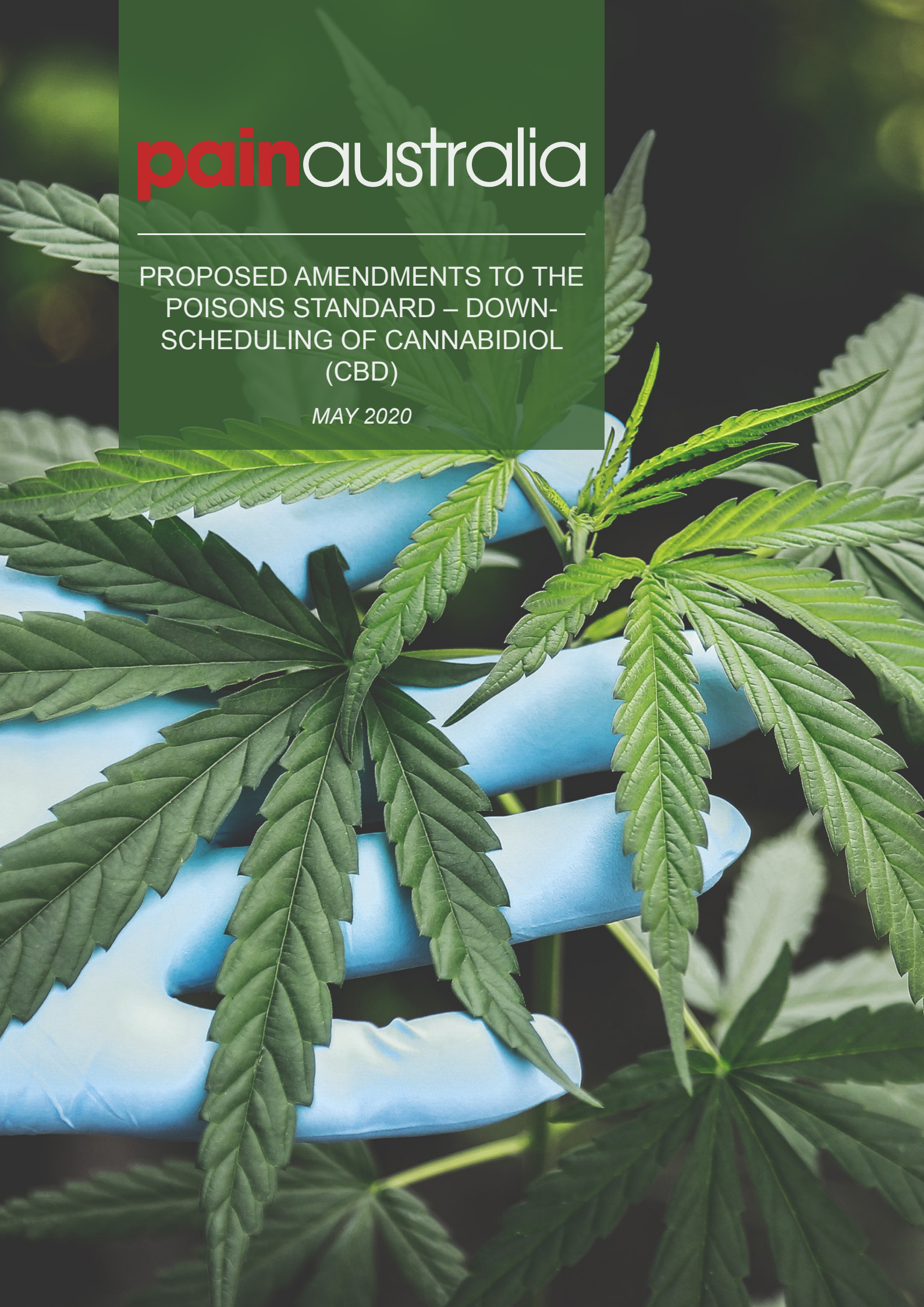
painaustralia

PROPOSED AMENDMENTS TO THE POISONS STANDARD – DOWN-SCHEDULING OF CANNABIDIOL (CBD)

MAY 2020



EXECUTIVE SUMMARY

Painaustralia welcomes the opportunity to provide input to the Therapeutic Goods Administration's (TGA) consultation on the proposal to down schedule cannabidiol (CBD) as an amendment to the current Poisons Standard for the meeting of the Advisory Committee on Medicines Scheduling (ACMS) and the Joint Advisory Committee on Medicines and Chemicals Scheduling (Joint ACMS-ACCS).

Painaustralia is the national peak body working to improve the quality of life of people living with pain, their families and carers, and to minimise the social and economic burden of pain. Members include pain and other specialists, health practitioners, health groups, consumers and researchers. Painaustralia works with our network to inform practical and strategic solutions to address this complex and widespread issue.

Painaustralia is cautiously supportive of the down scheduling of CBD to a Schedule 3 listing at a maximum dose of 60mg (preferable dose is 40mg as per new international conventions), however in implementing these changes, Painaustralia strongly recommends further education and awareness around the over the counter (OTC) use of CBD and its broader role in effective pain management to ensure that consumers are vigilant to both the benefits and risks posed by these pharmacological therapies.

Painaustralia recommends:

1. that careful consideration be given to the evidence of potential for OTC CBD to alleviate pain or related symptoms for over 3.7 million people living with chronic pain.
2. that the TGA consider increased pharmacovigilance to support the Schedule 3 listing of CBD.
3. that the TGA consider the broader health and mental health implications of enabling access to CBD
4. that the TGA consider the out of pocket cost implications of enabling OTC access to CBD.
5. that the TGA consider the models that enhance clinical oversight of the use of OTC CBD for pain management.
6. that OTC access to CBD be accompanied by a targeted education and awareness campaign around quality use of CBD and other medicinal cannabis products, drug interactions as well as an evaluation of the change.
7. that the TGA carefully regulate the availability of plant derived CBD products versus synthetic CBD products.
8. that the TGA consider the broader policy impact of enabling OTC access to CBD.

THE ISSUE

The majority of people who seek medicinal cannabis currently do so for pain management, and there is growing interest and expectation around the use of these products to treat a range of conditions.[1]

This may be due to increased awareness and availability of medicinal cannabis, a large and well-resourced world-wide industry promoting the benefits of these products, the recent establishment of a regulatory framework for these products or interest in seeking out alternatives to opioids and other pain medications.

Painaustralia acknowledges the widespread use of cannabis products, including CBD, and the large degree of community support for greater access to medicinal cannabis for a range of reasons. This situation highlights the significant gaps in access to, and understanding of, best practice pain management amid a rising pain burden.

Overall, while Painaustralia welcomes the easier access to another pharmacological intervention in the form of a CBD schedule 3 listing, we would also like to emphasise the need for any change to be undertaken with consideration of the context in which these products are used and the evidence base that supports the use of CBD for chronic pain. It is essential, that greater access to new pharmacological treatments for pain be accompanied by multidisciplinary treatment access to enable best practice pain management.

BACKGROUND

The growing prevalence and cost of pain

Painaustralia's report, The *Cost of Pain in Australia* prepared by Deloitte Access Economics, provides the most comprehensive analysis of the financial impact of chronic pain in Australia. It shows that chronic pain currently affects more than 3.37 million Australians. Chronic pain, also called persistent pain, is pain that continues for more than three months after surgery, an injury, as a result of disease, or from another cause.

For those who experience chronic pain, the pain can be debilitating and have an adverse effect on work, sleep, and relationships. Individuals with chronic pain may also commonly experience comorbidities such as depression, sleep disturbance and fatigue.

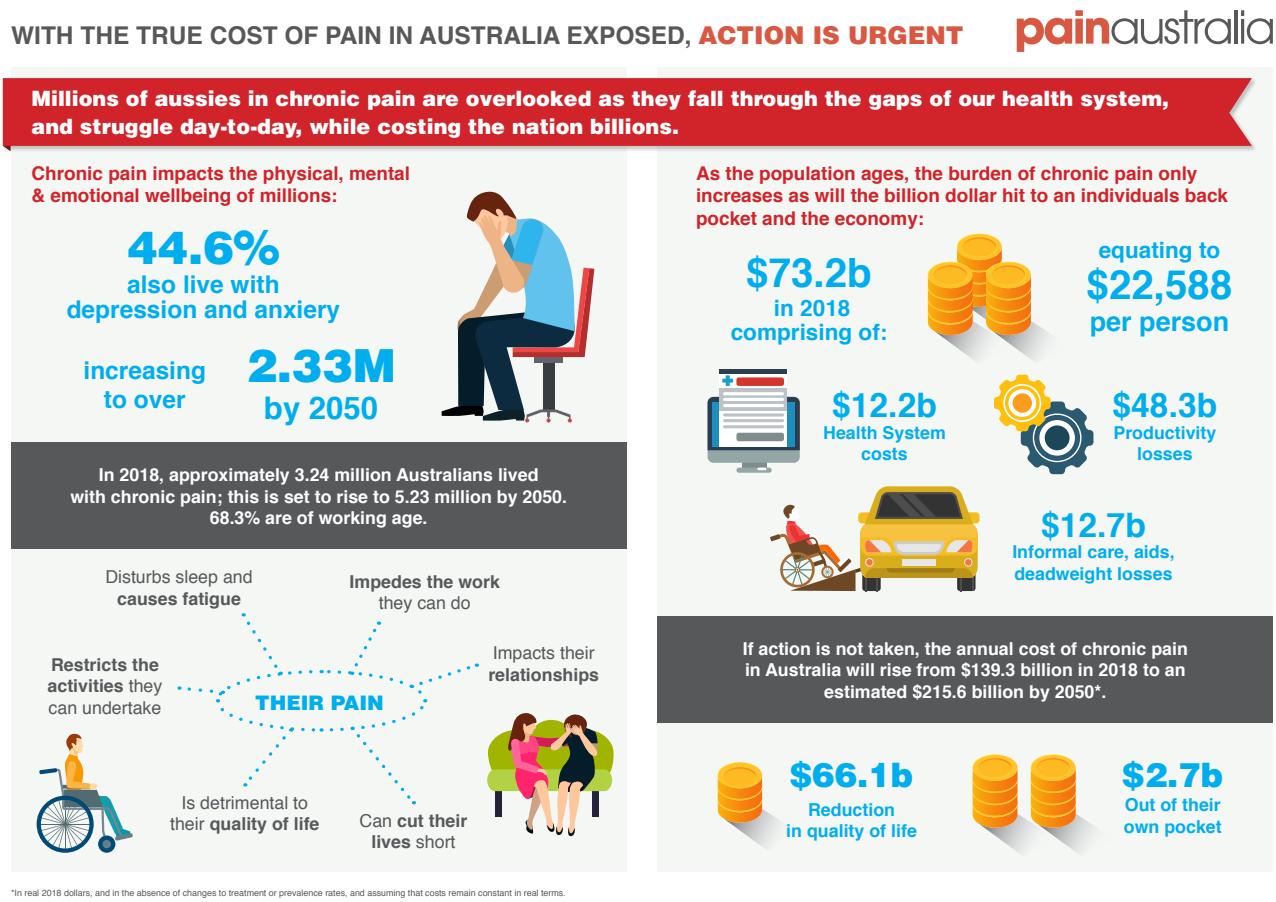
These comorbidities often contribute to worse health, societal and financial outcomes – for example, major depression in people with chronic pain is associated with reduced functioning, poorer treatment response, and increased health care costs. Nearly 1.45 million people in pain also live with depression and anxiety. Painaustralia's report finds that the reported comorbidity for chronic pain and depression or anxiety is estimated at 44.6% of patients, which is within the range of estimated values from the international literature.[2]

The consequences of these gaps are immense. The price paid by people with chronic pain is continued physical and psychological ill health, social exclusion and financial disadvantage. Opioids continue to be over-prescribed for pain, with unacceptable consequences including dependency and opioid-related deaths.

Society as a whole pays the price too. The total financial costs associated with chronic pain were estimated to be $73.2 billion in 2018, which equates to $22,588 per person with chronic pain.[3]

More than 68% of people living with chronic pain are of working age. Without action, the prevalence of chronic pain will increase to 5.23 million Australians (16.9%) by 2050.

In 2018, the staggering cost of chronic pain to taxpayers (including quality of life) was $139 billion. This was on top of the fact that in that year alone, Australians paid $2.7 billion in out of pocket expenses to manage their pain, with costs to the health system in excess of $12 billion.

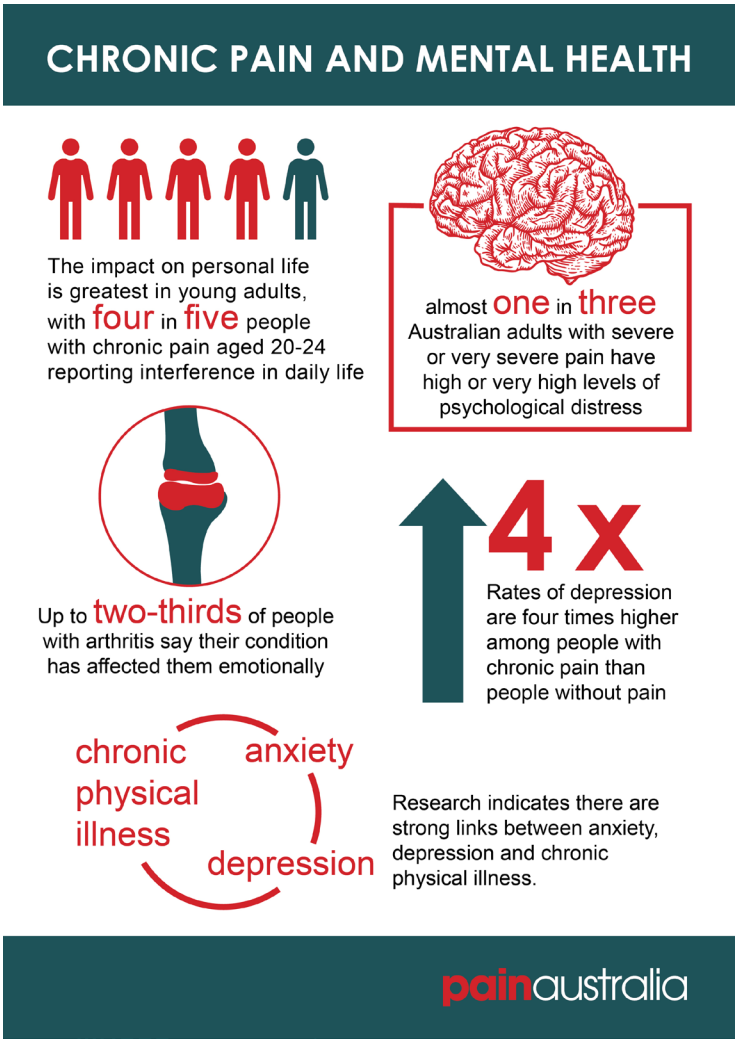


The Australian Institute of Health and Welfare (AIHW) latest report 'Chronic Pain in Australia' reinforces the findings of Painaustralia's report and the spiralling health, social and economic costs of chronic pain in Australia.[4]

AIHW's report found a significant 67% increase in GP visits related to chronic pain over the past decade, and more alarming statistics: 1 in 5 Australians aged 45 and over are living with persistent, ongoing pain, with many facing considerably poor health outcomes. Compared with people without chronic pain, those with chronic pain were 2.6 times as likely to have arthritis, 2.5 times as likely to have mental health problems, 2.5 times as likely to have osteoporosis and 2.4 times as likely to have other long-term health conditions or a long-term injury.[5]

The impact of inaction

Despite the burgeoning cost and impact of pain, our current clinical pathways are failing consumers. An epidemic of pain in Australia has seen problematic increases in the level of harm and deaths due to opioid misuse. With over three million people prescribed 15.4 million opioid scripts in 2016–17 it is unsurprising that opioids now account for 62% of drug-induced deaths, with pharmaceutical opioids now more likely than heroin to be involved in opioid deaths and hospitalisations.[6] In 2016–17 there were 5,112 emergency department presentations and 9,636 hospitalisations due to opioid poisoning, with three deaths per day attributed to opioid harm, higher than the road toll.[7]



Currently the MBS does not support a best-practice treatment model, leading to unnecessary use of hospital-based services and more significantly, an over-reliance on medication including opioids, which is associated with significant harm. Nearly 70% of pain management consultations end with a GP prescribing pain medication. Another 13% will end in imaging, but less than 15% can hope to be referred to an allied health professional.[8]

The AIHW's Chronic Pain in Australia report finds that Despite well-established evidence around the harms, people with chronic pain continue to be primarily sent down the pharmacological intervention path, with more than half (57%) dispensed analgesics, compared with 1 in 5 (21%) people without chronic pain. Alarmingly, people with chronic pain are almost 3 times as likely to be dispensed opioids and other analgesics and migraine medication as those without pain.[9]

This unfortunately means that for the 3.37 million people living with chronic pain, access to best practice care is problematic at best, and fatal at worst. Understandably the physical, mental and emotional toll of chronic pain impacts every facet of patients' lives. The lack of pain specialist care and GPs with limited options to deal with chronic pain means that millions of Australians are currently falling through the cracks of the country's health system.

Recommendation 1: Painaustralia recommends that careful consideration be given to the evidence of potential for OTC CBD to alleviate pain or related symptoms for over 3.7 million people living with chronic pain.

CBD AND CHRONIC PAIN

Without access to or knowledge of best practice pain management, people in pain are seeking alternative treatment options. Chronic pain has not received the same priority in policy and public awareness as other chronic health conditions and remains misunderstood and neglected, despite its significant prevalence.

Despite the legalisation and decriminalisation of cannabis in some jurisdictions in Australia and overseas, there is still limited availability of well-designed clinical studies to support quality evidence for the use of medicinal cannabis products such as CBD for chronic pain and much public opinion on its use is influenced by anecdotes.[10]

Painaustralia supports current efforts to enable quicker access to medicinal cannabis where it has been correctly prescribed, and we have supported commitments made at the April 2019 meeting of the Council of Australian Governments (COAG) Health Council to streamline the application and approval process for unregistered medicinal cannabis and progress the development of a single national online application pathway.[11]

However, we are concerned that the accelerated push to embrace CBD and medicinal cannabis for chronic pain across jurisdictions, may have some unintended consequences. At worst, this could see millions of Australians living with chronic pain offered 'false hope' of a treatment option that has limited benefit and diverts them from seeking and accessing best practice pain management that offers them the best chance for a good quality of life and return to function.

It is important to note that despite the assumption of its 'natural and green' image, CBD will remain a biomedical intervention, which has proven to be a demonstrably insufficient tool when used as a singular modality to manage complex chronic pain conditions.

Opioid prescription for chronic pain is not supported by evidence. However, high opioid prescription rates continue, and its misuse has had harmful effects in the community.[12] This highlights the importance of rigorous research to avoid unnecessary costs to various stakeholders and giving false beliefs of a "magic bullet" to people living with chronic and persistent pain.

The biopsychosocial framework that informs the assessment and management of people with chronic pain requires active engagement of patients in a multimodal management program, and this approach recognises the adverse effects that may be associated with polypharmacy in general and with cannabinoids in particular

Recommendation 2: Painaustralia recommends that the TGA consider the broader implications of enabling access to another pharmacological therapy for pain management

EVIDENCE-BASE FOR USE OF CBD FOR CHRONIC PAIN

When it comes to chronic pain, there is a need to expand availability of safe and effective treatments as current treatments are not adequate. Studies to date have not systematically addressed this question in a large population of people taking opioids for chronic pain.

There is little evidence about suitable doses of individual cannabis products like CBD, such as randomised controlled trials or systematic reviews, that enable definitive statements on effectiveness of medicinal cannabis for pain management. This lack of evidence makes it difficult for practitioners to prescribe, despite community expectations that these products will be made available to treat chronic pain.

"Synergy with THC appears to be required for neuropathic pain management; international approaches/consensus statement will suggest CBD first, titrate up to 40 mg before considering addition of THC"

Painaustralia Clinical Advisor

The strongest scientific evidence is for its effectiveness in treating childhood epilepsy syndromes, such as Dravet syndrome and Lennox-Gastaut syndrome (LGS), which typically do not respond to antiseizure medications. Painaustralia notes that these indications are the only ones that the Pharmaceutical Benefits Advisory Committee (PBAC) is considering for potential listing of CBD on the Pharmaceutical Benefits Scheme.

Recent NICE (National Institute for Health and Care Excellence) Guidelines also do not recommend offering CBD to manage chronic pain in adults unless as part of a clinical trial. The Guidelines note that the evidence did not show a reduction in opioid use in people with chronic pain prescribed medicinal cannabis.[13]

As noted by the Australian Centre for Cannabinoid Clinical and Research Excellence (ACRE) Prescribing Guidance Prescribing Cannabis Medicines for Non-Cancer Pain (CNCP), currently there is insufficient information to make a recommendation about the role of medicinal cannabis in the treatment of pain associated with arthritis and fibromyalgia. The best evidence of medicinal cannabis currently refers to neuropathic pain states, although it is constrained by similar methodological issues of limited sample size.[14]

The Australian Pain Society (APS) notes that evidence regarding specific doses of CBD is lacking, but preliminary data suggests a low risk of adverse effects at a dose of 60mg/day.

Comparatively, consumer support for this product may increase efficacy via placebo effects, although this remains to be tested.

"Synergy with THC appears to be required for neuropathic pain management; international approaches/consensus statement will suggest CBD first, titrate up to 40 mg before considering addition of THC"

Painaustralia Clinical Advisor

Potential for harm

The potential for drug-drug interactions of CBD with other commonly used medications is high[15,16,17]

The APS highlights that although there are mechanistic and animal studies suggesting that CBD inhibits inflammatory and neuropathic pain, there is a lack of human data to substantiate the claim that CBD improves pain control.

As noted in the TGA's own Review on the safety of low dose cannabidiol *"At low doses, CBD appears to have an acceptable safety and tolerability profile, although it was evident that there is a high potential for drug-drug interactions when used concomitantly with many other commonly prescribed drugs that are metabolised via cytochrome P450 (CYP) pathways. Currently there is insufficient evidence as to whether these would not occur with the use of low dose CBD."*

CBD is a strong inhibitor for Cytochrome P450 2D6 (CYP2D6) and Cytochrome P450 3A4 (CYP3A4) which are responsible for the metabolism for most pharmaceuticals.[18] CBD therefore has the potential to increase the serum drug level for most opioids, sedatives, anticoagulants,[19] antipsychotics, antidepressants, antiepileptics, cardiovascular agents, and cancer therapies.[20]

Overarching research suggests that potential CBD-related risks include liver injury, adverse drug interaction (e.g. with warfarin) and sedation (esp. if used with alcohol or other sedative agents)[21] As such, ***if access to CBD is enabled (even at low doses), this policy move must be supported by enhanced consumer information and decision-making support.***

This presents as a major issue for the chronic pain community, who often have multiple complex comorbidities, most of which are managed through the use of multiple medications. ***OTC access to CBD must therefore be supported by enhanced information about drug-drug interactions.*** Importantly, as the health risks associated with CBD and other cannabis products come under increasing scrutiny, pharmacovigilance during its use in growing numbers of people may uncover other problems.

Table 1.1Comorbidities associated with chronic pain, Australia 2018

Comorbidity	Percentage of patients
Depression or anxiety	44.6
Osteoarthritis and degenerative arthritis	29.3
High blood pressure	25.1
Diabetes	12.5
Heart disease	8.4
Rheumatoid arthritis	7.3
Ulcer or stomach disease	7.3
Lung disease	5.4
Stroke or neurological condition	5.3
Anaemia or other blood disease	4.7
Cancer	4.3
Kidney disease	3.1
Other medical problems	31.1

Source: Adapted from Tardif et al (2018).

Consumers have however noted that they already manage the risk of multiple medications and interactions.

"Noting that it won't be a silver bullet or suitable for all people experiencing chronic pain, I think it is important to also note that many traditional pain medications are "hit and miss" and work very differently for different people. Many people have to try a host of different treatments, many of which have bad side effects, before finding something that works effectively for pain management without life-impacting side effects. As such, I don't think "it isn't a miracle cure" is a good reason to not progress with making it more available as an option for those with chronic pain to try."

Input from Painaustralia's Consumer Advisory Group

Consumers also note that treatment accessibility is important, and downgrading CBD oil will hopefully make it more accessible to those who may benefit from it. This applies to those in regional areas who many not have a choice of doctors or specialists who are up to date with CBD as a treatment and may be unlikely to prescribe it, for those who struggle to find the time and the money to get prescriptions regularly, etc. .

Recommendation 3: Painaustralia recommends that the TGA consider increased pharmacovigilance to support the Schedule 3 listing of CBD.

Overarching health concerns with use of Cannabis Products

The use of cannabis (particularly its principal psychoactive constituent, tetrahydrocannabinol or THC) is associated with health risks including lung disease (when smoked), cardiovascular disease, acute pancreatitis, and cannabinoid hyperemesis syndrome.[22] Cannabis users are also at increased risk for occupational injuries, and cannabis-associated "drugged driving"—sometimes fatal—is increasing. Finally, the myth that marijuana is nonaddictive has been dispelled by studies of forced abrupt cessation of use indicating potential rebound hyperalgesia and craving.[23]

The Federal Department of Health coordinated a set of clinical guidance documents in late 2017 for prescribers treating a range of conditions, including chronic pain.[24] The reviews reveal in some ways the complexity of chronic pain, such as reporting of pain outcomes. In terms of prescribing, the guidance advises that the use of medications, including medicinal cannabis, is not the core component of therapy for chronic pain, favouring a comprehensive bio-social-physical assessment.

The Faculty Pain Medicine/Australian and New Zealand College of Anaesthetists (FPM/ANCZA) statement on the use of medicinal cannabis for management of patients with chronic pain concurs with this guidance.[25]

The APS notes that points to consider include advising consumers to inform their doctors that they are taking CBD and to collaboratively develop a pain management plan (if they don't already have one). Moreover, consumers should be advised of the evidentiary limitations regarding CBD for pain management including side effects, driving impacts and metabolic functioning.

As noted in the Royal Australian College of General Practice (RACGP)'s Medicinal Use of Cannabis position statement,[26] there is a need for more public and medical education. ***This education should reflect the current state of knowledge and contextualise the use of medical cannabis as a last-resort medication for specific categories of illness that can only be prescribed in rare circumstances after stringent legislative criteria are satisfied. This will be an important part of the implementation of the proposal to down schedule CBD as well, and must be prioritised if pharmacists will be able to provide OTC access.***

Overarching concerns around cannabis use and impact on mental health

Given the high cost associated with current access of medicinal cannabis products in Australia, it is important to consider the option to access both medicinal cannabis products with THC as well as unregulated cannabis products via the black market, which presents a cheaper and more affordable pathway to most consumers. The broader health implications of enabling access to cannabis should therefore be part of the consideration of down-scheduling.

It is also important to note that for those with psychotic disorders or at risk of developing them, medicinal cannabis may present higher risks. The comorbidity between mental and physical health problems is well documented, especially when illness becomes chronic. Nowhere do psychiatric and medical pathologies intertwine more prominently than in pain conditions.[27] Chronic pain deeply affects the capacity to work, mental health and wellbeing as well as relationships. Distressingly, it can also end in suicide.

As one of the peak bodies representing mental health expertise in Australia, the Royal Australian and New Zealand College of Psychiatrists (RANZCP) has particular insight into the significant psychiatric morbidity associated with cannabis use. They note that several studies linked cannabis use to increased risk for chronic psychosis as well as worse outcomes for people who already have psychosis.[28]

Rates of mental health and suicide are higher among people living with pain. Major depression is the most common mental health condition associated with chronic pain, with among 30-40% of people with a diagnosed mental health condition also presenting for treatment for chronic pain.[29] High rates of generalised anxiety disorder, post-traumatic stress disorder and substance misuse are often present for people living with chronic pain.[30]

Almost a third of Australian adults with severe or very severe pain experience high levels of psychological distress; around three times the rate of those with mild pain and six times the rate of those with no pain. One in five Australian adults with severe or very severe pain suffer depression or other mood disorders.[31]

Suicidal behaviour is also two to three times higher in people with chronic pain than the general population.[32] While these figures are dramatic, chronic pain has not received the same priority in policy and public awareness as mental health (despite its significant prevalence among people with mental health conditions) and remains misunderstood and neglected.

It is paramount that treatments for pain management are based on rigorous evidence. The experience and expression of chronic pain varies between individuals, reflecting changing interactions between physical, psychological and environmental processes. The diagnosis of major depression in patients with chronic pain requires differentiation between the symptoms of pain and symptoms of physical illness, so specific clinical knowledge is helpful.[33]

Emerging research has once again highlighted that that use of medical cannabis products, and their perceived efficacy, may be linked more to the mental health state of the individual as opposed to the severity of pain.[34] These findings are particularly important in the context of enabling access to yet another pharmacological intervention such as CBD, as there is well established research that indicates that among individuals with chronic pain prescribed opioids, depression has been associated with increased opioid dosage.

Increasing understanding that chronic pain is a disease of the person, and that a traditional biomedical approach cannot adequately address all pain-related problems is critical, and this needs to be a major consideration of any process that enables broader access to CBD or medicinal cannabis products.

Recommendation 4: Painaustralia recommends that the TGA consider the broader health and mental health implications of enabling access to CBD

OTHER MAJOR POLICY CONSIDERATIONS

Access versus Affordability

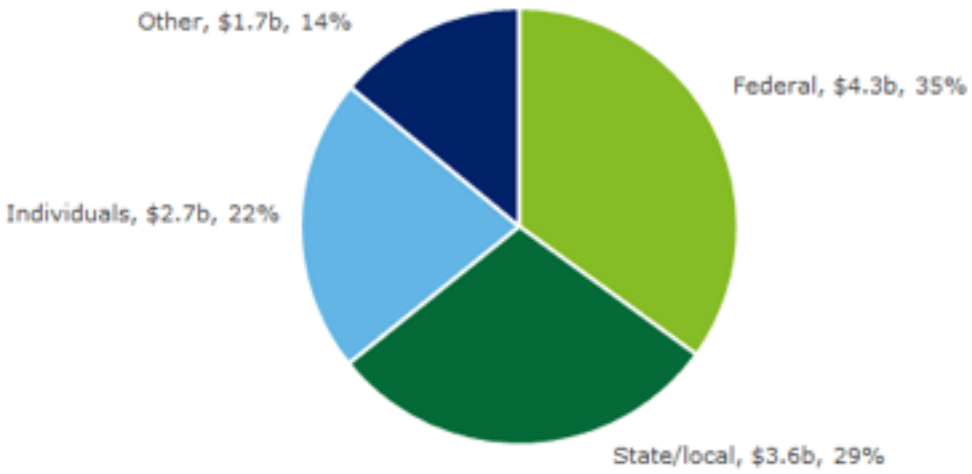
Research released by the medicinal cannabis sector in Australia indicates that people living with chronic pain who make up an estimated 60-70 percent of the market, are paying about $350 a month for their treatment using cannabis products.[36]

As there are currently no CBD medications subsidised by the Pharmaceutical Benefits Scheme (PBS), this means patients are required to cover all of the costs out of pocket.

OTC access to CBD has the potential to significantly add to the chronic pain related costs incurred by individuals in Australia. Painaustralia's cost of pain report showed that in 2018, individuals living with chronic pain bore about 22% of the health-related costs of chronic pain, a significant $2.7 billion dollars.

It is important to note that chronic pain may result in reduced employment either through disadvantages in job-seeking (for example difficulty in searching for work or keeping a job due to frequent absences) or self-selection out of the labour force. This can lead to significant productivity losses in the form of lost wages and other costs to the individual, such as reduced social engagement, so people living with chronic pain are already likely to be vulnerable to the cost of expenditure related to medications, including OTC.

Chart 1.1Costs of chronic pain by source of funds, Australia 2018



Source: Deloitte Access Economics analysis.

Additionally, CBD oil can already be purchased in Australia without a prescription, but because it is done without approval there is no real way for consumers to know what they are buying. Anecdotally, what is available to purchase without a script in Europe appears to be very different to what can be purchased in Australia. Consumers not that it would be a huge benefit to many to have a T***GA approved product that is easy to purchase at the chemist, as it would guarantee the quality and strength of the product and reduce risk of adverse events with fraudulent products and perhaps even lower the cost.***

Recommendation 5: Painaustralia recommends that the TGA consider the out of pocket cost implications of enabling OTC access to CBD.

Significance of Clinical Oversight

Painaustralia's founding members, the Australian Pain Society (APS) notes that chronic pain is typically a complex presentation, associated with multiple physical and psychological co-morbidities.

As such, medical intervention alone is frequently insufficient to improve the functioning or quality of life of individuals living with this condition. Best practice care for chronic pain involves multidisciplinary input spanning the physical, psychological and social factors associated with the onset and maintenance of pain.

These complexities can be exceedingly difficult to delineate, especially in a busy pharmacy setting (refer recruitment/enactment difficulties reported during the recent Pain Meds Check project). As such, ***although down-scheduling CBD may indeed serve to increase access in this country, it cannot be assumed with any confidence that this increased access will be associated with the provision of appropriate medical advice when accessed via pharmacist without a prescription.*** At the current CBD listing of Schedule 4, there are appropriate restrictions that ensure prescriptions are controlled by medical clinicians who are most familiar with the nuances of the individual patient; the general practitioner.

"I think the biggest issue with down scheduling is the loss of knowledge in the clinic. If GPs are required to prescribe then it would be expected that in time, feedback will increase their knowledge of response due to CBD particularly in the absence of good data. Prescribers can use this information to inform colleagues, industry, patients etc, of where it may be useful and where it may not."

Input from Painaustralia's Consumer Advisory Group

We also acknowledge that right now several access issues remain under the current Schedule 4 listing, with poor uptakes by hospitals and multidisciplinary pain services, leaving a large unmet demand across the chronic pain population group. This has made the sector vulnerable and open to exploitation through "access clinics" that are usually supported by the pharmaceutical industry and therefore expose consumers to the increased risk of single modality of care, as well as high out of pocket costs.

"I believe that if it is to be downgraded there needs to be more reliable information available to pharmacists about potential interactions with other medications and natural supplements. Given the status of CBD oil in Australia these are currently hard to find and it seems to be a bit of a guessing game, which impacts the safety of trialling CBD oil."

Input from Painaustralia's Consumer Advisory Group

Pain specialists have reported encountering many barriers in obtaining an authority to become an 'Authorised Prescriber". Even practitioners based at large hospitals who have applied with support of an ethics committee have been denied access, as the requirements include listing every single product they wished to use, which is a difficult task as products are constantly changing. Thus, practitioners are forced to rely on single person applications each time, with a continuous audit/research program, and additional barriers to access.

"Further lightening of restrictions will limit the need for health professionals education and rational/safe prescribing and use of product i.e. it will be increasingly consumer driven, health personnel will ignore/misunderstand potential benefit and harm (similar to current poor knowledge of naturopathic supplements). Proper pain assessments and management plans by well-trained clinicians will be replaced by a commercially promoted "supplement."

Painaustralia Clinical Advisor

While we consider a major policy shift such as down-scheduling, it is also ***important to consider if alternative measures, such as improving current pathways through which practitioners can become 'Authorised Prescribers',*** and which might provide better health outcomes for people living with chronic pain conditions.

Recommendation 6: Painaustralia recommends that the TGA consider the models that enhance clinical oversight of the use of OTC CBD for pain management.

Significance of informed decision making

As highlighted throughout our submission, it is vital to note that medication alone is not helpful for the management of chronic pain and patients need to adopt other strategies. All medications, including CBD, have side-effects and many can be harmful if used over the long-term. We need to monitor the impacts of changes to scheduling that considers societal costs of overuse of medications and a shift from lifestyle and holistic interventions to pharmaceutical interventions. In short, we need to weigh the costs versus the benefits.

"I believe it only provides a safeguard to the extent that people don't exceed the recommended daily dosing. As most people are presently taking substantially more to attain analgesia, improved sleep etc, it's difficult to assume that it will be used as directed."

Input from Painaustralia's Consumer Advisory Group

Many questions still remain around the effect of CBD on legal requirements around driving. The legal aspects relate to driving with THC in the system so trace amounts of THC may be found in CBD products (if plant derived), and given fat soluble/stored, can accumulate to detectable levels (and potentially impairment levels) with regular CBD use. There is a potential for false positive roadside tests and high sensitivity blood analysis being positive.

Consumers also expect all OTC drugs to be regulated for consistency. Consumers maybe unaware of small amounts of THC that remains in plant derived CBD concentrates, and the safety of high dose CBD.

Painaustralia therefore recommend that the d***own-scheduling be accompanied by a targeted education and awareness campaign around quality use of CBD and other medicinal cannabis products, as well as an evaluation of the change.*** The impact of down-scheduling particularly on adverse events such as polypharmacy and hospital presentations is also an important factor that must be monitored as a part of the TGA's proposed change processes.

Recommendation 7: Painaustralia recommends that OTC access to CBD be accompanied by a targeted education and awareness campaign around quality use of CBD and other medicinal cannabis products, as well as an evaluation of the change.

Ensuring consistency in product availability

As noted in the TGA's safety review, CBD is a chiral compound. Only the (-) CBD enantiomer is present in the cannabis plants. Consequently, plant derived cannabidiol is present only as (-) CBD and has low affinity for the CB1 and CB2 receptors, and thus is not psychoactive. Synthetic cannabidiol has the potential to be a racemic mixture, the non-psychoactive (-) CBD or the alternative (+) CBD enantiomer. (+) CBD and its derivatives have been reported to bind to both CB1 and CB2 receptors, displaying selectivity towards CB1[37,24] and is therefore likely to be psychoactive and present different pharmacological activity. Therefore, the use of ***synthetic CBD may have psychoactive potential that would not be found in plant-derived cannabidiol.*** This should be considered in any decision to down-schedule CBD.

It will also be important to monitor the potential for small concentrations of THC being present in plant-based products. For example, in the Netherlands, a maximum level of 0.05% THC is allowed in CBD products, even though, formally, any detectable trace of THC is illegal according to Dutch narcotics laws. This approach is based on the fact that even hemp varieties of cannabis produce a small amount of THC, and therefore naturally derived CBD extracts will carry some THC in the final products.[38] This issue around formulation also allows potential for high consumption of CBD OTC products, which may adversely impact consumers. Surveillance and testing of available products and clear definitions of allowable THC/other cannabinoids will be important in ensuring consumer safety.

I would suggest ratio of CBD to the/other cannabinoids be greater than 100:1. This means 2 x 40 mg CBD would administer <1 mg THC (which is about the lowest dose without psychoactive effects)

Painaustralia Clinical Advisor

Recommendation 8: Painaustralia recommends that the TGA carefully regulate the availability of plant derived CBD products versus synthetic CBD products.

Setting policy precedents

Down-scheduling (to non-prescription) may occur when:

- The medicine's level of risk is not as great as originally perceived and/or
- The potential health benefit of making the medicine more readily available outweighs any potential risk

As detailed through our submission, currently none of these criteria are met adequately.
There is a paucity of research on the effectiveness of CBD in managing chronic and persistent pain and also on its adverse short and long-term effects.[39]

International markets (e.g., Canada) have demonstrated that relaxing regulatory requirements can lead to the accelerated accessibility of a broad range of cannabis products, strains and strengths, many with limited to no therapeutic benefit. As per other listed medications, ***where low doses fail to provide sufficient pain relief, it is likely that stronger doses will be sought.*** This is expected to be independent of Scheduling level, although a lower Schedule may well expedite dose increases due to prescription availability.

Despite the legalisation and decriminalisation of cannabis in some places here and overseas, there have only been a limited number of well-designed clinical studies on medicinal cannabis[40] and its role in treating chronic pain. There may be a ***niche role, pending further research in the management of complex chronic pain with distress.***

Painaustralia has been involved in several policy and research forums that discuss the medical efficacy of medicinal cannabis products and in particular we are concerned to note that due to the current provisions of the Special Access Scheme in Australia, many manufacturers of medicinal cannabis products are reluctant to participate in research that can demonstrate the efficacy and effectiveness of these products.

This is a trend that was noted in the Senate report on current barriers to patient access to medicinal cannabis in Australia which notes evidence that large policy changes such as legalisation of marijuana have also removed incentives for the industry to fund controlled clinical research into the safety and effectiveness of cannabis based medicines. It has also not increased researchers' access to medical cannabis products for investigator-initiated clinical trials.[41]

There is a possibility of setting a dangerous precedent where scientific evidence is not considered in the decision-making process of down-scheduling CBD. Best practice management of persistent pain involves active engagement of the person experiencing pain. Promotion of a new passive intervention has the consequence of shifting the focus of management to a more biomedical and passive approach.

The APS notes that the ***evidentiary requirements regarding therapeutic efficacy are in place to protect consumers, and indeed prescribers, from avoidable harm. Duty of care requires the maintenance of these standards and cannabis should not be exempt from this process.***

Recommendation 9: Painaustralia recommends that the TGA consider the broader policy impact of enabling OTC access to CBD.

CONCLUSION

Despite the lack of a current evidence-base for chronic pain management, access to CBD is considered by many consumers as a viable treatment option.

While Painaustralia supports current efforts to enable and expedite access to CBD, we remain concerned about the unintended consequences of inappropriate OTC access for a uniquely vulnerable cohort of consumers. The development of a sound evidence base remains a critical enabler to ensure safe and effective use of medicinal cannabis in chronic pain and requires further research and investment as we still have much to learn about the role CBD can play in addressing chronic pain conditions.

Painaustralia is cautiously supportive of the down scheduling of CBD to a Schedule 3 listing at a maximum dose of 60mg (and ideally 40mg in keeping with international conventions), however in implementing these changes we strongly recommend further education and awareness around use of CBD and its broader role in effective pain management to ensure that consumers are vigilant to both the benefits and risks posed by these pharmacological therapies and to aid in informed decision-making by consumers.

Additional steps need to be taken to promote quality use of CBD and all cannabis derived products given the potential for accelerated usage and easy accessibility. We need to more effective multidisciplinary treatment and support to people living with pain if we are to reduce adverse events related to an over-reliance on pharmacological monotherapy in Australia.

The implementation of a National Strategic Action Plan for Pain Management, currently being considered by the Council of Australian Governments, is also an important step towards a national approach to raising awareness ensuring that consumers and health professionals have a better understanding of pain management and that the training, education and supports and services are in place to support these regulatory changes. This will become a key component to supporting better pain medication management and ensuring quality of life while limiting the escalating social and economic costs of unmanaged pain.

REFERENCE

1. Therapeutic Goods Administration 2017. Guidance for the use of medicinal cannabis in Australia Overview. Access online here.
2. Op. Cit. Deloitte Access Economics (2019).
3. Deloitte Access Economics (2018), The cost of pain in Australia, p.iv.
4. Australian Institute of Health and Welfare 2020. Chronic Pain in Australia. Access online here.
5. Op.Cit AIHW 2020.
6. Australian Institute of Health and Welfare 2018. Opioid harm in Australia and comparisons between Australia and Canada. Cat. no. HSE 210. Canberra: AIHW
7. Royal Australian College of General Practitioners (2018). Australian overdose deaths are increasing – and the demographics are changing. News GP. Access online here.
8. Deloitte Access Economics (2019), The cost of pain in Australia. Access online here.
9. Op.cit. AIHW 2020
10. Faculty of Pain Medicine Australian and New Zealand College of Anaesthetists 2015. Statement on "Medicinal Cannabis" with particular reference to its use in the management of patients with chronic non-cancer pain. Access online here.
11. Council of Australian Governments Health Council 2018. Communique. Access online here.
12. Royal Australian College of General Practitioners (2018). Australian overdose deaths are increasing – and the demographics are changing. News GP. Access online here https://www1.racgp.org.au/newsgp/ clinical/australian-drug-overdose-deaths-are-increasing-%E2%80%93-a
13. NICE 2019. Cannabis-based medicinal products NICE guideline [NG144]Published date: November 2019. Access online here.
14. Ware M. J Pain 2015; 16, p1221
15. Huestis, M.A., Solimini, R., Pichini, S., Pacifici, R., Carlier, J. and Busardò, F.P., 2019. Cannabidiol adverse effects and toxicity. Current neuropharmacology, 17(10), pp.974-989.
16. Qian, Y.,Gurley, B.J., Markowitz, J.S., 2019 The potential for Pharmacokinetic Interactions Between Cannabis Products and Conventional Medications. J. Clin Psychopharmacol. 2019 Sep/Oct, 39 (5) p462-471.
17. Expert Committee on Drug Dependence, World Health Organisation, Thirty-ninth Meeting, Geneva, 6-7 November 2017. https://www.who.int/medicines/access/controlled-substances/5.2_CBD.pdf
18. Kerstin Iffland*,1 and Franjo Grotenherme. An Update on Safety and Side Effects of Cannabidiol: A Review of Clinical Data and Relevant Animal Studies. Cannabis Cannabinoid Res. 2017; 2(1): 139–154. Published online 2017 Jun 1. doi: 10.1089/can.2016.0034
19. Stout SM, Cimino NM. Exogenous cannabinoids as substrates, inhibitors, and inducers of human drug metabolizing enzymes: a systematic review. Drug Metab Rev. 2014 Feb;46(1):86-95.
20. Melton ST. Stirring the Pot: Potential Drug Interactions With Cannabis. Medscape. 2017 Jun 8. https://www.medscape.com/viewarticle/881059#vp_1
21. US Food and Drug Agency 2020. FDA Regulation of Cannabis and Cannabis-Derived Products, Including Cannabidiol (CBD), Access online here.
22. Zhang MW, Ho RC. The Cannabis Dilemma: A Review of Its Associated Risks and Clinical Efficacy. J Addict. 2015; 2015():707596.
23. Carr,D. Schatman, M. Cannabis for Chronic Pain: Not Ready for Prime Time Am J Public Health. 2019 January; 109(1): 50–51. Published online 2019 January. doi: 10.2105/AJPH.2018.304593
24. Op. Cit TGA 2017
25. Op. cit. FPM 2015.
26. Royal Australian College of General Practitioners 2016. Medicinal use of cannabis products: Position Statement. Access online here.
27. Gatchel. R 2009. Comorbidity of chronic pain and mental health disorders: the biopsychosocial perspective. Am Psych 2009.
28. Royal Australian and New Zealand College of Psychiatrists 2017. Therapeutic Good Order No. 93 (standard for Medicinal cannabis) Access online here.
29. Alex Holmes, Nicholas Christelis and Carolyn Arnold 2013. Depression and chronic pain. Med J Aust 2013; 199 (6 Suppl): S17-S20. || doi: 10.5694/mja12.10589
30. Tang NK, Crane C. Suicidality in chronic pain: a review of the prevalence, risk factors and psychological links. Psychol Med. 2006 May;36(5):575-86. Epub 2006 Jan 18.
31. Blyth FM et al. Chronic pain in Australia: a prevalence study. Pain. 2001 Jan;89(2-3):127-34.
32. Tang NK, Crane C. Suicidality in chronic pain: a review of the prevalence, risk factors and psychological links. Psychol Med. 2006 May;36(5):575-86. Epub 2006 Jan 18.
33. Beyond Blue. Chronic physical illness, anxiety and depression. Access online http://resources.beyondblue.org.au/prism/file?token=BL/0124
34. Daniel Feingolda et al. Depression level, not pain severity, is associated with smoked medical marijuana dosage among chronic pain patients. Journal of Psychosomatic Research Volume 135, August 2020, 110130https://doi.org/10.1016/j.jpsychores.2020.110130
35. Sullivan, Mark 2018. Depression Effects on Long-term Prescription Opioid Use, Abuse, and Addiction The Clinical Journal of Pain: September 2018 - Volume 34 - Issue 9 - p 878-884 doi: 10.1097/AJP.0000000000000603
36. Cannabis Access Clinics 2018. Price of medicinal cannabis halves but still too expensive for many. Access online here.
37. Morales, P., Reggio, P.H. and Jagerovic, N., 2017. An overview on medicinal chemistry of synthetic and natural derivatives of cannabidiol. Frontiers in pharmacology, 8, p.422.
38. Hazekamp A.The Trouble with CBD Oil. Med Cannabis Cannabinoids 2018;1:65–72 https://doi.org/10.1159/000489287
39. Royal Australian College of General Practitioners 2016. Medicinal use of cannabis products: Position Statement. Use of medicinal cannabis products Position statement – 2019 update Access online here: https://www.racgp.org.au/advocacy/position-statements/view-all-position-statements/clinical-and-practice-management/medical-cannabis
40. Op. Cit TGA 2017.
41. Hall and Farrell, Submission 68, p. 10. Current barriers to patient access to medicinal cannabis in Australia

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