Massive population studies confirm alarming cannabis harm

50+ peer-reviewed studies from all 50 States in the US (325 million pop.) and 27 EU countries (511 million pop.) published 2021-23 have verified what had been known from in vitro and in vivo studies for decades, that cannabis is **genotoxic, mutagenic, carcinogenic** and **teratogenic**. These studies now verify that cannabis is causal in:

- **33 cancer types as against 14 for tobacco (Cannabidiol [CBD] is the most carcinogenic cannabinoid [12 cancers])**
- **the commonest forms of pediatric cancers which comprise 70% of cases**
- **89 of 95 birth defects tracked in Europe**
- **prematurely aging users by 30% at 30 years**

Medical Profession Many of our Australian professional organizations have made strong statements warning against widespread cannabis use. e.g. AMA, RACGP, AAP, ACOG, British Lung Foundation.

Common Pattern The almost ubiquitous pattern in which medical cannabis is used today is to treat decades long cannabis addiction, with the other indications serving as mere "tickets" to engage whilst simultaneously avoiding legal censure.

Higher Concentrations At 25-35% cannabis now is about ten times stronger than earlier and forms (Waxes, "Shatter", Dabs) up to 100% THC are coming. In USA organized crime is often associated with legal cannabis operations.

Parallel Drug Approval Pathway It is obvious that whilst all other drugs are held to a strict approvals and regulatory pathway cannabis products are held to no serious control whatsoever with the industry in an effectively unregulated exponential growth phase.

Limited Benefits Despite the international rhetoric of many governments and the cannabis industry there is either nil or very poor evidence for the efficacy of the vast majority of cannabinoid products in the management of most indications presenting to GPs (Ref RACGP Review).

Known Harms Alternately, there is increasing direct and indirect evidence from cellular, mechanistic, case data and epidemiological studies of "likely" harm from cannabis, both within and across generations (epigenetics). This is supported by large epidemiological studies, confirming increased cancers and neonatal congenital abnormalities in areas of increased cannabinoid use, not dissimilar from those used to identify links between tobacco or alcohol and morbidities. Numerous aging pathologies are accelerated 30% at 30 years.

Further Harms

1. **Gateway role** – Into other illicit drugs and criminal lifestyle is now well established by studies in numerous countries. Whilst few cannabis users progress to other illicits, virtually all users of other illicits have used cannabis, with much higher rates of drug and criminal progression amongst ever users of cannabis.
2. **Adult Brain** – Most major psychiatric syndromes have been linked with cannabis viz: sedation, amotivational state, anxiety, PTSD, serious mental disorders, depression, psychosis, bipolar disorder, schizophrenia, suicidal thoughts and completed suicides. Also linked with homicide and violence and over 70 mass shootings in USA thought to be linked with aggression (seen in both cannabis withdrawal and intoxication), impaired judgement and psychosis
3. **Child Brain** – ADHD-like and autism-like features; extreme aggression; impaired cortical processing; learning difficulties; smaller brain; microcephaly; anencephaly (which causes death within hours)

4. **Chest disease** – COPD, chronic bronchitis, emphysema, lung cysts, elevated residual volume, premalignant changes in upper and lower airways
5. **Immunomodulation** – Both immunosuppression and immunostimulation are described mediated via T-cells, B-cells, NK Cells, T-reg cells, antibodies and cytokines
6. **Endocrinopathy** – Central and peripheral hypogonadism, Prolactin elevated
7. **Cardiovascular** - accelerated coronary artery and atherosclerotic disease; strongly arrythmogenic (many tachyarrhythmias both atrial and ventricular; asystole kills within seconds); strokes.
8. **Driving, machine operating, workplace safety, critical skills** Evidence here is overwhelmingly negative and very concerning. Highly associated with motor vehicle fatalities (which kill). Alcohol-tobacco vehicular impairments are common.
9. **Overdose** Especially with new highly concentrated forms and in combination with alcohol and other drugs. In Colorado overdoses from cocaine, amphetamines, opioids and fentanyl have risen massively since legalization. Includes psychotic reactions. In Colorado, Texas and elsewhere fatal child overdose has become a major problem.

Genetic Toxicity These include gestationally and neonatal congenital abnormalities, cancers both childhood and adult, and the occurrence of premature age-related morbidities, and powerful direct effects on the aging process etc.

Known Mechanisms These findings are underpinned by clear cellular mechanistic studies on how cannabinoids (both THC and CBD based) can cause the above by interfering with normal cellular and body functions creating antecedents of disease. This of course is not surprising given the increasing understanding of the role of endogenous cannabinoids in normal development, body functioning, and cellular reproduction and maintenance, chromosomes, gene maintenance and control (epigenome) and that use of large doses or prolonged exogenous cannabinoids can significantly disrupt these functions.

"Do No Harm" Given the aforementioned, it is clear that caution needs to be applied to the medical use of cannabinoids, that although in the most positive interpretation may have a nominal impact managing morbidities, may in turn cause greater harm transgenerationally.

Multigenerational Impacts Genetic and epigenetic effects are believed to persist for at least three to four generations. Cannabinoids have been shown to be driving several childhood (and thus cross-generational) cancers including total childhood cancer. Cannabis, THC and cannabidiol have been shown to be linked with the cancers of the: breast, prostate, ovary and testis showing carcinogenesis to the reproductive organs. Also many birth defects including the absence of arms and legs and congenital brain, face, and heart defects. Also aging of the sperm and ovum themselves in rodents and humans.

Rigorous Trials – Evidence Base It is therefore not only reasonable but essential that each cannabinoid product marketed should be assessed by the established international standards for pharmaceutical development, and to which all other pharmaceutical products, prior to being released and used in populations must conform. There is need for a robust evidence base. At present cannabis is not performing impressively in hundreds of clinical trials. In the case of cannabinoids this must include rigorous and long term tests of genetic, epigenetic and epitranscriptomic toxicity including: genotoxicity, carcinogenicity, mutagenicity, teratogenicity and gametotoxicity in both sexes.

Not Incarceration We do not believe that period of incarceration for possession of small amounts of cannabis is appropriate. Nor has the law ever worked in this way either in this country nor in other western nations.

Education Needed Clearly widespread community education on this subject is needed. The leaders of our profession are superbly placed to spearhead the delivery of needed messages. However the educational effort needs to be a much broader whole of Government approach.

By Dr AS Reece - world authority on cannabis epidemiology and causality mechanisms