Is Cannabis Use a Contributory Cause of Psychosis?

The evidence and its implications for policy

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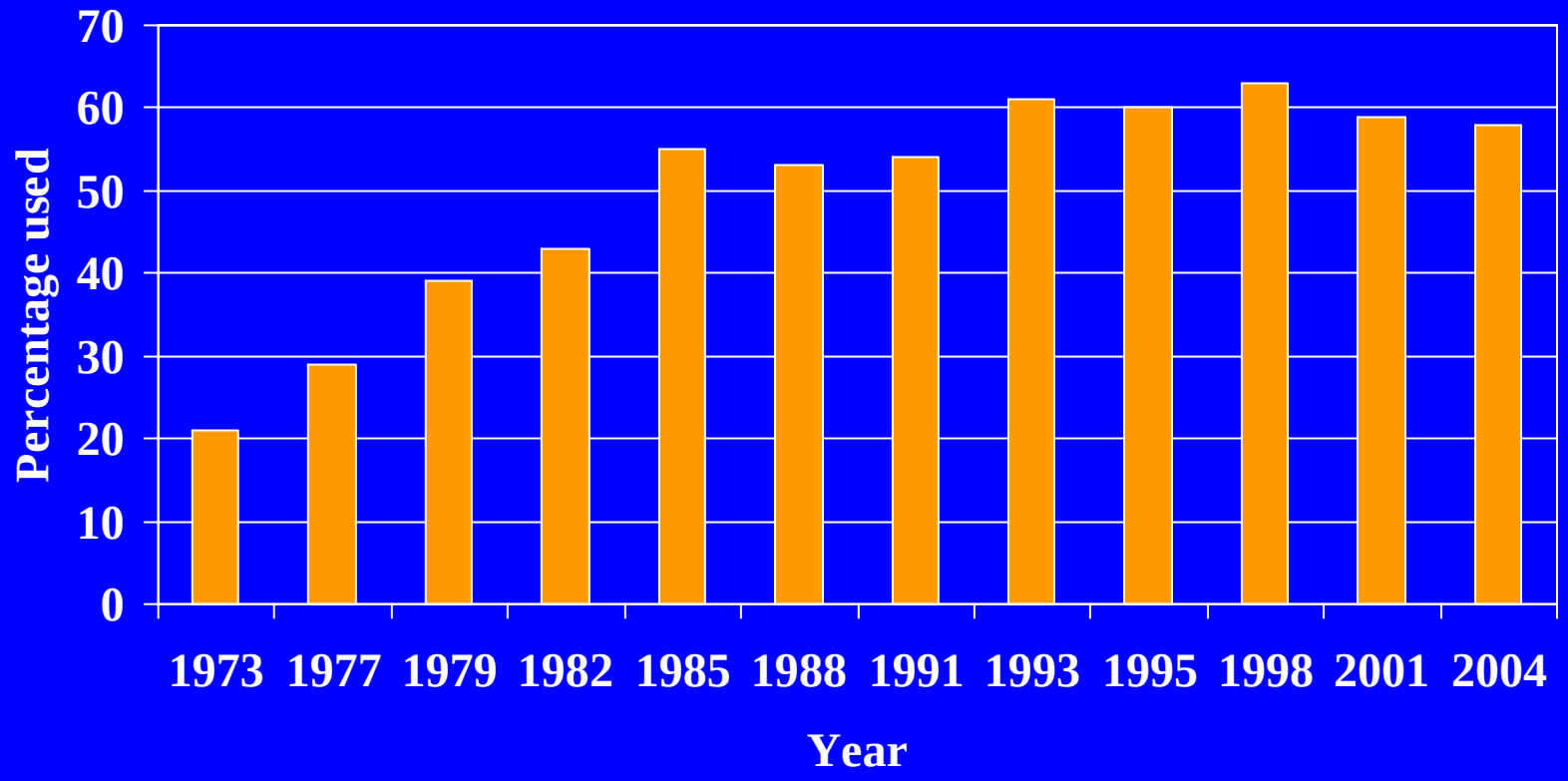
Outline

- 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

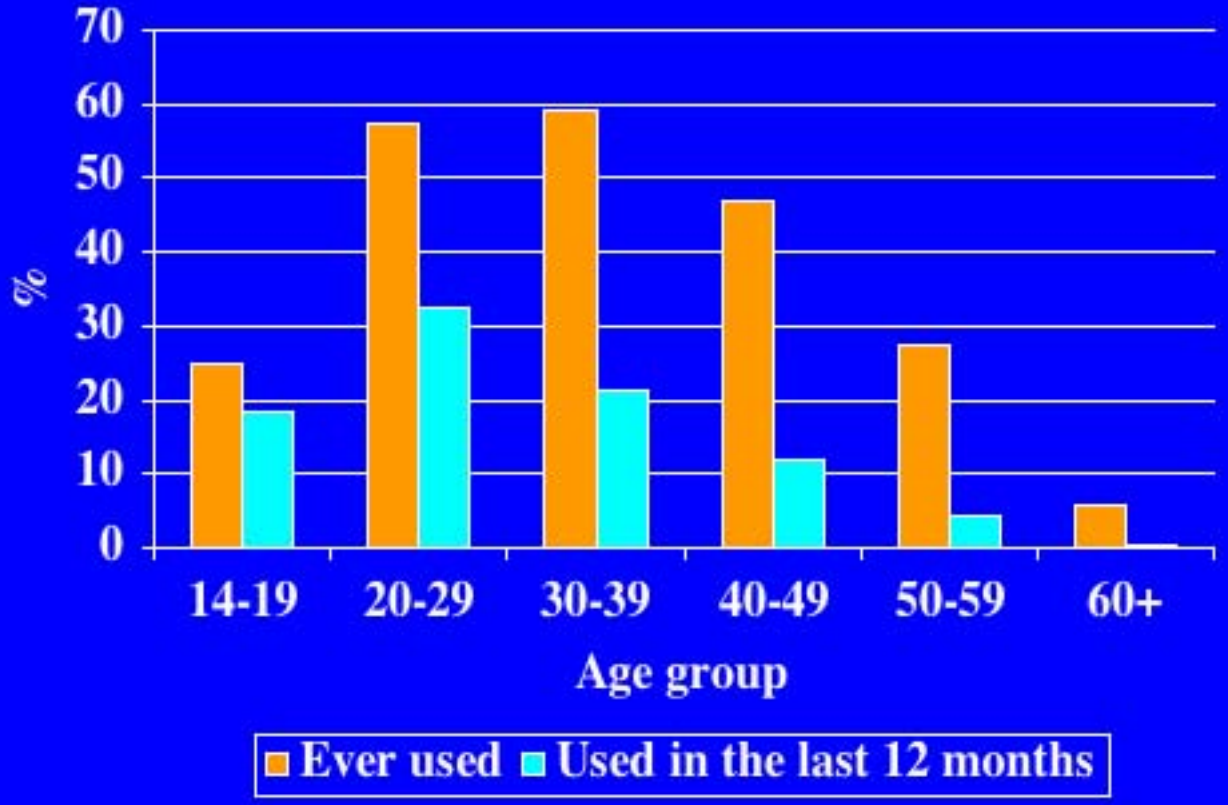
Reasons for Concern About Adolescent Cannabis Use

- 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

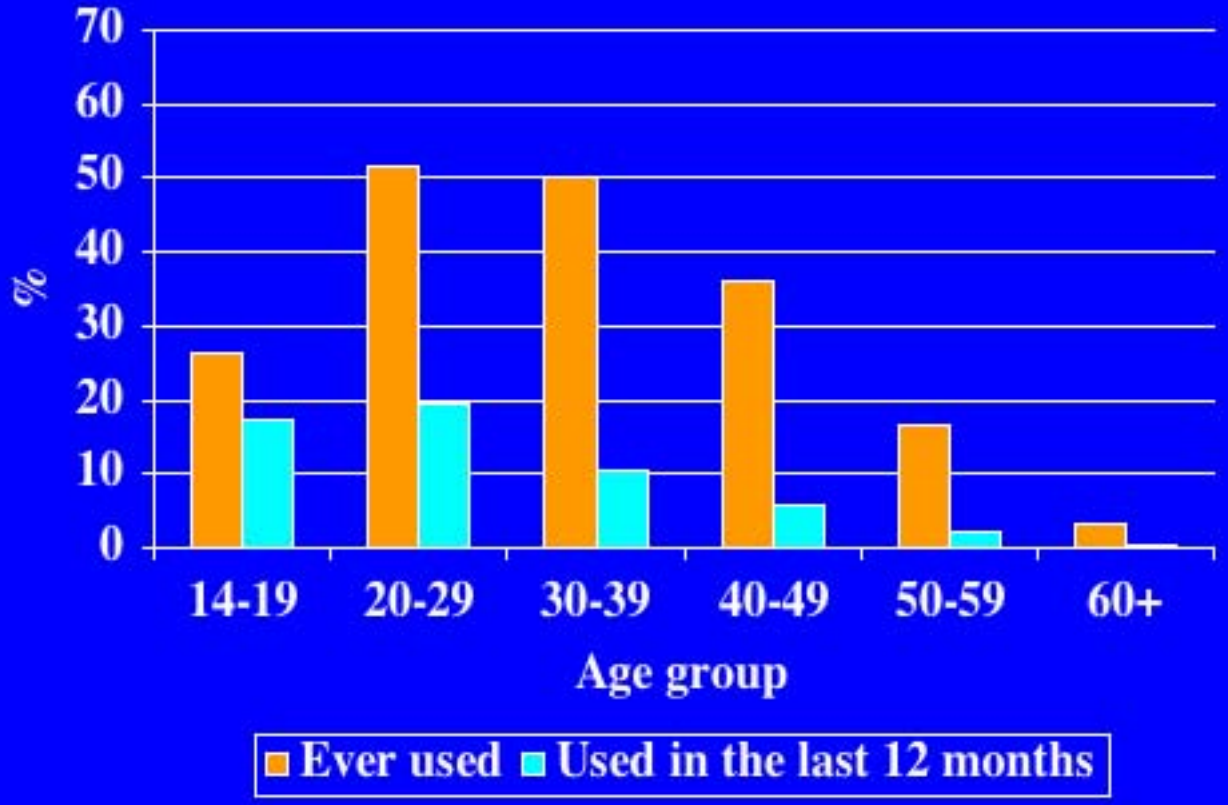
Lifetime cannabis use young Australians aged 20-29 years



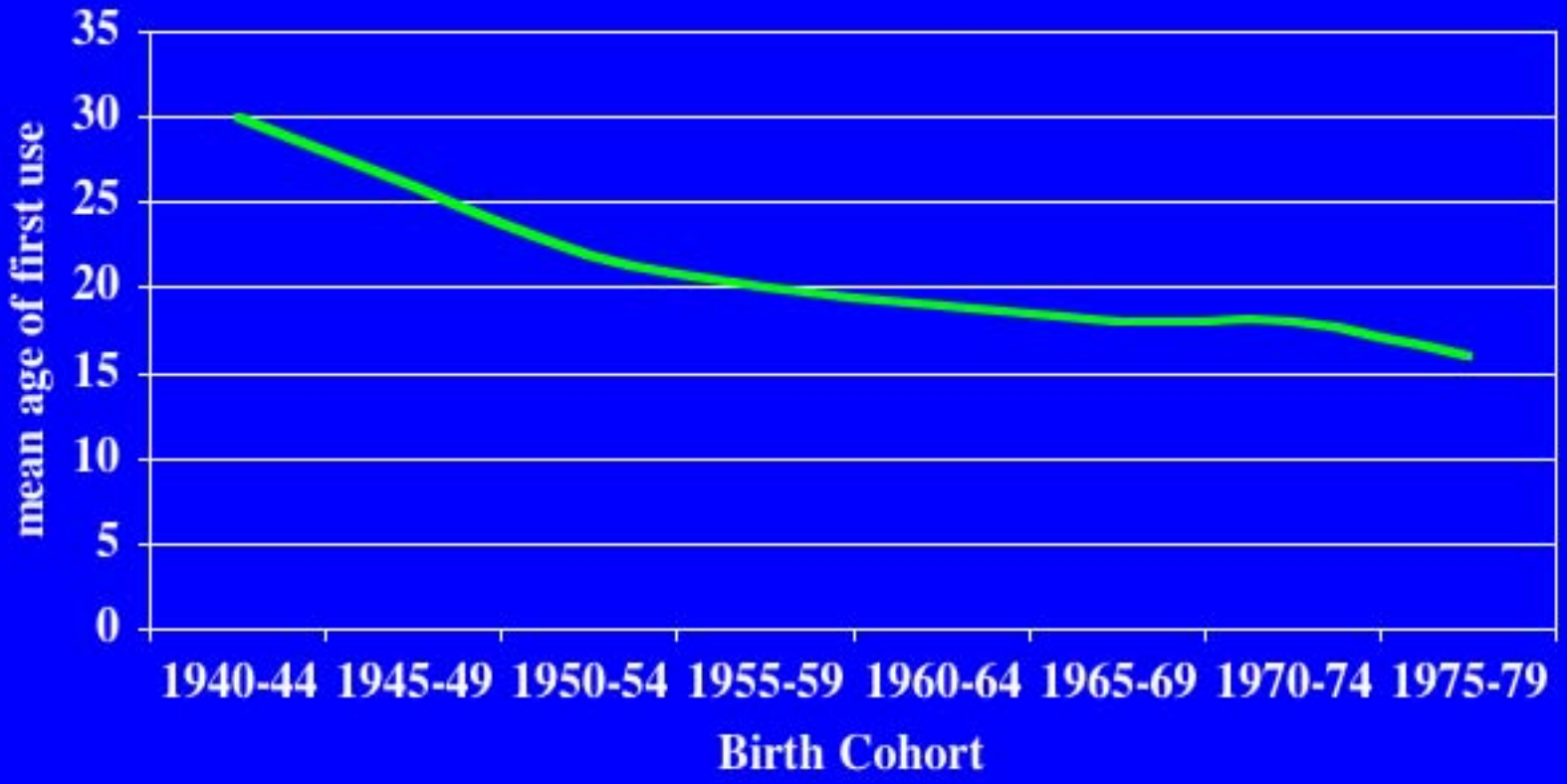
Cannabis Use 2004 in Australian males (14 and older)



Cannabis Use 2004 in Australian females (14 and older)



Trends in Age of First Use



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
- Henke et al (2004) 4 year follow up
  - 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 1

- 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

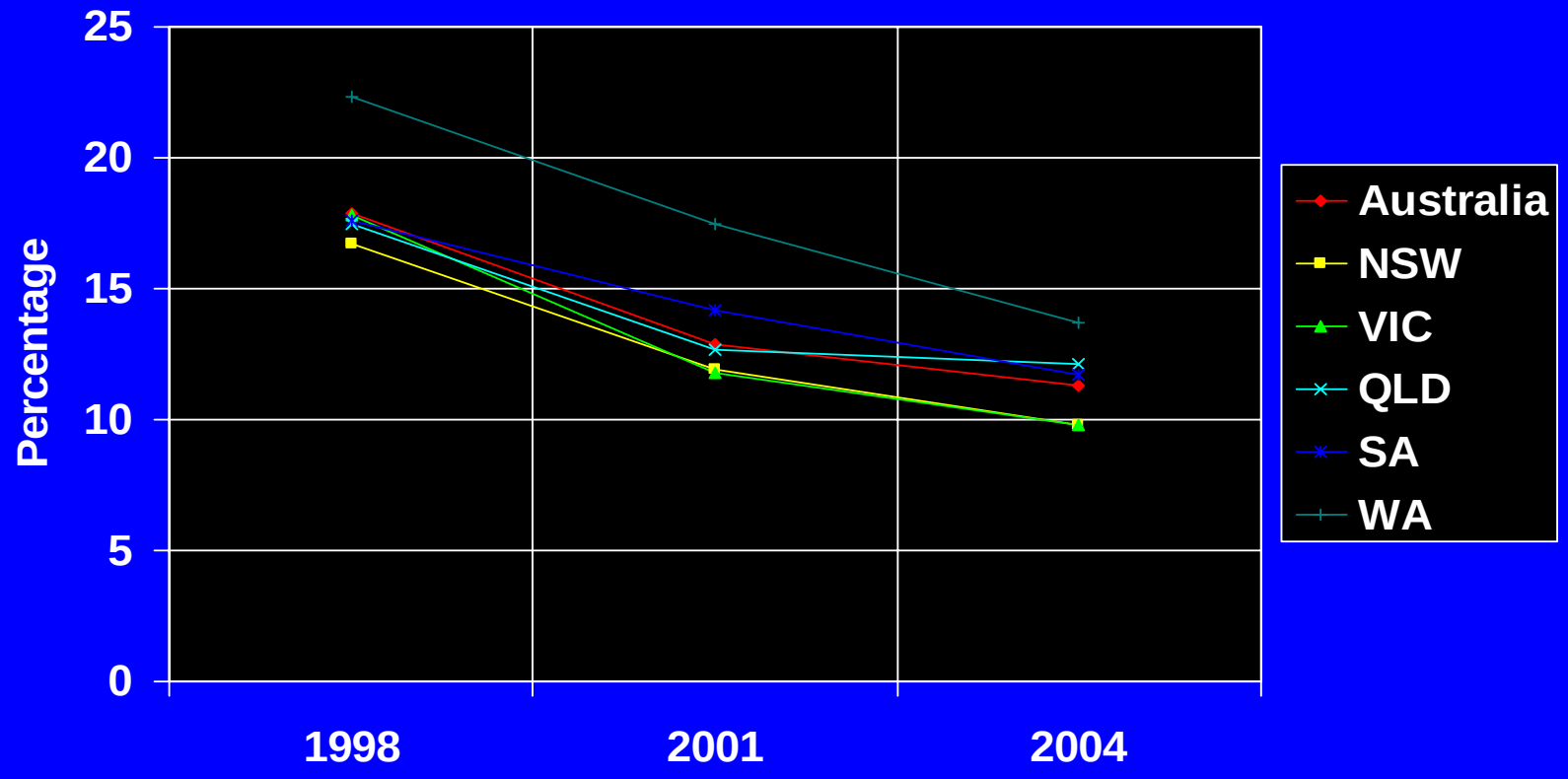
Arguments for Recriminalisation

- 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