THE HEALTH EFFECTS OF NONMEDICAL CANNABIS USE

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ACKNOWLEDGEMENTS AND DISCLOSURE

• Recipient of a Cassandra Miller-Butterworth Fellowship for a Clinician-Scientist PhD (2017-2020)

• Recipient of a South African National Research Foundation Thuthuka Grant

• No Conflicts of Interest
• The cannabinoid system
• Short term effects of cannabis use
• Long term effects of cannabis use
• Conclusions
• Recommendations
THE PLANT

- The cannabis plant has 3 major species
  - *Cannabis sativa*, *Cannabis indica* and *Cannabis ruderalis*
- *Cannabis sativa* plant
  - 750 chemicals
  - 104 cannabinoids
  - The principal cannabinoids are *delta-9-tetrahydrocannabinol (THC)*, *cannabidiol (CBD)* and *cannabinol (CBN)*
CANNABINOIDS

- Diverse chemical compounds that act on cannabinoid receptors
- 3 main sources
  - PHYTOCANNABINOIDs - cannabinoids produced by plants
  - ENDOCANNABINOIDs - neurotransmitters produced in the brain or peripheral tissue
  - SYNTHETIC CANNABINOIDs - synthesised in the laboratory

Benarroch, 2007
CANNABINOIDS

- THC is the primary psychoactive compound
  - Found at higher concentrations than CBD
  - Found in the resin that covers the flowering tops and the upper leaves of the female plant
  - Increases in THC content of cannabis sativa samples (in the US <2% in 1980 to 8.8% in 2008) (Mehmedic et al, 2010)

- CBD
  - Non psychoactive compound
  - Modifies the psychoactive effects of THC
CANNABINOID RECEPTORS

• CB1R:
  • Considered to have a role in motivation and cognition, synaptic plasticity, cell migration and neuronal growth.

• CB2R:
  • May have a role as part of ‘general protective system’
  • Are expressed in circulating immune cells, spleen, macrophages and microglial cells. It is expressed by some neuronal cells, but at a far lower level compared to CB1 receptors.
CANNABINOIDS & PREPARATIONS

- **Marijuana/ dagga/ intsango/ weed**
  - Prepared from dried flowering tops and leaves
    - Smoked in a joint mixed with tobacco
    - Vaporizing
- **Hashish**
  - Cannabis resin from flowering heads
  - Smoked as a joint or in a clay pipe, vaporized, food additive
- **Hashish Oil**
  - Solvent extracted liquid
  - Smoked, vaporized, food additive
  - Higher levels of THC
- **Synthetic cannabinoid receptor agonists**
  - 100% agonist
  - Novel psychoactive substances
  - **Spice, K2, Potpurri**
Epidemiology

- Cannabis is the most commonly used psychoactive substance under international control (UNODC, 2015, WHO, 2010).
- In 2013, 181.8 million people aged 15-64 used cannabis for non-medical purposes.
- In many developed and developing countries, the number of persons seeking treatment for cannabis use disorder has increased since the 1990's.
- In SA Youth Risk Behaviour survey, 12.8% of SA students (grade 8-10) used cannabis and 9.2% used in the past month (Bhana, 2015).
- In the Western Cape grade 8-10 students, 23.6% lifetime use.
- SASH study: 8.4% cannabis lifetime use.

**Table 1:** Primary drug of use (%) for all persons and persons under 20 years – selected drugs (2017b)

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1: Northern Region (MP & LP) 2: Central Region (FS, NW, NC)
SHORT-TERM EFFECTS OF CANNABIS

• **Cognition and co-ordination**
  - Cannabis acutely impairs a broad range of executive functioning, although effects not consistently observed
  - Including: attention, concentration, reaction time, memory (short-term, episodic and working memory) (Crean, Crane and Mason, 2011; Ranganathan & D’Souza, 2006)
  - Effects worse in less experienced cannabis users and dose dependent

• **Motor coordination**
  - Small causal impact of cannabis on traffic injury
  - Interferes with driving skills and increases risk of injuries (Hartmen & Huestis, 2013)
  - Driving while intoxicated may double the risk of MVA (Ashbridge, Hayden & Cartwright, 2012)
  - Studies in France compared 6766 culpable and 3006 non culpable drivers
    - Culpability higher in drivers with THC greater than 1ng/mL
    - Dose response relationship for THC and culpability persisted after controlling for BAC, age and time of accident
SHORT TERM EFFECTS OF CANNABIS

- **Anxiety and psychotic symptoms**
  - A minority of first time users become anxious, have panic attacks, hallucinate and vomit
  - Hallucinations increase with a pre-existing vulnerability to psychosis

- **Acute toxicity**
  - Fatal cannabis overdose by smoking of leaves and flowering tops is rare
  - Emerging data on cases of death from synthetic cannabinoids
  - In 2015- The Mississippi State Department of Health reported more than 1200 SC-related emergency visits and 17 deaths potentially related to SC use during this period, while the Alabama Department of Public Health reported more than 1000 such emergency visits and 5 such deaths (Trecki et al, 2015)
HEALTH AND PSYCHOSOCIAL OUTCOMES OF LONG-TERM USE
• Children exposed to cannabis may have higher rates of neurobehavioral and cognitive impairment (Tortoriello, 2014)

• Children exposed to cannabis in utero demonstrate impaired attention, learning and memory, impulsivity and behavioural problems and higher risk of using cannabis when they mature (Sonon et al., 2015; Noland et al., 2005; Goldschmidt, Day & Richardson, 2000; Goldschmidt et al., 2004; Goldschmidt et al., 2008; Day, Leech & Goldschmidt, 2011).

• Effects may not become apparent until later in development therefore exposed children should be followed up late into adolescence.
CANNABIS USE DISORDERS

- A SUD describes a problematic pattern of substance use that results in impairment in daily life or distress
- Must have at least 2 of the following within the same 12-month period:
  o Substance is taken in larger amounts or over a longer period of time
  o Worrying about cutting down, unsuccessful efforts to cut down
  o Spending more time using a substance, recovering from it, or obtaining it
  o Failure to fulfill major obligations; and/or giving up leisure activities
  o Craving, or a strong desire to use the substance
  o Important activities given up/reduced due to substance use
  o Continuing use despite problems caused or worsened by it, (1) in areas of mental (e.g., blackouts, anxiety) or physical health, or (2) in social relationships (e.g., using results in fights or arguments)
  o Recurrent use in a dangerous situation (e.g. driving or operating machinery)
  o Tolerance: using larger amounts over time to get the desired effect or less of an effect after repeated use of the same amount
  o Withdrawal symptoms (e.g. anxiety, irritability, fatigue, nausea/vomiting, hand tremor, etc.) after stopping use
CANNABIS DEPENDENCE

- Risk of dependence has been estimated at 16% in those who initiated cannabis use in adolescence (Anthony, 2006)

- Risk of dependence in 33-50% of daily cannabis users (van der Pol et al; 2013)

- Harmful use of cannabis and cannabis dependence are the most common forms of drug-use disorders in epidemiological surveys in Australia, Canada and the USA

- Approximately 13.1 million people cannabis dependent globally (Degenhardt et al; 2013)
Early and persistent cannabis users showed an average decline of 8 IQ points compared with peers who had not used cannabis (Meier et al; 2012)

Findings replicated in the US (Auer et al; 2005)

Impairments in attention, learning and memory, and an inability to switch between ideas or responses.

Even with sustained abstinence, cognitive functional recovery may not occur if cannabis use was initiated during adolescence (Meier et al., 2012; Moffitt et al; 2013; Solowij et al; 2011)

Neuroimaging shows structural changes in brain regions involved with memory and cognition
The use of cannabis before the age of 18 years is associated with an increased risk of psychosis compared to that association with initiation in adulthood.

15 year follow-up study of 50465 Swedish male conscripts found that those who used cannabis by the age of 18 were 2.4 times more likely to be diagnosed with schizophrenia (Andreasson et al, 1987)

Findings have been replicated in the Netherlands, Germany and New Zealand

Onset of psychosis occurred earlier in those with early initiation of cannabis (14 years).

Early onset of psychosis is associated with poorer course and outcome (Paruk & Burns, 2015)
CANNABIS AND PSYCHOSIS

ASSOCIATION between exposure and outcome.

- Systematic reviews of prospective studies have produced pooled odds ratios varying between 1.41 and 2.34.
- These reviews suggest a twofold increased risk of developing psychosis.

  Henquet et al (2005) – OR: 2.1
Temporal priority & Specificity:

Dunedin Study - Early cannabis use (15 years) produced a threefold increased risk of schizophreniform disorder. Other drugs did not produce these outcomes, therefore showing specificity.

Strength (dose-response relationship)

The Dutch NEMESIS study as well as the Swedish conscript study both demonstrated a dose-response relationship between cannabis use and risk of later psychosis.
CANNABIS AND OTHER MENTAL ILLNESSES

- High comorbidity between cannabis use and anxiety and depressive disorder, conduct disorders and eating disorders however longitudinal studies have not been able to demonstrate a causal relationship.

- Suicide
- Mixed results when controlling for confounders
- In adolescents the earlier the intense use of cannabis and the greater the frequency – the faster vulnerable individuals developed suicidal ideation.
- In general 9.5% of all toxicology reports for deaths by suicide show the presence of cannabis (Borges, Bagge & Orozco, 2016)
THE GATEWAY HYPOTHESIS

- Epidemiological studies in Australia, New Zealand and the USA found that regular cannabis users were more likely to use heroin and cocaine, and that the younger they were when they first used cannabis the more likely they were to use the other drugs (Kandel, 2002).

- Three explanations were offered for these patterns:
  - (a) that cannabis users had more opportunities to use other illicit drugs because these were supplied by the same black market as cannabis;
  - (b) that early cannabis users were more likely to use other illicit drugs for reasons that were unrelated to their cannabis use;
  - (c) that the pharmacological effects of cannabis increased a young person’s interest in using other illicit drugs (Hall & Pacula, 2010).

- Adult rats pre-treated with THC during adolescence and then allowed to mature to adults without THC are more likely to use heroin than rats not exposed to cannabis during adolescence.
300 nyaope users entering inpatient rehabilitation

The median age at enrolment was 27y (IQR 23-30y; range 18-47y)

The median age at first substance use was 14y (IQR 13-16y; range 7-25y)

94.7% used cannabis regularly prior to onset of nyaope use
UNDERSTANDING RISK IN PSYCHIATRY
OVERWEIGHT

HIGH CHOLESTEROL

HIGH BLOOD PRESSURE

DIABETIC
RISKS FOR CANNABIS INITIATION

EXEMPLARY POVERTY

SCHOOL FAILURE

LOW PARENTAL INVOLVEMENT

PARENTAL/SIBLING MODELING OF DRUG USE

MENTAL HEALTH FACTORS

RISKS FOR CANNABIS DEPENDENCE

LOW SOCIO-ECONOMIC STATUS & DIFFICULT FINANCIAL SITUATION

MENTAL HEALTH FACTORS

LOW-SELF ESTEEM, LOW SELF CONTROL

ANXIETY DISORDER

DEPRESSION

(Coffey et al., 2003; Fergusson, Horwood & Swain-Campbell, 2003; von Sydow et al., 2002)
LONG-TERM CANNABIS USE AN NON-COMMUNICABLE DISEASE

• Respiratory diseases
  • Chronic bronchitis - cannabis-only smokers were more likely to have reported cough, sputum and wheezing, but not more likely to report shortness of breath than controls who do not smoke cannabis (Aldington et al., 2007; Bloom et al., 1987; Moore et al., 2005; Tan et al., 2009; Tashkin et al., 1987; Taylor et al., 2000).
  • In follow-up studies of habitual cannabis smokers, those who quit show reductions in cough, sputum and wheeze compared to those who continue to smoke cannabis.

• Cardiovascular diseases
  • Limited number of studies
  • CB1 and CB2 receptors in the heart
  • Increase in heart rate with acute intoxication (tolerance in 2-4 weeks)
  • Increased occurrence of angina in people with pre-existing heart conditions (Aronow & Cassidy, 1974)
  • More recent case reports of increased CVD in younger cannabis smokers
LONG-TERM CANNABIS USE AND NON-COMMUNICABLE DISEASE

• Stroke
  • In the past decade stroke in young adults has increased
  • By 2015 around 100 cases of cannabis-related ischemic-stroke reported (Wolff et al, 2013)

• Cancer
  • Insufficient evidence regarding upper respiratory tract and lung cancers
  • Testicular cancer: 3 US studies have found a relationship between cannabis smoking and testicular cancer
    • No potential confounding by tobacco smoking
    • Cannabinoid receptors are found in the testes
CONCLUSIONS

• Cannabinoids are diverse chemical compounds that exert a range of effects

• There are significant health and social harms associated with cannabis use

• Early onset and higher quantities of cannabis use are most strongly associated with negative outcomes
RECOMMENDATIONS

- Scientists, NGO’s, policy makers and the media need to be mindful of the language used when conveying information about cannabis
- More South African research and longitudinal studies required:
  - prospective studies of adolescent populations
  - monitoring road traffic accidents
  - maternal cannabis use
  - cannabis and non-communicable diseases
  - culturally appropriate interventions from primary through to tertiary prevention
- Decisions regarding policy must take into account the views of all stakeholders