# Benefits and risks of cannabinoids

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**Article**

Cannabis is used by an estimated 219 million adults globally (4.3% of the population)[1] with a particularly high prevalence in North America (17.4% of the population). The 1961 UN Single Convention on Narcotic Drugs included cannabis with the opioids and cocaine as a controlled substance whose use was prohibited, but policies have changed considerably in recent decades. Medical use of cannabis is now permitted in large parts of North and South America, Europe, and Oceania, although patient access varies considerably across jurisdictions. The use of cannabis for non-medical purposes is also now permitted in Canada, 22 US states and Uruguay, and several other countries are considering allowing adult use in some form e.g., Germany, Luxembourg, Malta, the Netherlands, and Switzerland. In this rapidly changing cannabis policy climate, there is a compelling need for high-quality evidence on benefits and risks to inform policy and clinical practice.

Solmi et al.[2] report an umbrella review of benefits and risks of cannabis. Key strengths of their review are its inclusion of evidence from RCTs (n=51 meta-analyses) and observational studies (n=50 meta-analyses) and a range of interventions/exposures and outcomes. The interventions/exposures included cannabis, cannabinoids (drugs that act on the endocannabinoid system), and cannabis-based medicines. The cannabis plant produces over 100 cannabinoids including delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). THC and CBD have contrasting mechanisms of action and medical uses[3] (e.g. THC for the treatment of nausea and vomiting from chemotherapy; CBD for the treatment of seizures in childhood epilepsy syndromes). THC produces intoxicating effects and is responsible for the effects consumers seek from non-medical use. However, THC carries an increased risk of adverse events compared to other cannabinoids such as CBD.

Solmi et al.'s review[2] provides strong evidence of both benefits and harms for a range of medical indications. Results are particularly important from the 29.1% of RCT associations showing high to moderate certainty of evidence. For example, cannabis-based medicines reduced chronic pain but increased psychological distress, and reduced spasticity and pain in multiple sclerosis while increasing adverse events such as dizziness and somnolence. Cannabidiol reduced epileptic seizures and improved quality of life but increased adverse events such as diarrhoea and decreased appetite. In cancer, cannabis-based medicines improved sleep disruption but increased adverse events such as gastrointestinal disorders. For mixed conditions, cannabis-based medicines reduced nausea and vomiting, pain and spasticity, but increased adverse events including central nervous system, psychological and vision related events.

Taken together, this evidence could justify the introduction of medical cannabis in jurisdictions that do not allow any medical use and increase patient access in other jurisdictions. Balancing the benefits and risks of medical cannabis will require careful consideration of patient preferences, responses to other treatments, and the estimated magnitude of efficacy, adverse events, and cost effectiveness. Because of the inclusive nature of this review,[2] summary estimates were derived from a wide range of interventions with different doses, routes of administration, and cannabinoid profiles. As a result, they may not reflect efficacy or safety of any single medication, and it may be unclear which medication or dose to prescribe. Initiatives to improve consistency in research reporting, such as the standard THC unit endorsed by the US National Institutes of Health[4] could facilitate estimation of dose-response effects in future reviews.

The observational studies included in the review[2] primarily assessed non-medical cannabis use. Most evidence indicated no effect (49% of associations) or weak evidence (47% of associations). Convincing to highly suggestive evidence was found for associations of cannabis use with increased risk of psychosis in the general population, of car crash in drivers, and poorer birth outcomes following cannabis use during pregnancy. Given the wide range of cannabis exposures included, future research should estimate how different levels of exposure (e.g., frequency of use,[5] THC concentration[6]) modify risk. Such data could inform lower risk cannabis use guidelines[7] and policies for reducing harms (e.g. regulating levels of THC in legal markets).[8]

One important omission from the review was the lack of meta-analytic results on the risks of cannabis use disorder, a problematic pattern of use characterised by clinically significant impairment or distress.[9 10] It is critical to assess the risk of a cannabis use disorder when appraising benefits and risks. Results from a recent meta-analysis[10] estimate that 22% of people who have used cannabis will meet criteria for a cannabis use disorder. Cannabis use disorders are the primary contributor that cannabis use makes to the global burden of disease[11] and could increase the risk of further adverse cannabis outcomes because characteristic symptoms involve using more cannabis than intended, and difficulty controlling or cutting down use.[9] Given that cannabis use disorders are prevalent in people who use cannabis for medical as well as non-medical purposes,[12] preventing and treating CUDs should be a key focus in clinical practice and policies designed to maximise benefits and minimise risks.

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