Is Cannabis Use a Contributory Cause of Psychosis?

The evidence and its implications for policy

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Outline

• Concerns about cannabis use and psychosis
• Review evidence on relationship:
  • Population based longitudinal studies
  • Competing explanations
  • Biological plausibility
• Implications of the evidence for:
  • Mental health services
  • Health education of young people about these risks
  • Public policies towards cannabis use
Reasons for Concern About Adolescent Cannabis Use

• A “new” drug widely used by adolescents
• Adolescence an important psychosocial transition
• Associations between cannabis use, dependence and:
  • Psychotic symptoms and psychosis
  • Educational underachievement
  • Depression and poor mental health
  • Use of other illicit drugs
Lifetime cannabis use young Australians aged 20-29 years
Cannabis Use 2004 in Australian males (14 and older)

Age group

<table>
<thead>
<tr>
<th>Group</th>
<th>Ever used</th>
<th>Used in the last 12 months</th>
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<td>14-19</td>
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<td>20-29</td>
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<td>60+</td>
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Cannabis Use 2004 in Australian females (14 and older)

Age group:
- 14-19
- 20-29
- 30-39
- 40-49
- 50-59
- 60+

- Ever used
- Used in the last 12 months
Trends in Age of First Use

![Graph showing the trend in age of first use across different birth cohorts.](image)
Assessing the Effects of Adolescent Cannabis Use

- Cross sectional associations
  - with various adverse psychosocial outcomes
- Large longitudinal studies are needed
  - to separate effects of cannabis from
  - other drug use & user characteristics
- Social context of policy debate
  - polarised views about cannabis
  - A misleading policy simplification
The Cognitive Economics of the Cannabis Policy Debate

The leading media simplification of the debate

EITHER cannabis use is

• harmless and so it should be legalised
  OR
• is harmful and so should be prohibited
Countering Cognitive Economics

- Set aside the policy issues for the moment
- Apply standard criteria for causal inference
- Comparative analysis of other drug risks
  - Tobacco, alcohol and other illicit drugs
- Uncertainty, prudence and public health
- Implications for:
  - Mental health services
  - Health education of young people
  - Penalties for cannabis use
Cannabis & Schizophrenia

• Cannabis dependence & schizophrenia
  • in the general population: RR ~2
  • 20% in clinical populations vs 5% in community

• Cannabis use probably exacerbates disorder
  • Reasonable evidence from prospective studies
  • Reduced compliance or specific drug effect?

• Can cannabis use precipitate schizophrenia?
Evidence for Precipitation (Andreassen et al, 1987)

- Swedish conscript study: N = 50,000
- N times cannabis used by age 18
- Predicted risk of schizophrenia diagnosis
  - over next 15 years in a psychiatric register
  - In a dose response way
- Relationships persisted after adjustment for:
  - psychiatric history at age 18
  - parental history of divorce
Recent Evidence 1  
(Zammit et al, 2003)

- 27 year follow up of Swedish cohort
  - better register coverage
  - statistical control for more variables
  - covered most of the risk period for the disorder

- Replicated earlier findings:
  - RR = 3 for diagnosis & dose response relationship
  - Persisted after statistical adjustment
  - For whole period but weaker with time
  - AR of cannabis for schizophrenia: 13%
Recent Evidence 2

• Two New Zealand birth cohort studies
  • Dunedin (Arsenault et al, 2002) N = 759
  • Christchurch (Fergusson et al, 2003) N=900

• Both studies found that cannabis use
  • Predicted psychotic symptoms RR ~ 2
  • Stronger prediction for early onset cannabis use
  • Interacted with history of psychotic symptoms
Recent Evidence 3

- Van Os et al (2002) 4 year follow up
  - 4848 young Dutch adults
  - increased risk of symptoms & disorders
  - Attributable risk: 13%; 50% for more severe cases

  - N = 2437 German adolescents
  - Cannabis use predicted psychotic disorders
  - Stronger for those with a history of symptoms
  - Psychotic symptoms did not predict cannabis use
Recent Evidence 4

• Verdoux et al (2002) time sampling study N = 79 students
• Heavy cannabis users & vulnerable over-represented
• Cannabis use predicted psychotic symptoms
  – Stronger for those with a history of symptoms
• Psychotic symptoms did not predict cannabis use
Biological Plausibility

• D’Souza et al (2005) provocation study
  – 13 patients given 3 doses of THC:
    • Under double blind
    • placebo controlled
  – Dose response increases in
    • Cognitive impairment and + and - ive symptoms

• Evidence for G-E interaction: between COMT and THC
  • Caspi et al (2005) studied COMT allele in Dunedin birth cohort
  • RR of 10 in those with allele who smoked cannabis
    – no increased risk in those without COMT allele
Cannabis and Schizophrenia: Summary

• Reasonable evidence that
  • cannabis use exacerbates schizophrenia

• Consistent evidence that:
  • cannabis use can precipitate schizophrenia
  • Five longitudinal studies in 3 countries
  • consistent RR ~ 2 and AR ~ 13%

• Biological plausibility
  • Cannabinoid-dopamine interaction
  • Provocation study
  • COMT interaction
Common Responses to the Evidence on Cannabis and Psychosis

• Those who reject the link:
  • A beat-up: “reefer madness” revisited
  • “It never did me any harm”
  • Impeach individual studies

• Those who accept the evidence:
  • Cannabis is a “different drug” today
  • 30 times more potent than it was
Is Cannabis 30 times More Potent?

• Absence of good data:
  • testing not required or done regularly
  • Media publicize unusual cases: biased sampling

• US data show modest increase:
  • From 3% in early 1980s to 4% in late 1990s
  • Economic efficiencies & changing markets

• Changes in patterns of use
  • earlier initiation since early 1970s
  • heavier use of more potent forms via bongs
A Comparative Evaluation

- Comparisons encourage
  - evidential consistency and even-handedness
- Cigarette smoking and lung cancer:
  - Accepted on the basis of observational evidence
  - Absence of pathophysiological basis
  - But relationship stronger for tobacco than cannabis:
    - RR of 12 vs 2-3
- Biological plausibility
  - Arguably stronger for cannabis than tobacco in 1960s
A Comparative Evaluation 2

- **Alcohol and psychosis**
  - Case history evidence for delirium and hallucinosis
  - Experimental study: Isbell et al (1959)

- **Amphetamines and psychosis:**
  - More extensive case history evidence
  - Observational studies of contemporary users
  - Provocation studies in: volunteers and “addicts”
  - Biological plausibility: dopaminergic effects

- **Cannabis intermediate between the two**
  - Better epidemiological evidence than either
  - More limited experimental evidence
  - Reasonable biological plausibility
Evidence and Action: A Public Health Case for Prudence

• A game theoretic case for discouraging its use:
  • Cost if relationship is not causal:
    – foregone (or delayed pleasure) from using cannabis
  • Benefits if the relationship is causal:
    – Reduction in psychotic symptoms or disorders
    – Possible clarification of causal role
    – Reduction in: dependence, adverse psychosocial effects etc

• How best to discourage use is a separate issue
  • The current policy simplification misleads
Implications for Policy

• What should mental health services do?
• What should we tell young people?
  • What’s the most effective way to do so?
• How should it affect policies towards cannabis use?
  • Should we maintain the status quo?
  • Should we recriminalise cannabis use?
Implications for Mental Health Services

• Mental health services should:
  • routinely screen for cannabis & other drug use
  • counsel those who use cannabis to stop
    – or at least cut down and monitor the effects
  • offer to treat cannabis dependence
  • educate families of affected individuals

• Challenges: finding effective ways to:
  • persuade users to cease their use
  • helping them to do so if they try and fail
Health Educational Challenge

Providing credible advice on health risks given:

• Polarised views on cannabis in policy debate
• Inter-generational differences of opinion
  • About risks of cannabis use
  • About how to discourage use
• Scepticism among youth about health advice
  • double standards & scare campaigns
Advising Young People About Risks of Cannabis Use

• We need social marketing research
  • To identify credible messages about risks
  • Best ways to communicate about these risks

• Adults are poor judges of what’s credible
  • Political imperative to express voters’ concerns
    – especially via mass media campaigns

• Usual outcome an uneasy compromise:
  • Between what may work &
  • What parents want to hear
Advising Young People About Regular Cannabis Use

• Regular intoxication is not a good idea
  • whether with alcohol or cannabis

• Reduce social tolerance for drunkenness
  • especially among parents and adults generally

• Reinforce disapproval of intoxication
  • A sign that friends may need help
  • At risk of problems with
    – cannabis, alcohol & other drug use
Advising Young People about Cannabis and Psychosis Risk

• Drug use & mental health

• Intoxication not good for mental health
  • especially not when used to “feel better”

• Define high risks groups
  • Family history of psychosis
  • Bad experiences with cannabis & alcohol
    – self and others
  • Personal history of psychiatric disorder
What about cannabis policy?

• Reduced penalties for use in 1990s
  • Decriminalised in: SA, ACT, NT and WA
  • National diversion initiative 2001
• Driven by:
  • Widespread cannabis use in the community
  • Limited or discriminatory law enforcement
  • Arguments about harms from prohibition
  • Concerns about costs of law enforcement
The Cognitive Economics of the Cannabis Policy Debate

Given the leading media simplification of the debate
EITHER cannabis use
  – is harmless and so it should be legalised
OR
  – is harmful and so should continue to be prohibited

• Evidence of harm assumed to mean
  – return to criminal penalties for use
Arguments for Recriminalisation

• Make it easier to educate community
  • Simplifies cannabis laws
  • Avoids “mixed messages”
  • Sends a strong message of disapproval
  • Symbolically “zero tolerance”

• Deters young people from using cannabis
Cons of Recriminalising

• No evidence that penalties for use affect use
  • Rates increased equally in all states during 1990s
  • Same in Netherlands in 1970s and USA in 1980s
  • Rates declined equally in all states since 1998

• Costs of enforcement

• Non-enforcement of law
  • or arbitrary enforcement (as in USA)
Trends in past year use of cannabis 1998-2004
Cons of Recriminalising Cannabis Use

• A major distraction that may:
  • revive polarisation of policy debate
  • amplify scepticism about the evidence

• Better to look for common ground
  • Agreed health messages about the risks
  • Most effective and less coercive ways of discouraging adolescent use
Prohibition is not enough

- Psychosis has emerged under prohibition
- Law enforcement strategies may have contributed:
  - Reduced outdoor cultivation
  - Incentives for production of more potent products
  - Ready availability to young at risk males
- Need to consider changing incentives
  - Increase penalties for production of more potent products
  - Reduce penalties for home cultivation
Summary

• Good evidence for a contributory cause:
  • Longitudinal studies in 5 countries
  • Dose response relationships
  • Controlling for plausible alternative explanations

• Biologically plausible
  • Cannabinoids interact with the dopaminergic system
  • Challenge studies with THC
  • COMT interaction

• Evidence overall
  • Stronger than for alcohol and psychosis
  • Almost as good as for amphetamine–induced psychosis
Summary

• Sufficient evidence to act?
  • It would be if cannabis were a pharmaceutical

• Even if you’re still sceptical
  • prudence warrants efforts to discourage use
  • costs of doing so minor compared to possible gains

• Separate questions:
  • Who should we discourage?
  • How should we discourage?
Summary

• Implications for mental health services:
  • Screen for cannabis use
  • Recommend cessation or reduction in use
  • Research how best to discourage use and treat dependence

• Health educational implications
  • Ethical imperative to inform young people
  • Need social marketing research to identify how best to do so
  • To avoid the use of ineffective means that satisfy parents
Implications for cannabis policy

• Revisiting criminal penalties may be a major distraction:
  • Reviving polarisation and amplifying scepticism about the evidence
  • Without having much effect on rates of use
• Better to look for common ground
  • Agreed health messages about the risks
  • Most effective and least coercive ways of discouraging adolescent use
• Prohibition not enough
  • Need to change incentives for production of higher potency cannabis
  • Explore feasibility of higher penalties for more potent products