products", as they have received a marketing authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA, see section 2.1.2). Cannabis-based products for medicinal use in humans (CBPMs) include those cannabis-based products produced and used for medical purposes that are not separately scheduled under the 2001 Regulations. These are referred to as "CBPMs" or "unlicensed products" (as no CBPMs are currently licensed in the UK).

In this report the term "medical cannabis" encompasses both CBPMs and licensed cannabis-based medicines. However, this excludes both CBD supplements and cannabis products whose production, distribution or use is not exempt from criminal sanction, regardless of whether these are used for medical purposes. These are referred to as "CBD supplements" and "illicit cannabis", respectively.

The term "medical cannabis" does not imply that the risks or benefits of licensed products and CBPMs are different to those of illicit cannabis. Regarding risks and benefits to the user, they differ primarily in the reliability of the levels of active ingredients included in the product. There are also common differences in how they are taken, how they are acquired and the legal regime to which their producers and distributors are subject.

2.1.3 Research Questions

This research was conducted to identify evidence and report on the extent of the challenges medical cannabis use poses to road safety. The following research questions were explored:

Prescribing landscape and profile of users

- 1) What is the extent of medical cannabis prescribing in the UK / Great Britain, particularly prescribing to those who drive a motor vehicle?

Impact of medical cannabis on driving ability and road safety

- 2) To what extent does the use of medical cannabis impair driving ability?
 - Does the nature and the level of impairment depend on the type of medical cannabis prescribed?
- 3) Does the use of medical cannabis increase the risk of a road traffic collision or casualty?
 - Does the nature and extent of the risk depend on the type of the medical cannabis prescribed? If so, how?

Knowledge and understanding of how medical cannabis impacts driving ability and behaviours of prescribers and users

- 4) What do those prescribing medical cannabis know about its impact on driving?
 - Are risks communicated to patients and are they advised not to drive when taking the drug?
- 5) What do those who are prescribed medical cannabis know about its impact on driving?
- 6) To what extent do those who are prescribed medical cannabis follow the advice of medical professionals about driving when taking the drug?

2.2 Methodology

To address these research questions, we conducted interviews with key informants and a Rapid Evidence Assessment (REA) of academic and grey literature. The findings from the interviews and the REA have been drawn together in this report.

2.2.1 Key informant interviews

We conducted nine interviews with key informants in March 2021, aiming to capture a range of views on the current state of UK medical cannabis prescribing, the policy environment and road safety implications, and speculations on future developments. A potential list of interviewees was established through desk-based research and discussions with DfT. Participants held informed views relevant to the study and represented a range of stakeholder organisations and groups, including for example; academics, policy officials, lobbying groups, prescribers, registries and patient associations.

To guide the interviews, a topic guide was developed and agreed with DfT (see Appendix A for an overview of themes). The interviews explored:

- The prescribing landscape and demographic and driving profile of medical cannabis users;
- The impact of medical cannabis on driving ability and road safety; and
- Prescribers' and users' knowledge of how medical cannabis impacts driving ability, the advice given to users and users' behaviour.

Interviews lasted approximately 60 minutes, were conducted online via Microsoft Teams and audio recorded with participants' permission.

Interview data were managed and analysed using the Framework approach, a case and theme-based approach developed by NatCen to facilitate robust, systematic thematic analysis of qualitative data (Ritchie, 2013).

Verbatim quotations are provided to highlight the key findings and issues in participants' own words.

2.2.2 Rapid Evidence Assessment

REAs use systematic methods of searching, screening, critical appraisal, and synthesis of relevant literature to provide evidence on key topics and identify gaps for future research. The process used to conduct the REA included the following steps:

- We developed a search strategy in collaboration with DfT staff and experts to enable us to locate relevant literature from academic databases. A consultant search specialist developed search terms to capture academic and grey literature on medical cannabis and road safety (Appendix B). The search terms applied to four databases: Embase, Web of Science, PsychInfo and Transport Research International Documentation (TRID).
- Also in collaboration with DfT, we developed inclusion and exclusion criteria to determine which results from the database search ought to be considered for inclusion in the evidence review (Appendix C).
- We also conducted a search of key websites, a list of which is included at Appendix D.

We considered papers published from 2011 onwards, in English, that addressed one of several themes related to the research questions. The starting date of 2011 corresponds to when road deaths in Great Britain began to flatline (Department for Transport, 2021). When prioritising papers for data extraction we preferred those that were published more recently, reviews over non-reviews, and papers that addressed medical cannabis over those concerned with recreational cannabis. Reviews were prioritised over non-reviews as they cover a wide range of studies, increasing the confidence in the validity of the findings. We did not expect the research questions to be equally well addressed by the available literature and so we applied our prioritisation criteria with some flexibility. In total, attempting to cover all research questions and within our resource constraints, we included information from 26 documents from the literature searches, 10 documents papers suggested by key informants and DfT, and 20 documents from the website searches.

Following the identification of evidence, a process of initial screening took place. Titles and abstracts of all identified studies were screened against the inclusion criteria. Screening from website searches took place at source. Full texts of each paper that met the inclusion criteria were retrieved where possible and screened to assess their relevance for specific themes reflecting the research questions. Key information was then extracted and organised by theme.

Data from the interviews and literature review were analysed simultaneously and brought together in a narrative synthesis.

2.3 Methodological limitations

As was foreseen and discussed with DfT, the types and strength of evidence varied across research questions. For example, we found more data on the nature and degree of impairment caused by cannabis and the overall risk to road safety. There

was more limited literature on other topics, notably the profile of medical cannabis users, which was derived almost entirely from interview data.

Most published literature (particularly on risk) relates to North American contexts, with the majority of that from settings where cannabis is legally available for non-medical as well as medical use. There may therefore be some divergence in legal, regulatory, and cultural factors that affect the direct applicability of this evidence to the context of legalised medical cannabis in the UK. However, we have made clear where the evidence presented comes from.

With these limitations in mind, we are confident that the findings are an accurate representation of the state of the evidence as it currently stands. For the topics where our evidence is based solely on interview data, it is likely this represents the best evidence available.

2.4 Report structure overview

The rest of the report includes findings from the interviews and REA. The chapters are presented as follows:

- **Chapter 2** provides an overview of the legislation and regulations governing medical cannabis use in the UK and the types of cannabis that are available. It discusses health sector rules and practices related to prescribing and evidence on the effectiveness of medical cannabis.
- **Chapter 3** describes the number and types of prescriptions for medical cannabis in the UK at present, the relationship of prescribed cannabis with other drugs, and the demographic, health and driving profile of medical cannabis users in the UK.
- **Chapter 4** presents evidence on the nature and duration of driving impairments due to cannabis and the associated risks to road safety.
- **Chapter 5** outlines DVLA guidance on driving eligibility and medication and discusses the clinical guidance provided to patients using medical cannabis. It also presents evidence on patient adherence.
- **Chapter 6** reflects on possible changes in the coming years and their implications for road safety. It also outlines some research gaps for future consideration.

3 Setting the scene

Since the initial criminalisation of cannabis in the UK in the 1920s, several different laws and regulations have been implemented. The following chapter provides a description of the current legislative framework and health sector landscape in relation to cannabis use for either medical or recreational purposes. The chapter also outlines the types of cannabis products currently used for medical purposes and the rules and guidance followed by the NHS and the private sector. Finally, it briefly describes the existing evidence on the effectiveness of medical cannabis and the role of patients' registries in building this evidence base.

3.1 Legislative and regulatory framework

3.1.1 Legislation related to cannabis in the UK

Cannabis has long been used by humans, including for medical purposes. The psychoactive effects of delta-9-tetrahydrocannabinol (THC) have implications for population health and productivity and the supply and possession of cannabis have been criminalised in the UK since the 1920s, (Select Committee on Home Affairs, 2001) (Stevens, 2018) and most recently by the Misuse of Drugs Act 1971 (Misuse of Drugs Act, 1971). Cannabis also contains other compounds, the most important of which is cannabidiol (CBD, see Box 1).

The potential for cannabis to effectively treat a range of health conditions has had mainstream recognition in the UK since at least 1998 (Select Committee on Science and Technology, 1998). In 2018, following controversy over severely epileptic children being denied effective cannabis-based medication, the government amended the 2001 Misuse of Drugs Regulations (Schedule 2) to include "cannabis-based products for medicinal use in humans" (CBPMs) (Misuse of Drugs (Amendments) Regulations, 2018). This made cannabis-based products legal provided they were produced and used for a medical purpose and were prescribed by a doctor on the specialist register (that is, a consultant rather than a GP or junior doctor). In addition, three specific cannabis-based products are scheduled individually, outside the CBPM category (see section 2.1.3).

The relationship of cannabis to road safety largely concerns the impact of the psychoactive effects of THC on people's ability to drive safely. Since the Road Traffic Act 1988 it has been an offence to drive while unfit through drink or drugs (Drug Driving (Specified Limits) (England and Wales) Regulations, 2014).

In 2010 the North review of drink driving and drug driving, recommended bringing in threshold-based offences for driving with blood concentrations of certain drugs above named limits (called "per se" limits) (North, 2010). In 2012 the government amended the Road Traffic Act 1988 to establish a legal basis for per se limits for drugs, and commissioned expert evidence on the appropriate level at which those limits should be set. Reporting in 2013, the Wolff review recommended a limit of 5 micrograms per litre for THC (Wolff et al., 2013). The subsequent 2014 Regulations, which came into force in 2015, set the per se limit for THC at 2 micrograms per litre, lower than the Wolff review recommended (EMCDDA & CCSUA, 2018). See section 4.1.2, Box 2 for more detail on legal limits and impairment.

Ahead of the introduction of the per se limits in 2015, DfT issued guidance for healthcare professionals which set out the new statutory "medical defence" (Department for Transport, 2014). If medical cannabis has been lawfully prescribed for medical purposes and taken in accordance with instructions given by the prescriber, a

driver has a defence against a charge of driving with excess THC in their blood. (If there is evidence of impairment, the driver can nonetheless be prosecuted under section 4 of the Road Traffic Act 1988.)

Box 1: Components and physiological effects of cannabis

There are three components of cannabis that are important for its medical use, its implications for road safety or both: THC, CBD and terpenes. Overall, the main effect of concern is sedation or drowsiness. Other effects include distraction, blurred vision and dizziness.

Delta-9-tetrahydrocannabinol (THC) is the psychoactive compound that provides the high often sought in recreational cannabis use and some of the beneficial health effects desired by users of medical cannabis.

Cannabidiol (CBD) is a compound with no psychoactive effects but which gives various health benefits different to those offered by THC. While it is a component of many medical cannabis products, CBD alone is not a controlled substance and is available without prescription and commonly available from high street health shops.

Terpenes are a class of compounds found in high concentrations in cannabis. Terpenes are much less widely discussed than THC or CBD, (only two participants mentioned them) and they do not feature prominently in the literature on cannabis, impairment and road safety.

3.1.2 Regulatory framework for medical cannabis

The production and distribution of medical cannabis products is regulated by the Medicines and Healthcare products Regulatory Agency (MHRA). The MHRA sets rules and guidance for the production, import, distribution and marketing of medicines in the UK, and issues the marketing authorisations by which medicines become licensed. In exceptional cases the MHRA also has a role regulating unlicensed products of which it may not have assessed the safety, quality and efficacy.

Following the 2018 rescheduling of cannabis, the MHRA issued guidance on unlicensed CBPMs (Medicines and Healthcare products Regulatory Agency, 2020). The guidance outlines that such unlicensed products are exempted from the requirement for a licensing authorisation by reference to the “special needs” of an individual patient identified by a specialist doctor and under that doctor’s direct personal responsibility. The patient’s special needs must be such that a licensed product cannot adequately treat their condition; this is reflected in participants’ comments that for prescribing CBPMs for pain, patients must have previously been on two “traditional” pain medicines, generally through a pain clinic, before being eligible for CBPMs.

The guidelines for medical cannabis prescribing in the UK have been described by a leading advocate as “surprisingly liberal”, with no restrictions on indications or mode of CBPM administration apart from that they must not be smoked (Barnes, 2019).

3.1.3 Types of cannabis products used for medical purposes

The range of cannabis-based products used to treat health problems runs from licensed medicines through to illicit cannabis. These can be used alone or in combination, and the levels of THC and CBD, and how accurately these are known, vary. The different products are distinguished by whether they are legal or illicit, among legal products, whether they require a prescription, and among prescription products,

whether they are licensed and how they are scheduled in the 2001 Misuse of Drugs Regulations.

- **Licensed prescription cannabis-based medicines** are individually scheduled in the 2001 Misuse of Drugs Regulations. As outlined by the Advisory Council on the Misuse of Drugs, (ACMD) three cannabis-based medicines are currently scheduled individually: Epidyolex, Nabilone and Sativex (Advisory Council on the Misuse of Drugs, 2020, p. 6). All three are licensed, which means they have received marketing authorisation from the MHRA following an assessment of safety, quality and efficacy, and are prescribed by NHS doctors.
- There are currently no licensed CBPMs in the UK. **Unlicensed CBPMs** contain THC and CBD at a range of levels and in a range of THC:CBD ratios. The most common routes of administration include oils taken as oral drops or sprays, and flowers taken by vaping. Participants suggested that private clinics do not recommend smoking as a route of taking CBPMs due to the known negative health effects of smoking.

According to MHRA guidelines the THC/CBD content in unlicensed CBPMs ought to be quantitatively stated (Medicines and Healthcare products Regulatory Agency, 2020). However, it is not always easy to find out what these products contain: one participant attached to a registry reported that for the small proportion of products prescribed outside the registry formulary, they had to investigate what the THC/CBD content was.

- Legal, **non-prescription CBD supplements** from health food shops (most often oils or capsules) do not contain THC and tend to be regulated under “novel foods” legislation (unless created specifically for medical use as CBPMs) (Advisory Council on the Misuse of Drugs, 2020).
- There is also widespread use of **illicit cannabis** to treat health problems (Centre for Medical Cannabis, 2019). The THC levels in illicit cannabis are not predictable but given the narrow criteria for public sector prescriptions and the limited reach and sometimes high cost of private prescriptions, use of unregulated cannabis for medical purposes is perceived to be common. Participants said that many patients with chronic pain, in both NHS and private clinics, reported using illicit cannabis, especially if their requests for medical cannabis were declined. Clinicians prescribing medical cannabis reported that patients should stop using illicit cannabis as a condition of the prescription. Participants were clear that beyond differences due to dose and mode of administration, medical and illicit cannabis are fundamentally the same product with similar effects on impairment.

3.2 Health sector rules, guidance and practice

The National Institute for Health and Care Excellence (NICE) issues guidelines on health technologies which are used to guide clinical practice and inform prescribing policies in the NHS. Following the rescheduling of CBPMs in 2018, NICE published a guideline on cannabis-based medicinal products (NG144) (National Institute for Health and Care Excellence, 2019). NG144 recommends that doctors “consider Nabilone as an add-on treatment for adults with chemotherapy-induced nausea and vomiting” and “offer a 4-week trial of THC:CBD spray [Sativex] to treat moderate to severe spasticity in adults with multiple sclerosis”, as well as making a recommendation for research into CBD (Epidyolex) for severe treatment-resistant epilepsy. NICE recommends that doctors not offer THC or CBD to manage chronic pain, and the guideline makes no recommendations about other conditions.

In both the NHS and private sector, GPs cannot prescribe medical cannabis except as part of a shared care arrangement with a specialist. In the NHS, medical cannabis products are used when other treatments have failed, and in private clinics patients need to have had two previous failed treatments with non-cannabis medications before they are eligible for CBPMs (as mandated by the “special” categorisation of CBPMs).

3.2.1 NHS practice

The NHS describes medical cannabis as “only likely to benefit a very small number of patients” (NHS, 2018), related to the narrow set of conditions for which prescriptions are currently recommended. In line with the NICE guideline, the NHS offers licensed cannabis-based medicines for indicated conditions but does not support prescribing unlicensed CBPMs for pain conditions (NHS, 2018). The NHS states that THC carries risks that are currently unknown and recommends clinical trials be carried out. An NHS England report found that many clinicians would not prescribe THC due to the lack of evidence and knowledge of the products and their unknown long-term effects (NHS England and NHS Improvement, 2019).

Advocates of CBPMs are frustrated with the slow pace of their adoption by Clinical Commissioning Groups (CCGs), GPs and specialist consultants (Nutt, 2020). Given the limited availability within the NHS, most people using CBPMs obtain these through a private prescription (NHS 2019).

3.2.2 Practice in private clinics

Private sector doctors prescribe more medical cannabis than NHS practitioners. Interview participants told us that most prescriptions are for CBPMs rather than licensed cannabis-based medicines. The biggest difference compared to NHS practice is in the range of conditions treated, which, in addition to epilepsy and multiple sclerosis include for example, multiple types of pain; mental health and psychiatric conditions including anxiety, depression, attention deficit hyperactive disorder (ADHD), post-traumatic stress disorder (PTSD), agoraphobia and obsessive-compulsive disorder; cancer-related pain and appetite loss, substance use, neurological and gastrointestinal conditions.

Most notably, participants from private clinics and registries reported that a large proportion of patients – generally over half – use CBPMs for chronic pain. Across participants familiar with private prescribing, it was commonly reported that 50% to 75% of patients used CBPMs for pain, around 20% to 30% for psychiatric conditions anxiety and depression, and also attention deficit hyperactive disorder (ADHD) and smaller numbers for multiple sclerosis (MS), post-traumatic stress disorder (PTSD) and other indications.

Price may represent another difference between NHS and private provision. One participant from a private clinic, with long prior experience in the NHS, reported that even if prescribed by GPs under shared care arrangements, the cost of CBPMs was unlikely to be met by the NHS and the full cost would have to be covered out of pocket. What NHS prescriptions for CBPMs would cost is unclear, but it was felt they would be relatively expensive.

Although media reports commonly report private prescriptions costing thousands of pounds per month (Daily Express, 2020), several participants explained that they offered prescriptions for around £150 per month, deliberately set to be similar to what patients would commonly spend monthly on illicit cannabis.

3.3 Effectiveness of medical cannabis

There is some disagreement over the quality of the evidence that exists for the health benefits of medical cannabis. The main division is between experimental evidence derived from randomised controlled trials (RCTs) and observational “real-world evidence” derived from patients’ experiences with medicines prescribed in non-experimental routine care. RCTs are commonly viewed as a “gold standard” of evidence in medicine and RCT data is the primary form of evidence used by bodies such as NICE.

Evidence for the efficacy of medical cannabis from RCTs is mixed. For example, a 2017 systematic review reported the effects of medical cannabis for chronic pain in 27 RCTs and 3 cohort studies, for chronic neuropathic pain, pain from multiple sclerosis and other pain conditions (Nugent et al., 2017). The methods and findings were heterogeneous and the results most often showed a limited benefit of cannabis, either statistically insignificant or lower than the threshold of clinical relevance. A recent literature review on medical cannabis in oncology also found mixed results, with several studies showing important improvements in cancer-related pain and others showing no statistically significant effect (Abu-Amna et al., 2021).

Despite these mixed findings, a 2018 review found that there was “conclusive or substantial evidence of efficacy” for using medical cannabis to manage chronic pain in adults (MacCallum and Russo, 2018). A recent review drawing on other major reviews as well as real-world evidence presents a slightly different assessment of the strength of evidence for different conditions, but agrees it is relatively strong for pain conditions, for which there are high numbers of potential patients (Schlag et al., 2021a).

Compared to RCT evidence, real-world evidence often shows higher efficacy. This may partly be because the patient population self-selects into the treatment, for example by requesting CBPMs when they have already had positive health benefits from using illicit cannabis. Nonetheless, real-world evidence suggests that for some conditions, CBPMs can be highly effective, as reflected in a paper on a series of 10 children with severe epilepsy and associated pain (Zafar et al., 2020).

With this evidence in mind, some literature points toward increasing interest in and acceptance of CBPMs for pain, including in other countries. For example, a 2017 survey of doctors in Israel (in which 50/79 pain specialists responded) found that 95% prescribe CBPMs in their pain practice; 20% found CBPMs “very effective” and 43% found CBPMs “effective to some extent” in treating intractable chronic pain (Sharon et al., 2018).

Another example is reported in a paper currently in preprint showing data from an expert conference in the UK to rate the benefits and risk profiles of drugs for chronic neuropathic pain. A range of experts took part in a structured process to rate the benefits and risks of drugs including THC, CBD, THC/CBD, gabapentin, amitriptyline, opiates and others (Nutt et al., 2021). The cannabinoid drugs were ranked highest overall on the benefit–safety balance; on the specific risks of cognitive impairment, drowsiness and dizziness, THC/CBD and THC were considered comparable to or better than all other serious pain drugs (that is, excluding ibuprofen).

Experimental evidence is not however always necessarily convincing: one doctor cited a recent randomised trial that showed no impairment from vaping CBD-dominant cannabis compared to placebo (Arkell et al., 2020), the doctor thought the trial dose of 13.75mg CBD was implausibly low compared to a plausible prescription dose of over 600mg.

Mixed views regarding the effectiveness of medical cannabis, and particularly of unlicensed CPBMs, for improving health were also shared by interview participants. This disagreement largely related to the quality of evidence required to make clinical judgments, as outlined above. As might be expected, people involved in clinics

prescribing CBPMs regarded the quality of the evidence for psychological and pain conditions as higher than others, including NHS stakeholders.

3.3.1 Registries and the future of evidence

This quick overview demonstrates that there is still much to be learned about the health benefits of medical cannabis; calls for further research are common among authors and were also made by many interviewees. The absence of more conclusive evidence may continue to slow the adoption of CBPMs among NHS practitioners, but it seems likely that patient numbers in private clinics will continue to increase. This presents an opportunity to gather data, albeit observational rather than experimental, through registries involving patients from private clinics or networks of private clinics.

Registries serve primarily to build the evidence base on efficacy and safety. Two such large registries already exist: the Drug Science Project Twenty21 registry and the Sapphire clinic network both collect data explicitly for research purposes (Drug Science, 2021) (Sapphire Medical, 2021). One participant suggested that another private registry was being planned. There are also plans for a registry of NHS medical cannabis patients, although this registry may take a long time to generate evidence (Business CANN, 2020).

4 Prescribing landscape

This chapter explores the current prescribing landscape by presenting some estimates on the number of patients using medical cannabis, the types of products prescribed in terms of concentration of active ingredients and mode of administration, and the use of other drugs together with prescribed cannabis. It also outlines the profile of medical cannabis users in the UK by focussing on three areas: the demographic characteristics, health conditions and driving profile of medical cannabis users.

4.1 Numbers of patients

The number of people using medical cannabis in the UK varies according to the type of product under consideration:

- By one estimate over 1 million people in the UK use illicit cannabis with medical intent (Centre for Medical Cannabis, 2019).
- There are no formal estimates of the number of prescriptions for unlicensed CBPMs. However, participants suggested that most clinics have patient numbers in the low dozens, and the networks associated with the two large registries, Project Twenty21 and Sapphire, have between 500 and 1000 users each. **Participants' estimates of the total number of prescriptions varied substantially, from under 1000 (certainly an underestimate) to around 5000**, broadly suggesting the number is likely to be in the low thousands.
- A report from 2020 indicates that only three patients have NHS prescriptions for unlicensed CBPMs (Business CANN, 2020).
- Prescriptions for licensed cannabis-based medicines through the NHS number in the low hundreds. There are signs that this may be increasing: NHS prescriptions in the five months from November 2019 were higher than those for the entire previous year (328 vs 320) (Advisory Council on the Misuse of Drugs, 2020). ACMD (2020) considered this increase to “probably” be related to NICE publishing guideline NG144, which may have raised the profile of medical cannabis.

The current effect of medical cannabis use on the number of drivers on the road per se is probably negligible: the DVLA's senior doctor states that 757,000 people told DVLA about a medical condition in 2020 (Jenkins, 2021). People prescribed medical cannabis are a tiny fraction of that number, and a substantial proportion of medical cannabis users are likely to be too sick to drive (see section 3.4.2 below).

4.2 Types of prescriptions

Medical cannabis varies by level of THC and CBD, by THC:CBD ratio, and by mode of administration. Mode of administration is important for the maximum concentration of THC, affecting degree of impairment, and duration of THC presence in the body, potentially affecting duration of impairment and the time for which someone may be over the legal limit.

Interview participants unfamiliar with private sector activities suggested that more knowledge was needed of prescribing practice in the private sector. Private prescribers were willing to give details of their prescribing practice, albeit in the context of not being identified (and one remarked on the secrecy that exists between proprietors of different clinics). Even if detailed data on private prescribing is not shared publicly, basic

breakdowns are available at least from the large Project Twenty21 registry (Project Twenty21, 2021).

The main CBPM preparations offered by private clinics are orally administered oils (in THC-dominant, THC/CBD-equivalent and CBD-dominant preparations), and dried flowers, (high THC and THC/CBD-equivalent) administered most commonly by vaping (in which the flower is heated in a vaporiser and the patient inhales the vaporised THC). Among interviewees attached to private clinics, all prescribe CBPMs and none mentioned prescribing licensed cannabis-based medicines.

Prescribers from medical cannabis clinics outlined the types of prescriptions they make for different conditions. One participant described the following typical daily prescriptions:

- Pain: CBD 50mg / THC 14mg (oral oil). Patients who need rapid relief of symptoms, (acute pain, for example) are prescribed dried flowers. The average prescription is 70gr of dried flowers a month;
- Anxiety spectrum / Autism: CBD 100mg / THC 20mg;
- Epilepsy (adults): CBD 450mg;
- Multiple sclerosis: CBD 20mg / THC 30mg

A pain doctor said that their clinic tends to begin new patients on a preparation that includes at least some THC, following discussions with more experienced colleagues in Canada about what is effective. For a patient new to cannabis (that is, no prior use of any cannabis including illicit cannabis) they might offer a daytime preparation of 0.3mL of oil with 5/20 THC/CBD mg/mL, generally to be taken three times daily (that is, 4.5mg THC daily). For patients with experience of cannabis (including illicit use) they might offer 0.5mL of oil with 10/10 THC/CBD mg/mL (15mg THC daily).

Mode of administration is also important for impairment. Vaporised (and smoked) cannabis have much higher maximum blood concentrations of THC, with much faster onset of the maximum concentration (Schlag et al., 2021b). In contrast, with oral administration, such as ingestion of cannabis oils, concentrations remain elevated for longer, but at much lower maximum levels. Patients who used substantial THC to relieve symptoms before sleeping would typically be given a flower to put in a vaporiser.

A review from 2018 seeking to offer guidance to doctors on prescribing states that consuming more than 20 to 30mg of THC daily risks psychoactive side effects (MacCallum and Russo, 2018), which is consistent with the example daytime prescriptions outlined above. Additional warnings about driving and other responsible or dangerous activities are recommended for prescriptions with a higher THC content, including those given to relieve pain at night.

4.3 Relationship of prescribed cannabis with other drugs

Participants involved with medical cannabis clinics reported two groups of drugs were commonly used by patients instead of (or in some cases in addition to) medical cannabis:

- Some patients (primarily with chronic pain) used illicit cannabis before they presented to a private clinic. Wanting to avoid the psychoactive effects of illicit cannabis and knowing exactly what they were taking were reported as key

motivations for some patients to access a medical cannabis prescription through a private clinic, especially if they had been declined a CBPM in the NHS.

- Other pain drugs such as gabapentin, amitriptyline and opiates were also commonly used. Prescribing physicians interviewed felt these drugs were less safe for driving than medical cannabis:

“We generally try and reduce other medicines once they’re settled on cannabis medicines ... If we can get people onto cannabis medicines and wean the gabapentin and the tricyclic then actually in a complicated way that improves risk profiles overall for the patient.” (Interview participant)

4.4 Medical cannabis user profile

There is little published information on the characteristics of medical cannabis users in the UK. A recent review on medical cannabis and cannabis dependence (Schlag, 2021b) presents data from several countries and a range of settings on the differences between medical and recreational use and users of cannabis. The review highlights that compared to recreational users, medical cannabis users are older, usually have poorer general physical health and psychological wellbeing and lower quality of life scores, and mainly use cannabis to alleviate their symptoms. Additionally, they are less interested in ‘getting high’, take lower, controlled doses and are less likely to have a substance use disorder. Beyond this, the data on the characteristics of users detailed below comes from the interviews.

Table 1: Characteristics of medical vs recreational use and users, from Schlag et al. 2021b

Medical Use	Recreational use
Often daily (55.9% of users report daily use, 23.5% report weekly use) (Stewart, 2020)	Full range from rarely to daily; only some daily users are addicted (Cuttler and Spradlin, 2017)
Various routes of administration (Borodovsky et al., 2016)	Often smoked with tobacco in the UK (Winstock et al., 2017)
Lower controlled dose of known quantity of cannabinoids/cannabis (Cash et al., 2020)	Higher THC dose, often unknown, cannabinoid and content usually unknown (Cash et al., 2020)
Regulated quality (e.g., cGMP)	Unknown quality
Poorer general physical health (Lin et al., 2016)	Usually good general health (Lin et al., 2016)
Poorer psychological well-being (Goulet-Stock et al., 2017)	Generally good psychological well-being (Goulet-Stock et al., 2017)
Lower physical QoL scores	Generally normal range of QoL
Higher age (>50 years) (Turna et al., 2018)	Lower age (Winstock et al., 2019)
Main aim to alleviate symptoms (Stith et al., 2018)	Main aim enjoyment, relaxation, social effects (Geraint et al., 2008)
Little desire to get 'high'. Represented in a sample of MS patients with high dropout rate from Sativex (THC based medication) (Carotenuto et al., 2020)	Liking effects of THC (Osborne and Vogel, 2008)
Lower prevalence of substance use disorder (including alcohol) (Compton et al., 2017)	Often other psychoactive drug use (Compton et al., 2017)

4.4.1 Demographic profile

Interview participants reported that the population of patients using medical cannabis is diverse. In terms of age, users ranged from very young to elderly patients, although they tend toward middle age and patients aged under 25 are rare. The majority of patients (around 60%) are male. Patients have a range of work and activity profiles. Some are too disabled to work, while others work in a range of occupations, or are students, retirees, or full-time carers. The relatively high cost of prescriptions and products means that users are often economically stable. However, in recent years there has been a reduction in the cost of products and prescriptions which may have moved people from the illicit market to the legal one. Finally, participants noted that many patients previously used (or were using) illicit cannabis at the time of accessing medical cannabis.

4.4.2 Health profile

The health profile of medical cannabis users is also diverse given the number of conditions that are currently treated, mainly by private clinics. According to interview participants, medical cannabis users were often patients with multiple health conditions, referred to by one participant as:

“Some of the most disabled people in the country.” (Interview participant)

This affects their quality of life and contributes to the emergence and exacerbation of other conditions, some of which are also treated with CBPMs. For example, anxiety and depression were often treated with CBPMs alongside other conditions.

“[Chronic pain] patients almost always have anxiety and depression as well, and it’s a circular argument: anxiety and depression predispose you to having real physical pain because they affect your nervous system, and having long term pain of course gives you anxiety and depression, so we’re always aware we are treating [anxiety] as a secondary condition.” (Interview participant)

Although symptom profiles are diverse, participants reported that in their opinion, patients tend share a common wish to improve their health-related quality of life:

“If you ask me to pick a characteristic, the only one is that they are all people who want to improve their quality of life. That’s the only thing [they] all have in common.” (Interview participant)

The importance of quality of life for users of medical cannabis is also described in the recent review of evidence on medical cannabis and dependence (Schlag et al., 2021b).

4.4.3 Driving profile

There are currently no studies on the driving profile of medical cannabis users in the UK. This information gap was discussed with the key informants who reported their impressions and experiences. For example, one participant from a network of private clinics estimated that four out of ten (39%) of their patients drive: a quarter of them drove socially, eight per cent commuted to work by driving, three per cent drove a car for work, and less than one per cent (0.4%) drove a light or heavy goods vehicle for work.

The health conditions of users emerged as one of the main challenges to driving, and the presence of different conditions at the same time (multimorbidity) means that medical cannabis users may be less likely to drive compared to the general population. In addition, some of the conditions treated with medical cannabis, such as epilepsy, are considered incompatible with driving by DVLA unless they are under control and a number of specific criteria are met (DVLA, 2021a) (DVLA, 2021b). For other conditions, such as anxiety, PTSD, and agoraphobia, patients are advised to inform DVLA if these may affect one's ability to drive safely. In most cases, interview participants indicated that their patients had informed the DVLA of their health conditions. While this may prevent individuals with particular conditions from driving, participants also added that some patients had reported that the use of medical cannabis enabled them to drive by lessening the physical and cognitive impact of their symptoms (discussed further in chapter 4).

Differences linked to the location of practices and patients were also highlighted as impacting on driving. For example, participants reported that patients in rural areas and in towns with poor transport systems may find it necessary to drive to get around.

5 Driving impairment and road safety

The type and extent of impairment caused by using cannabis (either for medical or recreational purposes) depends on a number of different factors, such as an individual's medical conditions, previous experiences with cannabis, THC intake and mode of administration. This chapter addresses the nature and duration of impairment through cannabis and how impairment varies between different types of medical cannabis product. It also discusses how medical cannabis use may interact with impairment caused by other drugs or by health conditions. Finally, it addresses the level of risk posed to road safety by driving impaired by cannabis use.

5.1 Driving impairment and cannabis use

5.1.1 Nature and duration of impairments associated with cannabis use

Interview participants stressed the wide range of possible effects of cannabis on the body and mind, and the subjective nature of individual responses to the drug. Several effects that may impact on driving safety were mentioned by participants. These included drowsiness and sedation, impaired judgement, slower reaction time, poorer control of motor skills, lack of concentration, confusion and blurred vision. The extent of impairment varies considerably, and a physician who works for a private clinic described the most severe cases as comparable with the effects of morphine, such as feeling sleepy, tired or dizzy, and confused (NHS 2018). Participants had differing views on how (and when) to assess impairment (see Box 2).

Studies from the USA, Australia and Europe investigating impairment often experimentally compare users' performance in simulated driving environments after taking THC, THC/CBD, or placebo. These tend to be small studies and have mixed results. For example, a test of 14 volunteers who received either 125 mg of vaporised cannabis-based products (THC-dominant or THC/CBD equivalent) or a placebo found that cannabis increased lane weaving during a car-following exercise and reduced the subjects' confidence in driving (Arkell et al., 2019). However, a second test which did not require the volunteers to follow another car in the simulation found that neither mean speed nor lane weaving were affected. Further studies found similar results (Arkell et al., 2020) (Tank et al., 2019). In these studies volunteers continued to feel impaired up to four hours after inhaling cannabis, and considered themselves still impaired, even though observable drug effects had disappeared by that point. Impairment was self-assessed and reported by the participants and also tested through cognitive and psychomotor tests sensitive to THC impairment (Arkell et al., 2020) or via medical examination (Tank et al., 2019). A recent review of literature on impairment and use of medical cannabis (Eadie et al., 2021) reported that the usual duration of neurocognitive impairment (difficulty in articulating and processing information which may affect attention, manual dexterity, coordination, and reaction time) following use of medical cannabis containing THC is four hours or less. The authors note that studies of impairment in recreational use (usually smoking) show a strong dose-response association. The evidence we reviewed did not include any similar estimate of the duration of impairment following recreational use of cannabis. However, there is no reason to think that for a given dose and mode of administration in a person of given tolerance, there would be any difference in impairment according to use for medical versus non-medical purposes. As noted above, a population of medical users may well use lower and more consistent doses than a population of recreational users.

A further study with 20 participants (Micallef et al., 2018) explored the effects of cannabis consumption on driving in both simulated and real settings. It found that impairment was more pronounced during the simulation than during the real driving. The researchers suggested that this may be due to several factors related to higher levels of attention in the real setting and absence of adequate sensory stimulation in the simulation.

A further factor is the long-term effects of cannabis consumption on users. A recent meta-analysis of previous studies (Lovell et al., 2020) found that regular use of cannabis products was associated with a mild to moderate loss in some areas such as cognition, executive function, learning, memory and decision-making. These losses were persistent (that is, observed when the user had not recently taken cannabis) and may impact on an individual's ability to drive safely.

More targeted but smaller studies broaden our understanding of this issue. For example, a study of non-intoxicated regular users of recreational cannabis (Dahlgren et al., 2020) found that "chronic cannabis use is associated with impaired driving performance even in the absence of acute intoxication" (p. 7) (chronic use was defined as using cannabis at least 5 days a week, having used it at least 1500 times in their lifetime, and having urine testing positive to cannabinoids). During the simulated driving test, cannabis users showed higher levels of impairment compared to the control subjects. They also had more accidents, drove faster, showed increased lateral movement, and were less able to follow the rules. However, the research also reported that driving impairment was mainly found in those cannabis users who had started using cannabis before the age of 16, and that impulsivity had an impact on how users and non-users performed. According to the researchers, the role played by impulsivity is unclear, although potentially significant: it may be one of the factors that determined an early onset of cannabis use, but it may also be the result of the neurological impact of cannabis on individuals younger than 16.

5.1.2 Relationship of impairment to types of medical cannabis

Different medical cannabis products contain different levels of THC and CBD and different THC:CBD ratios, which can impact on impairment in different ways. The effect of THC is dose dependent (Eadie et al., 2021) and the impact of the level of THC on potential impairments was emphasised during the interviews. Interviewees did not regard CBD as a concern for road safety, although some noted that sedation is a side effect for a minority of users of the CBD-only product Epidyolex.

Studies offer a mixed picture of the interaction of CBD and THC in relation to driving impairment. For example, a study on 705 people in Norway looked at THC/CBD levels in blood samples taken after an accident or after having been stopped for suspected drug driving (Havig et al., 2017). The results suggest that THC causes impairment, but CBD does not. By contrast, small simulator studies have found that CBD increased the concentration of THC in the subjects' plasma and in some cases worsened driving impairment (Arkell et al., 2019). Another small study found that CBD did not reduce impairment but that THC:CBD-equivalent cannabis increased driving confidence compared to THC-dominant cannabis (Arkell et al., 2020). Increased confidence may not positively affect driving ability, although the authors did not comment on this.

Apart from CBD, other chemical compounds that are found in cannabis products may contribute to driving impairment. For example, some interview participants suggested that terpenes may have a role in producing some of the effects typically associated with the use of cannabis such as sedation. A 2021 systematic review (Eadie et al., 2021) reported that myrcene, a terpene, may increase the sedating effects of THC, and suggested that future studies should "monitor and record in detail the quantities and

concentrations of the other constituents of the cannabis being studied, as the individual or “entourage” effects of these on cognitive impairment is largely unknown” (p. 11).

Interview participants explained that the administration route is also linked to differences in impairment. Inhaling vaporised flowers has a more intense and quicker onset, but the duration of the effects including impairment is shorter (about 4 hours for a typical dose). Oils have a slower onset but the effects last longer (about 6 hours). The differences in onset and effects due to the administration route are also indicated by a study (Celius and Vila 2018) comparing smoking cannabis containing 34 mg of THC content with taking eight oral sprays of Sativex administering 22 mg of THC. Despite the broadly similar levels of THC taken in, the maximum concentration of THC in the blood plasma was 162 µg/L at 9 minutes post-inhalation for smoked cannabis compared to 5.4 µg/L at 60 minutes after spraying for Sativex.

Box 2: Legal limits and impairment

There is disagreement over whether per se limits or impairment form the best basis for offences of driving under the influence of cannabis:

Interview participants highlighted the fact that long-term cannabis users may have elevated levels of THC in their blood despite not having used cannabis recently and would therefore not be impaired to drive safely. One individual raised concerns that long-term users might be criminalised without presenting an elevated risk, and equally that other patients on lower doses and with less THC in their blood may have much greater impairments, depending on other contextual factors:

“Some patients on higher doses of medical cannabis may reach that [upper limit] but might not be affected; while some patients on lower doses, who are nowhere close to the legal cut-off are severely affected and should not drive.” (Interview participant)

The literature supports this view, highlighting a poor correlation between blood THC levels and impairment. For example, one study found that a minority of long-term users may exceed legal blood THC limits even after several days of abstinence (Peng et al., 2020). Another concluded that per se limits “do not reliably represent thresholds for impaired driving” (Arkell et al., 2021, p. 107), and a review describes “equivocal evidence correlating specific blood levels of THC with psychomotor impairment” (Chow et al., 2019, p. 1304).

Although the evidence suggests that per se limits may not be an accurate interpretation of impairment in all cases, one participant explained that the argument misses the point: limits such as those in the contemporary UK drug driving legislation are not primarily about impairment but about liability. In addition, concentrations of THC at 5mg/mL are associated with increased collision risk, even if there is variation in individual impairment at that level: “Impairment is a very dangerous word... because it's very difficult to assess. It's very subjective.” (Interview participant)

In practice, enforcement of drug-driving laws based on impairment is available to police and prosecutors. The per se limits aim to deter drug-driving regardless of impairment, and the medical defence provides prescribed drug users do not risk being prosecuted for drug driving simply for using their medication as advised (Crown Prosecution Service, 2019).

5.1.3 Comparisons to driving without medication or with illicit cannabis or other drugs

Although there is a clear risk of impairment from taking THC, driving may also be impaired by users' health conditions and by other drugs they are using including illicit cannabis and other medications.

It is possible that overall impairment may be less when using medical cannabis. Some studies show improvements in driving capabilities as a result of taking medical cannabis for specific health conditions. A study conducted on a multicentre, observational program by Etges and colleagues (2016) analysed the data of 941 patients, (including 761 from the UK) who were taking Sativex to treat spasticity and other symptoms of multiple sclerosis or other health conditions such as chronic pain. The study found that adverse events from the THC, such as dizziness and fatigue, were mainly reported during the first month of treatment, but there were no long-term safety concerns and driving impairment was not significant. Additionally, more study participants reported an improvement in their driving ability than reported a worsening (15% vs 4% of those driving).

A recent literature review (Celius & Vila, 2018) also highlighted similar improvements. Regarding the influence of Sativex on the driving ability of multiple sclerosis patients, the review highlighted that it does not impair driving, unless there are adverse events, and improves the patients' driving ability by controlling spasticity. Improved driving ability for patients treated with medical cannabis was also reported by interview participants. Examples provided by participants included patients with chronic pain who were not able to drive before starting using CBPMs due to intense pain, patients with PTSD who reported that CBPMs allowed them to focus on driving and avoid being distracted by intrusive thoughts, and a patient with chronic pain and ADHD who said he was calmer and less distractible after taking CBPMs which reduced the risk of driving and work accidents.

Risks were perceived to increase with higher levels of THC, which were known to be higher in illicit cannabis than medical cannabis. For example, one interview participant reported that the THC content was the main difference between illicit cannabis, which has a high THC content (up to 80%), and medical cannabis, which has a lower THC content (up to 23%). The same participant added that:

“Illegal cannabis is more likely to be mixed with other drugs, which means there could be a higher risk of being sedated or experiencing toxic effects because it [cannabis] can be mixed with anything.” (Interview participant)

Similarly, a review (Eadie et al. 2021) found that studies on recreational use of cannabis reported on average a THC content of 225 mg in each joint and an impairment lasting up to 24 hours, while studies that used doses more typically found in medical cannabis treatments (no more than 34 mg of THC) reported an impairment lasting no longer than 4 hours.

Participants described the impact of medical cannabis on road safety as similar to other prescription medicines that can cause sedation or affect the patient's reaction times. Some considered traditional pain medicines (such as gabapentin, amitriptyline and opiates) as worse for driving than medical cannabis prescribed in moderate doses. One issue with other drugs is the perceived level of impairment:

“Patients often don't recognise how impaired they are by [traditional pain drugs] gabapentin or tricyclic amitriptyline.” (Interview participant)

5.2 Cannabis and risks for road safety

This section explores the level of risk connected to the impairment caused by using cannabis. With some exceptions (Lee et al., 2018; Cook et al., 2020), most of the studies found for this review refer to recreational cannabis rather than medical cannabis, which is the focus of this study. This challenge was also highlighted by interview participants.

5.2.1 Degree of increased risk

A recent systematic review of reviews on cannabis-related harms (Campeny et al., 2020) found that use of cannabis was associated with increased odds of a motor vehicle collision, of being considered responsible for the collision, of non-fatal collisions, of becoming involved in an accident, and of fatal collision. The increased odds of these outcomes varied, with odds ratios of 1.6 to 2.7. While compelling, the authors also found that most of the reviewed studies did not describe accurately the frequency and quantity of cannabis used, or had difficulty isolating use of alcohol as a confounding factor. Such limitations highlight “the need to include data on quantity, frequency and patterns of use in future studies” (p. 31). More detail on these factors and on type of cannabis used, would help define different types of users, (for example ‘heavy users’) and how risks link to each typology of user.

An earlier assessment of several studies (Rogeberg & Elvik 2016) found a somewhat lower increased odds of motor vehicle crash due to the use of cannabis when controlling for confounding factors (such as alcohol intoxication). Controlling for these factors reduced the risk associated with cannabis alone to a “low-to-moderate” magnitude (odds ratio of 1.4). The authors also suggested two interpretations of the results that help explain the data:

- Cannabis users tend to be more aware of their impairment compared to alcohol users. This might mean that only those who do not feel impaired drive, lowering the risk of crashes. However, they also express concern that this could, in the future, convince new users that driving while intoxicated by cannabis is not problematic, making them overconfident and increasing the risk of crashes.
- Alternatively, they suggested that “deciding to drive while intoxicated is a decision correlated with traits that predict higher crash risk independently of cannabis use” (p. 10). Therefore, the estimation of crash risk linked to use of cannabis may be pushed upwards by individuals who would be ‘high-risk’ drivers independently of the use of cannabis.

Culpability studies are a further approach to assess the potential risk for road safety derived from the use of cannabis. These studies look at all the factors that may have contributed to an accident, which include not just the actions of the driver but also, for example, road type, vehicle conditions, crash type, and other parties’ responsibilities (Brubacher et al., 2014).

A review of culpability studies (Rogeberg, 2019) found that the attributable risk fraction from cannabis-impaired driving (the proportion of crashes that would be avoided if cannabis-impaired driving was eliminated) is below 2% in all but two reviewed studies, which shows that impairment linked to use of cannabis increases the risk of accidents, although with a low magnitude. The authors indeed state: “While this indicates that the overall public health impact of cannabis impaired driving is minor relative to that of alcohol-impaired driving, it does not imply that cannabis impaired driving is safe, and the low average is consistent with the presence of a smaller group of high-dose drivers with more substantially raised risks” (Rogeberg, 2019: 78). Most included studies were from the USA (as well as France, New Zealand and Australia) but many pre-dated more recent cannabis legalisation and related to illicit cannabis use.

It is worth noting that the degrees of increased risk noted for THC are much lower than those for driving impaired by alcohol. For example, a study from the US found that the odds ratios for fatal injury for drivers with a blood alcohol concentration of 0.08% (the legal limit in England) compared to sober drivers were 19.7 among drivers aged 16 to 20 and 7.5 for drivers aged 35 and over; the odds of fatal injury for drivers positive for marijuana was not significantly different from 1 (Romano et al., 2014). A study using data from several European countries found an odds ratio for fatal collision of 23.0 for

drivers with between 0.05% and 0.08% alcohol in blood, alongside a non-significant odds ratio of 1.3 for people positive for THC alone (Bernhoft et al. 2012).

5.2.2 Differences in risk according to legal and policy framework

The evidence suggests that risks in relation to road safety are not necessarily impacted by medical legislation, but that they can increase (even just for a short period) when cannabis is decriminalised or legalised, for example:

- In an analysis of fatal vehicle accidents in the USA between 1993 and 2014, (Seigny, 2018) 8.8% of drivers tested positive for cannabis, more than other drugs but less than alcohol (about a quarter of drivers tested positive for alcohol). However, the legalisation of medical cannabis was not found to be associated with an increased rate of drivers who tested positive for cannabis. The only exceptions were those states with medical cannabis licensed dispensaries, where the odds of driving under the influence of cannabis increased to 14%. This difference was explained in terms of legal and practical differences. For example, point-of-sale quantity limitations or the existence of dispensaries with a wide range of prices and products may encourage users to travel longer distances and more frequently. Similarly, restrictions on the number of dispensaries and prohibition of home cultivation may mean users drive more frequently.
- A study in the USA compared data on fatal crashes involving cannabis in states that moved from prohibition to medical legalisation with states that moved to decriminalisation or full legalisation. The authors found significant increases in fatal crashes in states that had decriminalised or fully legalised cannabis but no evidence of any change in fatal crashes where only medical legalisation was introduced (Lee et al., 2018).
- The same pattern was found in another study (Cook et al., 2020) that compared the rates of fatal crashes in US cities that had decriminalised cannabis use and those that had legalised medical cannabis only. The authors found that the effect of introducing policies on the use of cannabis for medical purposes had decreased the number of fatal crashes by 14% on average for people aged 15 to 24. Conversely, cities that decriminalised cannabis saw an increase of fatal crashes of 13% on average, (although this effect was only temporary, and the rate of fatal crashes fell back to pre-decriminalisation rates after 6 months).

In addition, some evidence suggests that the legal frameworks and their implementation and interpretation might impact on road safety. For example, a study on the implementation of recreational cannabis laws in Colorado and Washington State and fatal traffic accidents found that the legalisation of recreational cannabis was associated with an increase of fatalities in Colorado but not in Washington State (Santaella-Tenorio et al., 2020). This was interpreted as a consequence of the different ways the laws were implemented in the two states, including for example, purchasing limits, home cultivation, density of retail stores, prevalence of last-month use, allowed cannabis potency, route of administration, and cannabis tourism.

5.2.3 Limitations of risk estimates

Both the Cook and colleagues (2020) and Lee and colleagues (2018) studies used data from the US Fatality Analysis Reporting System (FARS), which limits the study only to the fatal accidents and makes it impossible to infer any relation between cannabis and less severe traffic accidents (Cook et al., 2020). This limitation was also

described by Romano and colleagues (2017) who pointed out that cannabis may make a driver more at risk of inattention-related accidents than those linked to aggressive driving. Conversely, the estimated risk associated to use of cannabis is usually assessed against the total number of accidents, which is larger than the number of inattention-related crashes. This may reduce the estimate of the actual extent of cannabis contribution to specific types of accidents. Romano and colleagues (2017) also found that crash risk estimates are highly dependent on the quality of the data collected.

In conclusion, the literature review suggests that people who have consumed cannabis have an increased chance of being involved in motor vehicle collisions. Interview participants also thought there were increased risks to road safety from using medical cannabis containing THC. However, much of the evidence on risk comes from studies in jurisdictions with general decriminalisation, or relate to illicit use, and as outlined, there is some evidence that legalisation for medical use does not increase crash risk at population level.

6 Driving guidance for patients using medical cannabis

This chapter discusses regulations on driving eligibility, guidance on driving while using medication, the advice patients receive from their prescribers on potential impairment, and patients' adherence.

6.1 Regulations around driving eligibility

Misuse of or dependence on cannabis is a basis on which the DVLA may refuse or revoke a driving license (DVLA, 2016). However, prescribed medical cannabis is treated differently, in line with other prescribed medications.

The DVLA requires by law that drivers tell the agency about any medical condition that could affect driving, and for certain named conditions, depending on the class of vehicle and details of the condition and treatment, the DVLA must be informed (DVLA, 2021a) (DVLA, 2021b). The DVLA will make an assessment, which may involve tests or contacting the patient's doctor. They may then revoke or change the duration of the patient's license or require them to adapt their vehicle. Patients must also inform DVLA and give up their licenses if their doctor tells them to stop driving for three months or more, or a medical condition affects their ability to drive safely for the same period.

The only condition requiring mandatory notification for which medical cannabis is commonly used is epilepsy (DVLA, 2021b). Most prescriptions are for conditions that do not carry a legal requirement of notification, although prescribers reported advising patients to notify the DVLA of their prescriptions to comply with the law and to avoid risking losing their insurance coverage in the case of a collision.

The DVLA produces guidance for medical professionals on assessing fitness to drive, to help professionals advise patients on whether to notify the DVLA of a medical condition (DVLA, 2021c). This guidance states that "doctors and other healthcare professionals should":

- advise the individual on the impact of their medical condition for safe driving ability;
- advise the individual on their legal requirement to notify the DVLA of any relevant condition; and
- notify the DVLA directly of an individual's medical condition or fitness to drive, where they cannot or will not notify the DVLA themselves.

The DVLA guidelines refer to patients being "free from any medication effects that would impair driving" as a condition for continuing to drive or resuming driving following medication. The guidelines give an outline of the elements required for safe driving, (such as attention and concentration, good reaction time, and coordination) but it is down to the individual driver to judge whether their ability to drive safely is impaired. Both guidance documents and interview participants suggest this judgement is often made following discussion with the driver's doctor. Participants commented on there not being a clear test for impairment, though some mentioned the type of thing they would advise patients to look out for, reflecting these element required for safe driving. One mentioned carefully assessing patients' speech for slurring during consultations, particularly as a sign of impairment by traditional pain medicines. One key informant mentioned having to ask DVLA for direct guidance on several occasions as the information on their website was "unclear".

Other resources also exist, such as the detailed Training Manual for Physicians and Pharmacists on Medicinal Drugs and Driving, developed for the European Commission (DRUID Consortium, 2009), which describes the steps doctors should take for prescribing safely to drivers. These include being prepared to answer questions patients have about advice on the label; outlining signs of impaired driving (such as trouble with vision, concentration or alertness, surprise at normal events such as changing traffic lights, difficulty in driving straight or staying in lane); close monitoring of and advice on other factors that may affect impairment by the medicine (such as concurrent use of other medicines or alcohol; and higher vigilance in the initial stages of a new medicine. These steps and others reflected what some prescribers described doing with their patients.

One participant explained that some patients mistakenly believe that they automatically lose their driving license if they start using medical cannabis. Therefore, they felt that some individuals might choose to continue using illicit cannabis because they are afraid that if they are prescribed medical cannabis, they will need to disclose it to the DVLA and therefore lose their licence. The implication here was that receiving a prescription increased the patient's accountability and made other actors aware of their activities. According to the participant, such patients can drive thanks to the use of cannabis which mitigates the symptoms of their conditions, but do not want to move to prescribed CBPMs due to a fear of losing their driving license.

6.2 Prescribers' advice to patients and patient adherence

Prescribers reported that they gave patients advice on driving while using medical cannabis, as they would with any other medication. This advice was not reported to be highly detailed but covered the main point that the patient should not drive if they feel impaired. Advice was given both verbally and in information leaflets. Prescribers also described considering the interaction of medical cannabis with other medications that a patient may be using and emphasised ongoing monitoring of how patients were responding to their medication, including those likely to impair driving. Finally, they advised greater caution when a patient first started taking a new drug.

Interview participants emphasised that judgements about fitness to drive safely were ultimately made by patients themselves. A participant speaking from a patient's perspective agreed:

"It is about being sensible as a patient. You know in your head if you are OK to drive or not, generally." (Interview participant)

In certain situations, prescribers reported giving more specific guidance to support safe consumption. Examples included:

- Prescribing a high-potency preparation for pain of a 0.5g flower at 20% THC that would deliver 100mg of THC to be taken at night. The guidance given alongside this stated that the dose should be taken after childcare, cooking and other tasks were finished and without any driving for 12 hours following consumption.
- Some patients seeking CBPM prescriptions may have these denied in certain circumstances due to their driving profile. For example, it was reported that one patient worked as a heavy goods vehicle driver and the clinic decided it was inappropriate to prescribe THC-containing CBPMs. It was not known whether this patient already used illicit cannabis, and therefore overall whether the risk to road safety is in fact reduced by such policies.

- In other situations, the guidance was vaguer – for example one prescriber advised that nobody should drive within an hour of vaping, with longer prohibitions for higher doses of THC.

Generally, prescribers expressed little concern that patients would not adhere to the guidelines and did not see compliance with medical cannabis as being inherently different to compliance with any other prescription medicine. According to the Crime Survey for England and Wales, in 2019/20, 3.8% of drivers (those who had driven at least once in the prior 12 months) self-reported having driven after taking medication where they were advised not to do so (Department for Transport, 2020). This proportion was higher for men than women (4.6% vs 2.9%) and lower for drivers aged over 30, (<4% across age groups) than for those under 30 (4.8% to 6.6%). As noted above, medical cannabis users tend to be male and older.

Much of the literature on adherence and attitudes to driving under the influence of cannabis (DUIC) comes from recreational cannabis users rather than medical cannabis users. While the potential for impairment by given blood concentrations of THC is unlikely to vary according to the reason for use, there are differences between the user populations that suggest that adherence may be higher among users with a medical need. In particular, there is evidence that medical users are older, and there is evidence that propensity to take risks decreases with age (Gomes-Franco et al., 2020). It is also worth noting that the main aim of medical cannabis users in using cannabis, as reported among multiple sclerosis patients using Sativex, is to alleviate symptoms rather than to 'get high' (Schlag et al., 2021b), which matched what interview participants said.

A study using the 2016/17 US National Survey on Drug Use and Health found that older users are less likely to report DUIC (Lloyd et al., 2020), although the same study showed distinctly increased odds of DUIC among people who used cannabis for both medical and recreational purposes, compared to those who only used for medical purposes. This raises the important caveat that for a minority of users, motivations for using cannabis may overlap and suggests that doctors may need to investigate patients' motivations and adjust their guidance accordingly.

7 Possible changes in the future

This chapter presents possible changes that could affect the level and nature of medical cannabis use in the UK in the future, regarding regulation and prescribing practices, and discusses the implications for road safety of potential growth in patient numbers. It concludes by outlining some areas where further research might be useful.

7.1 Regulatory changes

Aspects of the regulatory regime around CBPMs could change. Currently, the MHRA advises that:

“The unlicensed CBPM is a ‘Specials’ medicinal product, formulated in accordance with the specifications of a Specialist doctor, and for use by an individual patient under his direct personal responsibility.” (Medicines and Healthcare products Regulatory Agency, 2020, p. 7)

Interview participants identified the categorisation of CBPMs as “specials” as a limitation on their uptake, both in reference to who can prescribe but also with regard to the licensing and supply implications. Although some regarded the restriction as unjustifiable and damaging to health, nothing from the research suggested this categorisation was likely to change soon. Participants thought that the somewhat ‘last-resort’ nature of medical cannabis, requiring two previous failed treatments, was likely to remain.

Given the NICE guidance and the common view in interviews and literature that the evidence base needs improvement, it seems likely that any regulatory change (including expansion of NHS CBPM prescribing to further conditions) would require either improvement of the evidence base or a change in the approach of regulators to consider non-RCT, “real-world” evidence. A participant advocating the effectiveness of CBPMs commented that RCTs for rare conditions “will never happen”, as patients are too few and RCTs are not financially viable. Although observational evidence is less robust there are circumstances in which consistent strong observational evidence may be adequate to guide clinical practice (Potts et al., 2006), as is evidently happening in private clinics. NICE has procedures for including observational evidence in its assessments (Faria et al., 2015) and these could guide studies conducted by researchers working with registry data. Even if the “true” effectiveness of CBPMs is modest, the number of potential patients is nonetheless large given the reports of over one million people in the UK currently using cannabis with medical intent. Some participants suggested that policies and guidance should be updated in light of the increasing number of patients on CBPMs and suggested that looking at other countries’ experience and approaches may be helpful.

Nothing from the research suggests that any aspects of the legal regime related to drug driving or DVLA regulatory regime around driving eligibility and medical conditions are likely to change in the near future, and participants largely felt that changes were not necessary.

One phenomenon that may increase is the Cancard+ scheme for medical cannabis users that helps avoid arrest if found in possession of illicit cannabis (Cancard+, 2021). This scheme has the support of police chiefs (Medical Cannabis Network, 2020). This is not, however, supported by the British Medical Association or Royal College of General Practitioners, who state “The BMA and RCGP cannot however support the use of the Cancard+, nor the suggestion that UK registered GPs sign a declaration confirming a diagnosis in order for the card to be issued.” (BMA & RCGP, 2021).

Prescribers however advise patients to keep a copy of their prescriptions with them to explain their possession of cannabis, in case this should be necessary.

The Cancard+ website implores card holders to: “be considerate in your actions after you have taken a dose of medicine”. A 2017 study of 416 drivers in Washington state, USA, included 34 who held a “medical card” (Ward et al., 2017). In this group, intention to drive under the influence of cannabis was far higher among those who believed they would not be arrested than among those who thought they would, suggesting the importance of clear communications to potential card-holders (in contrast, perhaps, to the “Get out of jail” characterisation in media headlines (Vice, 2021)).

7.2 Changes to prescribing practices

Prescribing practices could change even without regulatory changes. The volume of patients registered with private clinics seems likely to continue to increase, although participants did not agree on how quickly this might happen. Indicators of change reported by some participants included:

- Increasing awareness of medical cannabis among both the public and doctors, which they thought would increase demand substantially in the coming years. Although doctors, may be starting from a low level of knowledge (MacCallum and Russo, 2018) participants felt there was an appetite to know more.
- The steady emergence of ‘real-world’ evidence from CBPM registries, which would make changes in NHS guidance inevitable.
- Pressure from patients, with doctors and nurses reporting increased patient enquiries about CBPMs following the 2018 change in the law (Cogora, 2019).

Other participants felt that growth would be steady but not dramatic. One participant pointed to various barriers to access that limit the potential for growth; the need for a serious, diagnosed chronic health condition with two failed prior treatments, and the cost of prescriptions. This participant thought that if these conditions continue to characterise eligibility and access, the number of prescriptions in a few years’ time will remain under 50,000.

Regarding the cost barrier, prices of private prescriptions have fallen in recent years. It is plausible that CBPM costs will reduce as more patients create incentives for producers to enter the market and potentially also to undertake more trials to build the evidence base which could in turn encourage more prescribing. A prescriber who does not offer CBPMs described an additional pressure in favour of increased CBPM use in the near future: opiate use for patients with chronic pain is declining due to safety and efficacy concerns. Given the size of the patient population, replacements for opiates could be hugely profitable, which may further drive attempts to fill the evidence gap in coming years. This is consistent with the higher overall benefit–safety balance found for cannabinoids over opiates and other drugs by an expert decision conference (Nutt et al., 2021).

7.3 Potential implications for road safety

Several participants discussed the somewhat complex theoretical relationship between road safety, driving behaviour and patients’ medication profiles. Road safety in relation to medical cannabis is primarily affected by the likelihood of given levels of impairment in drivers, as well as their driving behaviour in terms of extent of their driving and awareness of any impairment. Driving can be impaired both by physical and mental

health problems and by medications taken to treat those problems. Likelihood to drive at all can also be affected by both the illness and the drugs.

Participants talked about the potential for medical cannabis to make people safer drivers by reducing impairments from illness including pain, stiffness and mental distraction due to anxiety and ADHD. Taking medical cannabis may also reduce impairment caused by other drugs (be they prescription pain drugs or illicit cannabis), although according to guidance, patients using those drugs ought not to be driving if impaired. On the other hand, the evidence suggests that the psychoactive effects of THC may increase impairment through drowsiness or confusion even as it reduces impairment through reducing the severity of symptoms. With new medication and changes in their perceptions of impairment, people may conceivably move between not driving and driving.

Participants acknowledged that in some cases people may become willing to drive through an improvement in their symptoms but still be somewhat impaired; we also note that some patients report that their driving improves when using medical cannabis, which implies that they were driving previously. This may suggest non-adherence to doctors' advice, but it also suggests that in practice there are different degrees of impairment among drivers, even though legal rules and medical guidance are that patients should not drive if their driving "is impaired". Participants criticised the idea of impairment as a binary phenomenon, with some preference for understanding impairment by degrees.

In short, increased use of medical cannabis may improve road safety through its positive effects on other sources of impairment, but it may decrease road safety through having people driving under the influence of THC. It may also enable people to drive who previously felt unable. We cannot easily estimate the net effect of these factors for road safety.

As discussed in chapter 5, starting to take medical cannabis ought to be accompanied by guidance from prescribers on potential risks to driving. It is also important to bear in mind, particularly if thinking about road safety priorities, that relative changes in the road safety profile of the population of actual and potential medical cannabis users need to be assessed in the larger context of the populations of all users of prescription drugs and of illicit cannabis.

Lastly, it is also important to approach the road safety implications of medical cannabis in the wider context of driving impaired through intoxication, particularly regarding alcohol. As one study put it, "The lower contribution of drugs other than alcohol to crash risk relative to that of alcohol suggests caution in focusing too much on drugged driving, potentially diverting scarce resources from curbing drunk driving." (Romano et al. 2014: p. 56). This is particularly salient regarding medical cannabis, given its relatively low dosage and the likelihood of a using population relatively well apprised of the risk of impairment.

7.4 Further research

Due to the limitations of the REA process in terms of comprehensive coverage, it is possible that important questions are already answered by the literature but that we simply have not prioritised that evidence. With that in mind, we have identified several possible areas for further research:

- A systematic investigation of the effectiveness of safe driving communications among medical cannabis users, taking account that they may be differently susceptible to communications compared to either other users of prescription medicines or recreational cannabis users.

- Given that medical cannabis users are likely to be long-term users of low-to-moderate doses, it might be beneficial to have stronger evidence on whether chronic users with permanently elevated blood THC levels are impaired through this ongoing exposure. Existing evidence on impairment without acute intoxication in long-term recreational users may not extrapolate well to medical users.
- It may be possible to explore data collected by the various registries that currently exist in parallel, and to explore routine inclusion of driving-related indicators in these. (Eadie et al., 2021)
- Consider the interaction between medical cannabis and different substances.

Some issues that arose relate to road safety and impairment more broadly rather than just to medical cannabis use:

- It may be useful to investigate the consistency of drivers', doctors' and regulators' understandings of what constitutes impairment.
- We did not find evidence on the number of arrests or prosecutions of people for driving-related offences (either infringing per se limits or driving while unfit), or the outcomes of such cases including the number of people successfully using a medical defence. Such data may be held by the DVLA, and if not may be available via police forces or the Crown Prosecution Service.

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Appendix A. Interview topic guide

Tailored topic guides were used to ensure a consistent approach across all the interviews and between members of the research team. The guides were used flexibly to allow researchers to respond to the nature and content of each discussion, so the topics covered and their order varied between interviews. Researchers used non-leading questions, and answers were fully probed to elicit greater depth and detail where necessary.

The main headings and subheadings from the topic guides used for interviews with key informants is included below.

1. About the participant role and experience

- Can you tell me a bit about your role in that work and how it relates to MC products?
- What kind of involvement do you have in the context of medical cannabis prescription and /or road safety?
- What are your perceptions of the current use of MC in the UK?
- What are in your opinion the main implications for road safety of the use of MC?

2. Prescribing landscape

- How does the prescription of MC work in the UK / Great Britain? We are interested in both NHS/public and private prescribers and any differences between these groups.
- Facilitators and barriers to physicians prescribing MC (generally)
- What are the main characteristics of MC users? Note: *we are interested in approximations and estimates based on participants views/ other anecdotal sources if they do not have access to data. Probe for sources/ where views come from.*

3. Use of medical cannabis and driving ability

- What kind of driving impairment is usually caused by the use of MC?
- To what extent and how is driving impaired?
- Does impairment vary according to the type and dosage of MC prescribed?
- In your opinion, (and based on the discussion on possible impairments) what is the extent of challenges to road safety related to MC?

4. Prescribing physicians: awareness of impact on driving

- Views on how prescribing physicians consider / assess the potential impact of MC on driving

5. Medical cannabis users: awareness of impact on driving and medication compliance

- Views on the extent to which MC users aware of the impact of MC on driving
- Views on the facilitators and barriers to users' awareness of the impact of MC on driving?
- Views on the extent to which MC users follow the prescribers' advices and why / why not?
- Extent to which advice might be supplemented with other views/ information independently researched?

6. The future

- Thoughts on how the situation regarding MC and its impact on driving might develop in the future:
- Views on the needs for change – probe for views on the balance between extending prescribing and managing risks to road safety
- Benefits / potential challenges of anticipated changes to policy and possible mechanisms for change (e.g. lobbying, drawing on evidence from other countries, further research etc.)
- Key priorities that should be taken into account when formulating future policy in this area
- Final thoughts/ reflections

Appendix B. Search strings for database searches

1. Embase Classic+Embase (Ovid) <1947 to 2021 February 26> Searched 2nd March 2021

- 1 exp United Kingdom/ or ("united kingdom" or UK or britain or british or english or scottish or scots or welsh or england or scotland or wales or "northern ireland" or ulster).ti,ab,kw. (882877)
- 2 (driving or driver* or vehicle* or ((road or traffic) adj3 (safety or accident* or death* or fatalit*)) or crash* or collision*).ti,ab,kw. (446029)
- 3 car driving/ or aggressive driving/ or distracted driving/ or driving ability/ or drunken driving/ or reckless driving/ or road rage/ or "speeding (driving)"/ or traffic accident/ (83760)
- 4 or/2-3 (478937)
- 5 (cannabis or marijuana or THC or tetrahydrocannabinol or cannabinoid or cannabidiol or anandamide or cannabichromene or cannabidivarin or cannabielsoin or cannabigerol or cannabinal or dexanabinol or dextronantradol or dronabinol or ehp101 or endocannabinoid or lenabasum or levonantradol or methanandamide or nabiximols or nantradol or noladin ether or palmidrol or virodhamine).ti,ab,kw. (71629)
- 6 exp cannabinoid/ (73922)
- 7 or/5-6 (93711)
- 8 exp canada/ or exp united states/ or exp france/ or exp germany/ or netherlands/ or exp denmark/ or sweden/ or exp australia/ or new zealand/ or austria/ or belgium/ or chile/ or colombia/ or czech republic/ or denmark/ or estonia/ or finland/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or south korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or norway/ or poland/ or portugal/ or slovakia/ or slovenia/ or exp spain/ or switzerland/ or turkey/ (3077108)
- 9 (australia or austria or belgium or canada or chile or colombia or czech or denmark or estonia or finland or france or germany or greece or hungary or iceland or ireland or israel or italy or japan or korea or latvia or lithuania or luxembourg or mexico or netherlands or "new zealand" or norway or poland or portugal or slovak or slovakia or slovenia or spain or sweden or switzerland or turkey or "united states" or usa).ti,ab,kw. (2101595)
- 10 or/8-9 (3985778)
- 11 4 and 7 and 10 (1122)
- 12 limit 11 to yr="2011 -Current" (675)
- 13 1 and 4 and 7 (125)
- 14 limit 13 to yr="2011 -Current" (73)
- 15 (impair* or reflex* or concentrat* or conscious* or unconscious* or subconscious* or automat*).ti,ab,kw. (4173267)
- 16 mild cognitive impairment/ or intellectual impairment/ or visual impairment/ (112516)
- 17 orienting reflex/ or muscle reflex/ or reflex/ or visual reflex/ or conditioned reflex/ (61257)
- 18 consciousness/ or attention/ or consciousness level/ or awareness/ (253662)
- 19 or/15-18 (4441664)
- 20 4 and 7 and 10 and 19 (480)
- 21 limit 20 to yr="2011 -Current" (**317**) - OECD
- 22 1 and 4 and 7 and 19 (57)
- 23 limit 22 to yr="2011 -Current" (**36**) - UK

2. Web of Science (SSCI/SCI) – Searched 2nd March 2021

- # 11 **556 [OECD]**
#8 NOT #9
10 **136 [UK]**
#6 NOT #9
9 1,099,633
TS=("animal model" or mouse or mice or rat or rats or (laboratory NEAR/2 (animal* or model*)))
8 768
#5 AND #4 AND #2 AND #1
7 2,256

#4 AND #2 AND #1

6 185

#3 AND #2 AND #1

5 2,154,751

TS=(impair* OR reflex* OR concentrat* OR conscious* or unconscious* OR subconscious* or automat*)

4 14,558,299

TS=(australia or austria or belgium or canada or chile or colombia or czech or denmark or estonia or finland or france or germany or greece or hungary or iceland or ireland or israel or italy or japan or korea or latvia or lithuania or luxembourg or mexico or netherlands or "new zealand" or norway or poland or portugal or slovak or slovakia or slovenia or spain or sweden or switzerland or turkey or "united states" or usa) OR CU=(australia or austria or belgium or canada or chile or colombia or czech or denmark or estonia or finland or france or germany or greece or hungary or iceland or ireland or israel or italy or japan or korea or latvia or lithuania or luxembourg or mexico or netherlands or "new zealand" or norway or poland or portugal or slovak or slovakia or slovenia or spain or sweden or switzerland or turkey or "united states" or usa)

3 1,846,738

TS=("united kingdom" or UK or britain or (british NOT ("british columbia")) or english or scottish or scots or welsh or england or scotland or wales or "northern ireland" or ulster) OR CU=("united kingdom" or UK or britain or england or scotland or wales or "northern ireland" or ulster)

2 40,660

TS=(cannabis or marijuana or THC or tetrahydrocannabinol or cannabinoid or cannabidiol or anandamide or cannabichromene or cannabidivarin or cannabielsoin or cannabigerol or cannabinol or dexanabinol or dextronantradol or dronabinol or ehp101 or endocannabinoid or lenabasum or levonantradol or methanandamide or nabiximols or nantradol or "noladin ether" or palmidrol or virodhamine)

1 967,511

TS=(driving or driver or vehicle* or ((road or traffic) NEAR/3 (safety or accident*))) or crash* or collision*)

3. **APA PsycInfo (Ovid) <1806 to February Week 4 2021> Searched 2nd March 2021**

1 ("united kingdom" or UK or britain or british or english or scottish or scots or welsh or england or scotland or wales or "northern ireland" or ulster).ti,ab,lo. (300923)

2 (driving or driver* or vehicle* or ((road or traffic) adj3 (safety or accident* or death* or fatalit*)) or crash* or collision*).ti,ab. (69570)

3 driving behavior/ or aggressive driving behavior/ or driver distraction/ or driving under the influence/ or motor traffic accidents/ or transportation accidents/ (16473)

4 or/2-3 (70714)

5 (cannabis or marijuana or THC or tetrahydrocannabinol or cannabinoid or cannabidiol or anandamide or cannabichromene or cannabidivarin or cannabielsoin or cannabigerol or cannabinol or dexanabinol or dextronantradol or dronabinol or ehp101 or endocannabinoid or lenabasum or levonantradol or methanandamide or nabiximols or nantradol or noladin ether or palmidrol or virodhamine).ti,ab. (25175)

6 cannabis/ or hashish/ or marijuana/ or cannabinoids/ or tetrahydrocannabinol/ (13800)

7 or/5-6 (25790)

8 (australia or austria or belgium or canada or chile or colombia or czech or denmark or estonia or finland or france or germany or greece or hungary or iceland or ireland or israel or italy or japan or korea or latvia or lithuania or luxembourg or mexico or netherlands or "new zealand" or norway or poland or portugal or slovak or slovakia or slovenia or spain or sweden or switzerland or turkey or "united states" or usa).ti,ab,lo. (737505)

9 4 and 7 and 8 (254)

10 limit 9 to yr="2011 -Current" (163)

11 1 and 4 and 7 (35)

12 limit 11 to yr="2011 -Current" (21)

13 (impair* or reflex* or concentrat* or conscious* or unconscious* or subconscious* or automat* or reaction* or risk* or attention or awareness).ti,ab. (1170006)

14 cognition/ or mind wandering/ or cognitive impairment/ or reaction time/ or cognitive processing speed/ or exp selective attention/ or exp visual attention/ or exp attention/ or exp focused attention/ or sustained attention/ or exp attention span/ or concentration/ or vigilance/ or

consciousness states/ or awareness/ or sleepiness/ or wakefulness/ or visual perception/ or risk perception/ or risk factors/ (316361)

15 or/13-14 (1266226)

16 4 and 7 and 8 and 15 (175)

17 limit 16 to yr="2011 -Current" (117) - OECD

18 1 and 4 and 7 and 15 (23)

19 limit 18 to yr="2011 -Current" (13) – UK

4. Transportation Research Board TRID (US) – Searched 2nd March 2021

1. UK = 7

(cannabis or marijuana or THC or tetrahydrocannabinol or cannabinoid or cannabidiol or anandamide or cannabichromene or cannabidivarin or cannabielsoin or cannabigerol or cannabinol or dexanabinol or dextronantradol or dronabinol or ehp101 or endocannabinoid or lenabasum or levonantradol or methanandamide or nabiximols or nantradol or "noladin ether" or palmidrol or virodhamine) AND (medical OR prescription OR prescribed OR therap*) AND ("united kingdom" or UK or britain or british or english or scottish or scots or welsh or england or scotland or wales or "northern ireland" or ulster)

2. OECD – 53

(cannabis or marijuana or THC or tetrahydrocannabinol or cannabinoid or cannabidiol or anandamide or cannabichromene or cannabidivarin or cannabielsoin or cannabigerol or cannabinol or dexanabinol or dextronantradol or dronabinol or ehp101 or endocannabinoid or lenabasum or levonantradol or methanandamide or nabiximols or nantradol or "noladin ether" or palmidrol or virodhamine) AND (medical OR prescription OR prescribed OR therap*) AND (australia or austria or belgium or canada or chile or colombia or czech or denmark or estonia or finland or france or germany or greece or hungary or iceland or ireland or israel or italy or japan or korea or latvia or lithuania or luxembourg or mexico or netherlands or "new zealand" or norway or poland or portugal or slovak or slovakia or slovenia or spain or sweden or switzerland or turkey or "united states" or usa)

Appendix C. Inclusion and Exclusion Criteria

These criteria guided the prioritisation process as well, alongside consideration of the thematic

Criterion	Inclusion criteria	Exclusion criteria
Relevance	<ul style="list-style-type: none"> Data on the extent to which medical cannabis impairs driving or affects road safety. If data is lacking on medical cannabis and road safety, data on the extent to which THC from non-medical sources impairs driving or affects road safety. Data on medical cannabis prescribing data in the UK. Data on physicians' knowledge about the impact of medical cannabis on driving and how this is communicated to patients. Data on users' awareness of the impact of medical cannabis on driving and their medication compliance. 	<ul style="list-style-type: none"> Data on non-medical cannabis use, with the possible exception of data on road safety and non-medical sources of THC (if data on impairment and risk are not available for medical sources). Evidence not related to humans.
Evidence type	<ul style="list-style-type: none"> All types of evaluative studies (where available): reviews (including systematic, scoping and rapid reviews/evidence assessments, meta-analyses, narrative analyses), randomised controlled trials, quasi-experimental studies (including cohort and pragmatic trials, case and observational studies including surveys. Grey literature (those publications or policies not published in peer reviewed journals). 	<ul style="list-style-type: none"> Protocols, opinion pieces, popular media (e.g., blogs, social media feeds and/ or newspaper articles). Single studies where adequate review evidence on the same topic is available. Non-review data on non-medical THC and driving impairment
Methods	<ul style="list-style-type: none"> All paradigms (i.e., quantitative, qualitative, mixed methods). 	<ul style="list-style-type: none"> Where methods are unclear, do not respond to the research question and/ or are of low-quality.
Date	<ul style="list-style-type: none"> Publication January 2011 – January 2021. Prioritise more recent literature 	<ul style="list-style-type: none"> Research over 10 years old
Geography	<ul style="list-style-type: none"> No inclusion/exclusion but prioritise UK-based studies. All OECD countries (34 countries) as second priority. 	
Language	<ul style="list-style-type: none"> English 	<ul style="list-style-type: none"> Information not in English.

Appendix D. Website searches

Organisation	Primary information sought
European Monitoring Centre for Drugs and Drug Addiction	Impairment and risk data (RQ1 and 2)
Canadian Centre on Substance Use and Addiction	Impairment and risk data (RQ1 and 2)
Department for Transport	Road safety statistics (RQ1 and 2)
NICE	Guidance on prescribing of medical cannabis (RQ4 and 5)
MHRA	Detail of medical cannabis products (RQ3)
DVLA	Licensing criteria, guidance and statistics (RQ3)
NHS	Guidance on prescribing of medical cannabis, statistics (RQ3 to 6)
Project Twenty21	Extent of and practice around prescribing (RQ3 to 6)
Centre for Medicinal Cannabis	Extent of and practice around prescribing (RQ3 to 6)
Medical Cannabis Network	Extent of and practice around prescribing (RQ3 to 6)
Open Access Government	Any (most likely RQ1 and 2)
Social Science Research Network	Any (most likely RQ1 and 2)
Openprescribing.net	Data on prescribing (RQ3)