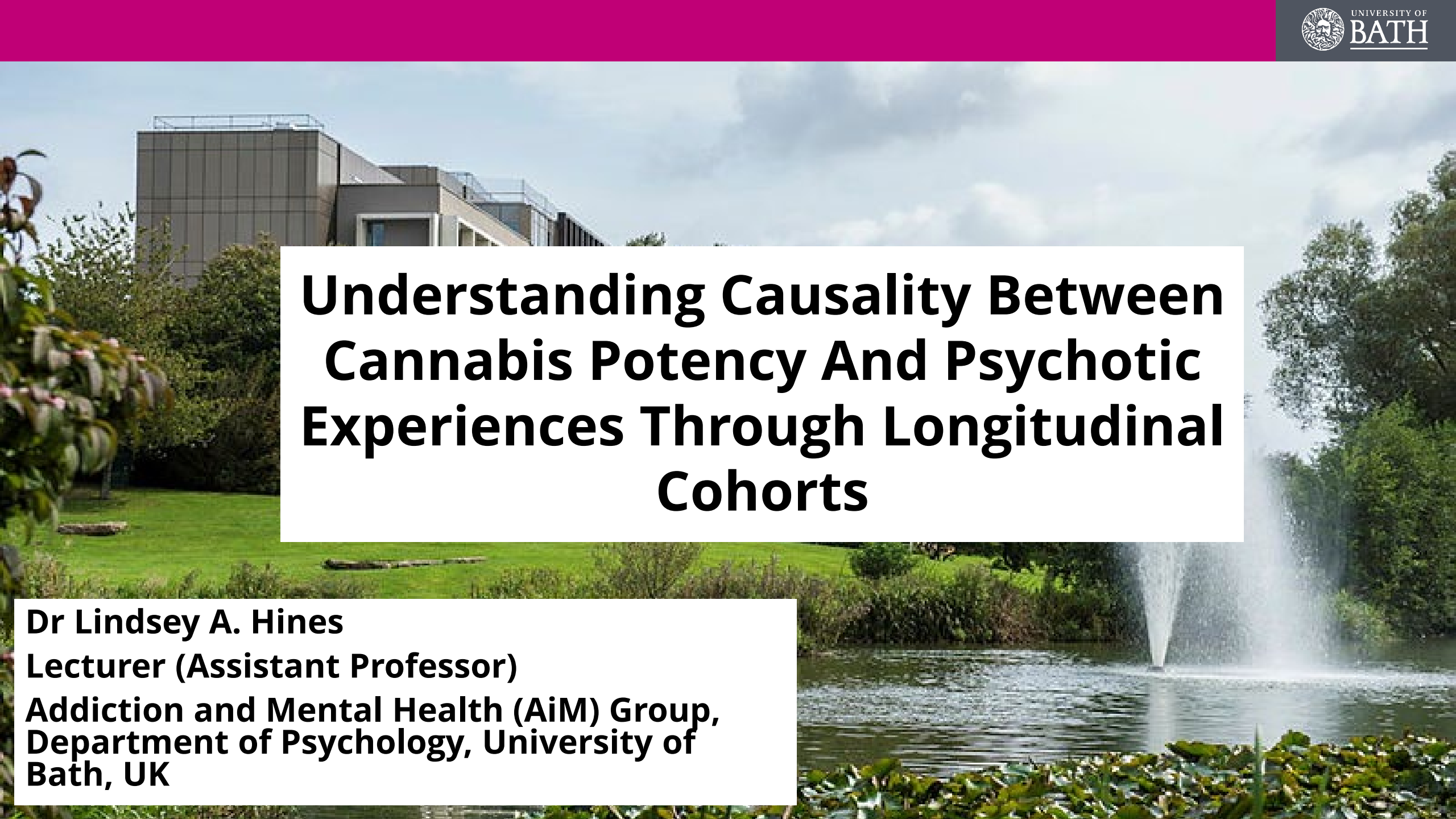


Understanding Causality Between Cannabis Potency And Psychotic Experiences Through Longitudinal Cohorts

Dr Lindsey A. Hines

Lecturer (Assistant Professor)

Addiction and Mental Health (AiM) Group, Department of Psychology, University of Bath, UK

Cannabis use

Globally, the most commonly used internationally regulated drug

In the UK:

- Illegal, except for medical cannabis (very limited conditions and difficult to access)
- Up to 5 years in prison for possession, 14 years for supply; and/or an unlimited fine
- Cannabis use is prevalent amongst adolescents; estimated lifetime prevalence 30%-60% in the UK (age 16-24 year olds)

Cannabis use

Associations with mental health disorders are strong when use is frequent

Associations with, and possible causal role in development of, psychosis

Concerns about rising potency of cannabis in both regulated and unregulated markets

Cannabis potency and psychosis: review

- Reviewed all the studies on cannabis potency and mental health
- 8 studies (with multiple papers) focussed on psychosis
- Overall, increased risk of psychosis with use of higher potency cannabis compared with lower potency cannabis
- Higher potency cannabis use has also been associated with an earlier onset of psychosis, more symptoms of psychosis, and an increased risk of relapse

Petrilli K, Ofori S, Hines L, Taylor G, Adams S, Freeman TP. Association of cannabis potency with mental ill health and addiction: a systematic review. Lancet Psychiatry. 2022 Sep;9(9):736-750.

Cannabis potency and psychosis: review

Limitations:

- Cannot establish direction of association
  - Reverse causation: participants with poorer mental health outcomes could use higher potency cannabis as a form of self-medication
- The most effective intervention targets are *causes* of the disorder we are seeking to prevent ("correlation is not causation")
- To establish causality from potency we need longitudinal data and causal inference approaches

Petrilli K, Ofori S, Hines L, Taylor G, Adams S, Freeman TP. Association of cannabis potency with mental ill health and addiction: a systematic review. Lancet Psychiatry. 2022 Sep;9(9):736-750.

Methods:
The Avon Longitudinal Study of Parents and Children (ALSPAC) cohort

AKA
“The Children of the 90s”

ALSPAC: Children of the 90s

- Prospective population-based birth cohort study: recruited parents of ~14,000 children born 1991-1992 in South-West England
- Mothers completed surveys during pregnancy
- Their children then participated in research from birth – age 30 (and still going)

Available data

During pregnancy

1990

Available data

During pregnancy

1990

Childhood

1990-2000

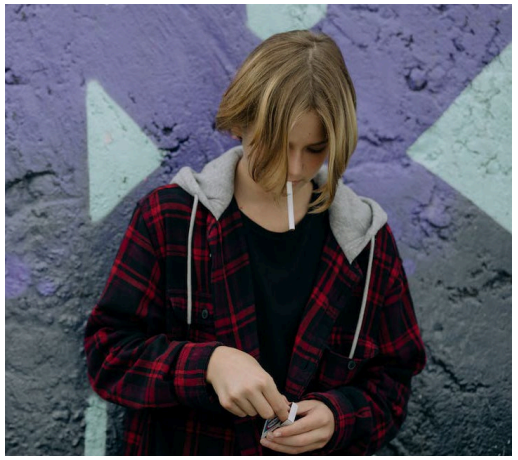
Available data

During pregnancy

1990

Childhood

1990-2000



Adolescence

2000-2015

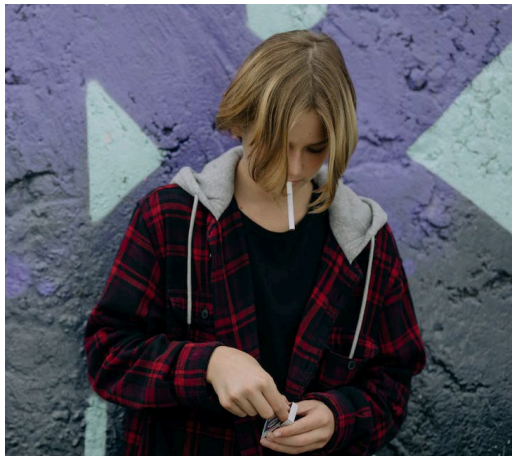
Available data

During pregnancy

1990

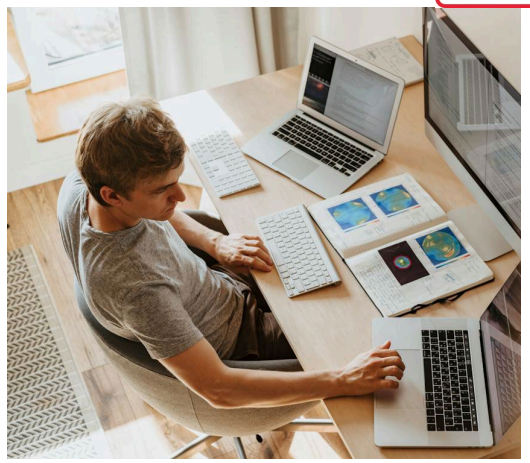
Childhood

1990-2000



Adolescence

2000-2015



Adulthood

2015 onwards

Aim of study

Explore whether use of high-potency cannabis in adolescence is associated with **incident** psychotic experiences

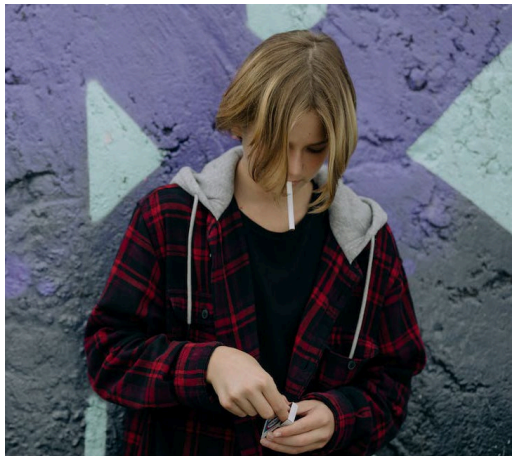
Available data

During pregnancy

1990

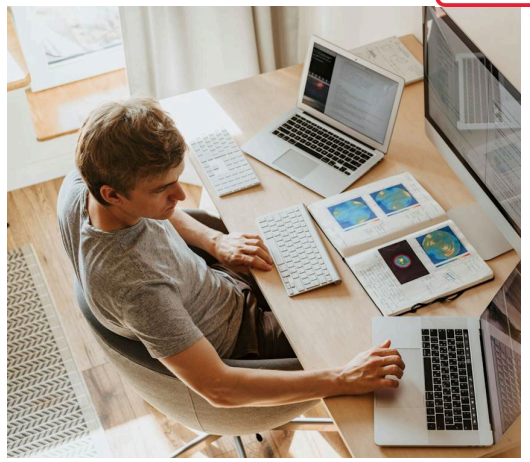
Childhood

1990-2000



Adolescence

2000-2015



Adulthood

2015 onwards

Psychologist-assessed measures of psychotic experiences (e.g. hallucinations, delusions) age 12, 18 and 24

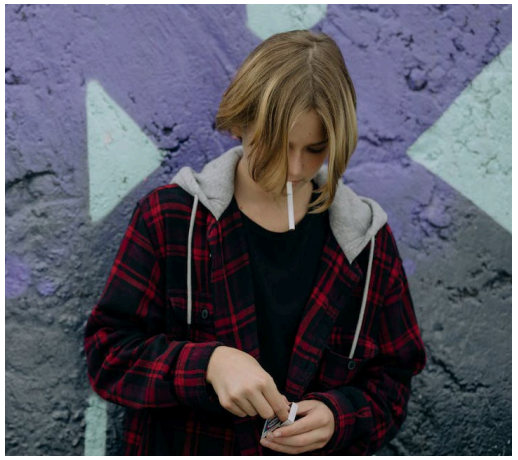
Available data

During pregnancy

1990

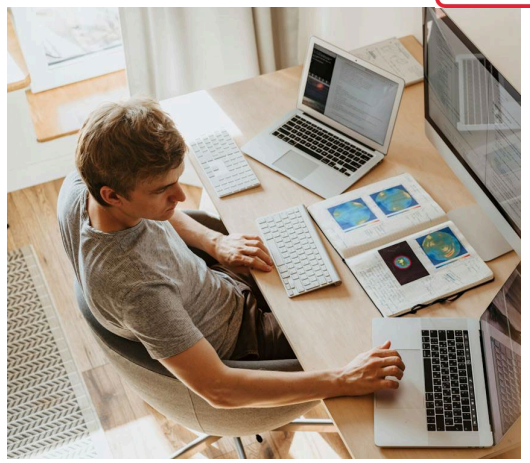
Childhood

1990-2000



Adolescence

2000-2015



Adulthood

2015 onwards

Use, and frequency of use, of cannabis self-reported age
13, 14, 15, 16, 18, 22, 24

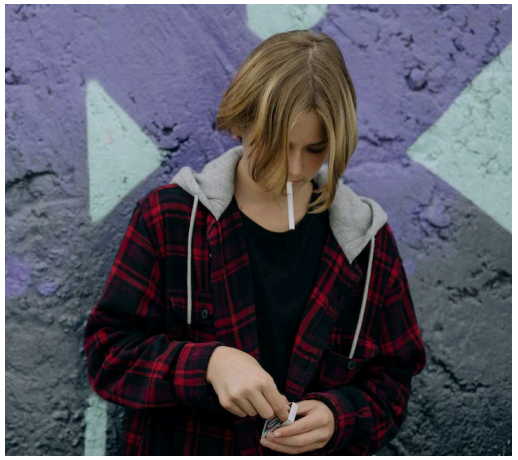
Available data

During pregnancy

1990

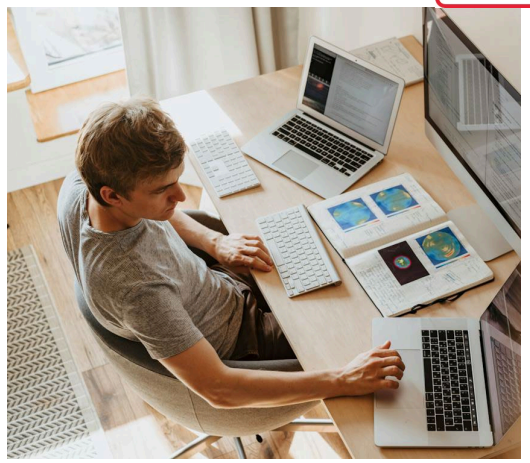
Childhood

1990-2000



Adolescence

2000-2015



Adulthood

2015 onwards

Self-reported type of cannabis most commonly used since first using cannabis (options: ‘herbal cannabis/marijuana’, ‘skunk/other stronger types of herbal cannabis’, ‘hashish/resin/solid’)
at age 24

Results

ADDICTION
SSA SOCIETY FOR THE STUDY OF ADDICTION

SHORT REPORT | Open Access

Incident psychotic experiences following self-reported use of high-potency cannabis: Results from a longitudinal cohort study

Lindsey A. Hines, Jon Heron, Stanley Zammit

First published: 13 May 2024 | https://doi.org/10.1111/add.16517 | Citations: 2

Funding information: L.A.H. is funded by the Wellcome Trust (209158/Z/17/Z). S.Z. is supported by the National Institute for Health and Care Research Biomedical Research Centre at University Hospitals Bristol and Weston National Health Service (NHS) Foundation Trust and the University of Bristol. The work was undertaken with the support of the Medical Research Council (MRC) (MR/M006727/1) and the MRC and Alcohol Research United Kingdom (UK) (MR/L022206/1).

https://onlinelibrary.wiley.com/doi/10.1111/add.16517

Results (1560 people)

Age 12-18

No psychotic experiences

Age 12-18

No psychotic experiences

Results (1560 people)

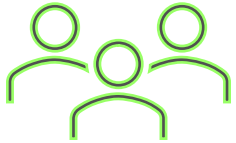
Age 12-18

No psychotic experiences

16-18 use high-potency cannabis (N=145)

Age 12-18

No psychotic experiences



16-18 use lower-potency cannabis (N=1415)

Results (1560 people)

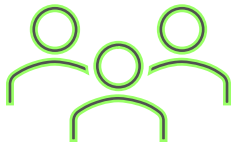
Age 12-18

No psychotic experiences

16-18 use high-potency cannabis (N=145)

Age 12-18

No psychotic experiences



16-18 use lower-potency cannabis (N=1415)

Age 19-24

High-potency cannabis use associated with **twice the likelihood** of having incident psychotic experience
(OR 2.38, 95% CI 1.30-4.38, P=0.005)

Adjusted for tobacco use age 16–18, social class, maternal education, sex and depression symptoms at age 16

Results (5570 people)

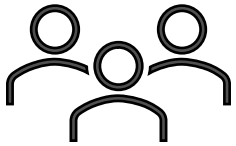
Age 12-18

No psychotic experiences

16-18 use any cannabis (N=2037)

Age 12-18

No psychotic experiences



16-18 no cannabis use (N=3533)

Results (5570 people)

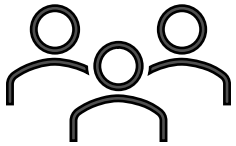
Age 12-18

No psychotic experiences

16-18 use any cannabis (N=2037)

Age 12-18

No psychotic experiences



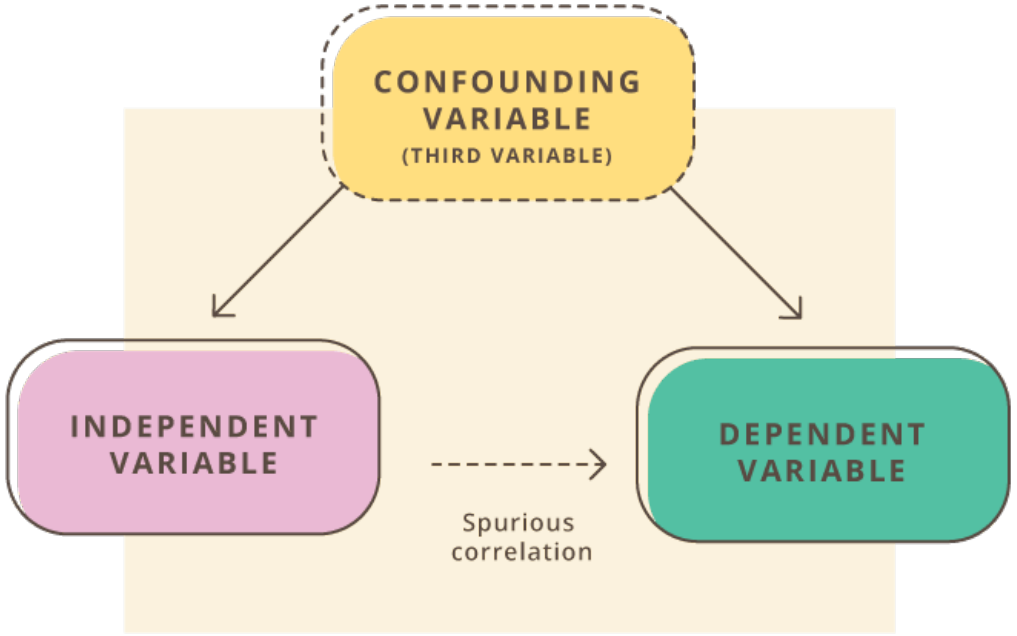
16-18 no cannabis use (N=3533)

Age 19-24

No difference between these groups in risk of incident psychotic experiences

Adjusted for tobacco and alcohol use age 16–18, social class, maternal education, sex and depression symptoms at age 16

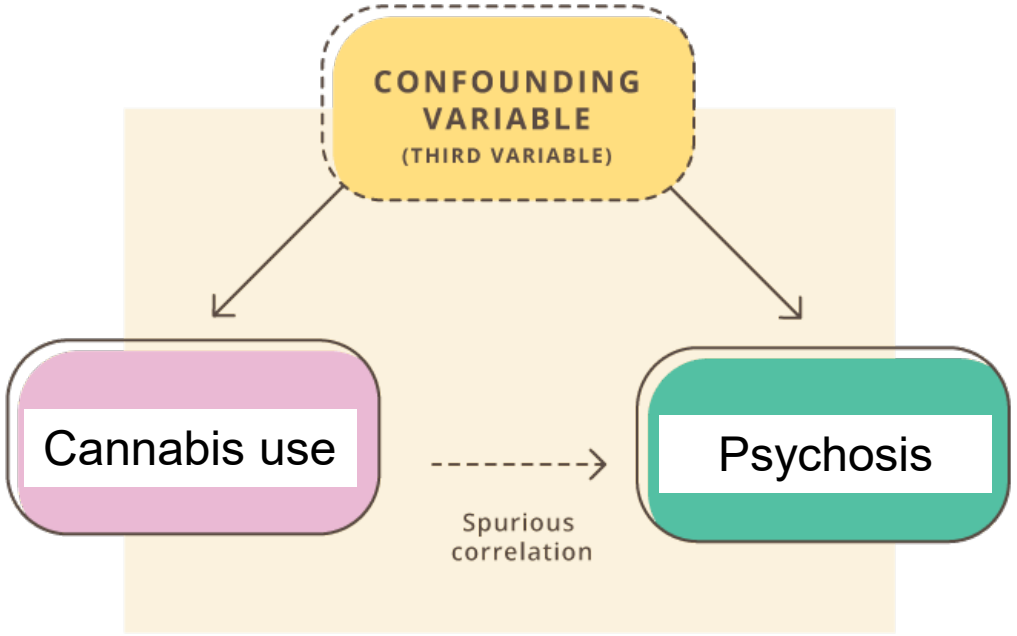
What about confounding?



What at first looks like a causal relationship between IV and DV is ultimately spurious. The confounding variable is the hidden explanation.

From https://explorable.com/confounding-variables/discuss/

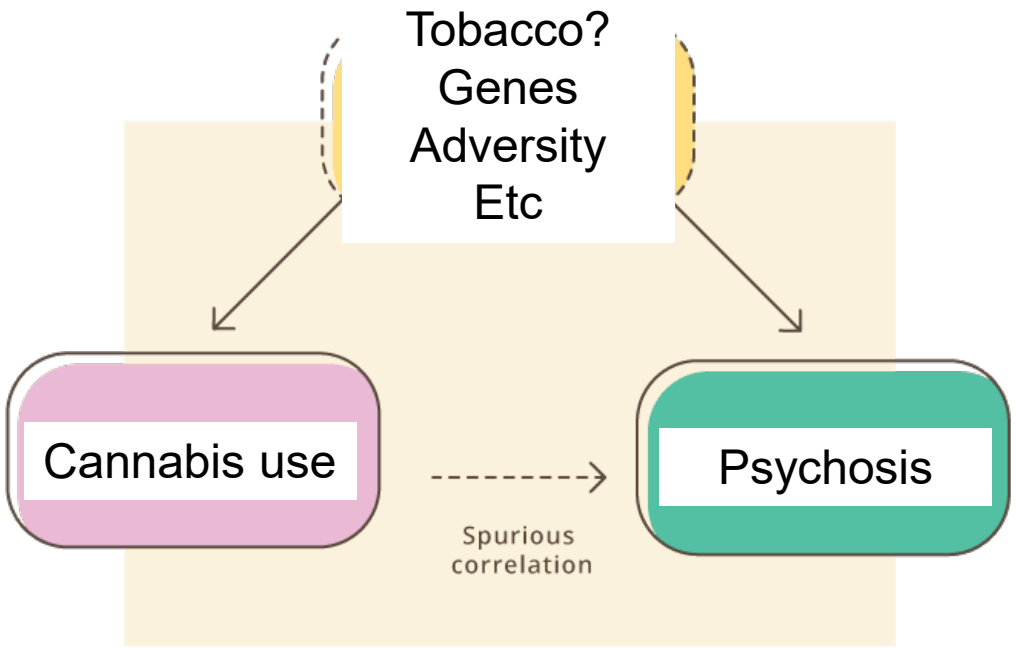
What about confounding?



What at first looks like a causal relationship between IV and DV is ultimately spurious. The confounding variable is the hidden explanation.

From https://explorable.com/confounding-variables/discuss/

What about confounding?



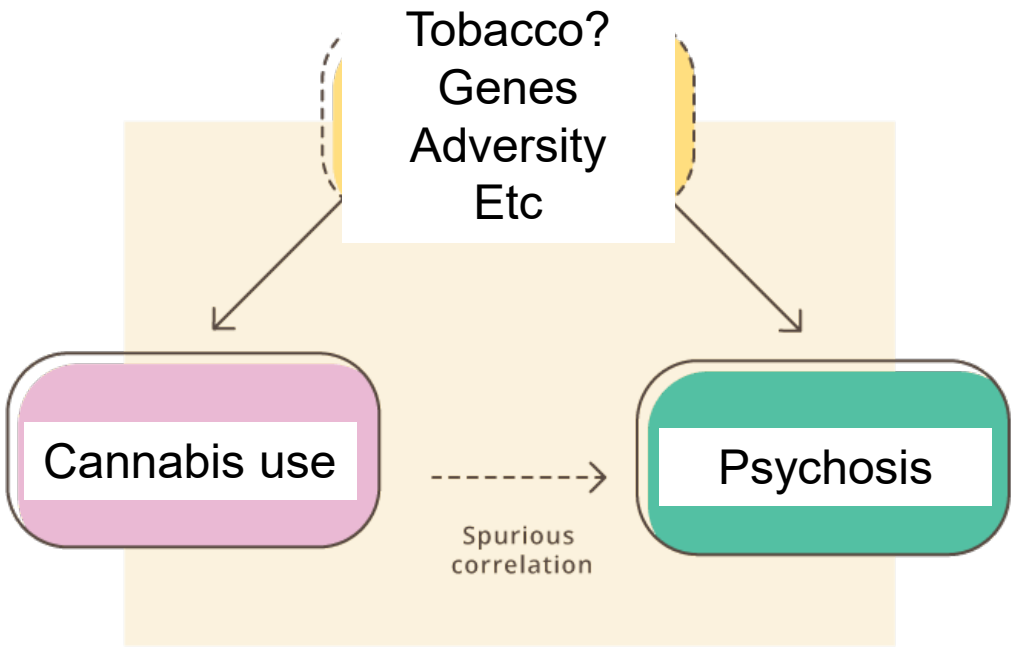
What at first looks like a causal relationship between IV and DV is ultimately spurious. The confounding variable is the hidden explanation.

From https://explorable.com/confounding-variables/discuss/

What about confounding?

Importance of the comparison group: do we have the same confounding with potency…?

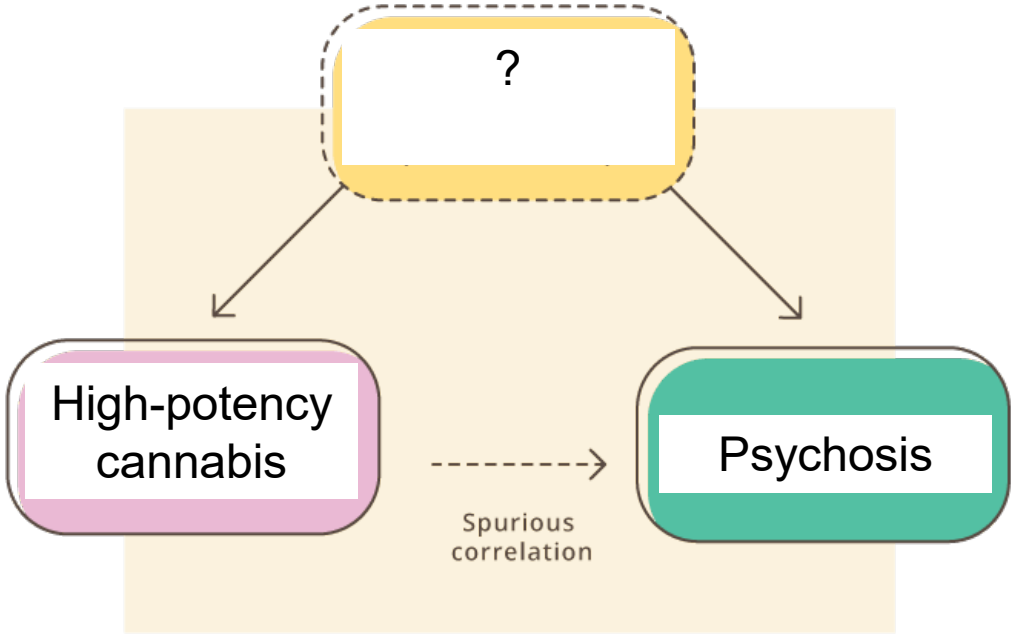
We don't yet know much about what might lead to differences in choosing high v. low potency strains



What at first looks like a causal relationship between IV and DV is ultimately spurious. The confounding variable is the hidden explanation.

From https://explorable.com/confounding-variables/discuss/

What about confounding?



What at first looks like a causal relationship between IV and DV is ultimately spurious. The confounding variable is the hidden explanation.

From https://explorable.com/confounding-variables/discuss/

Results (1560 peopl

Differences in known confounders e.g. Genes, adversity etc
Are likely to be minimal between these groups

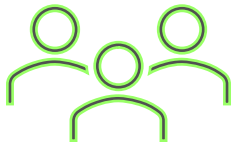
Age 12-18

No psychotic experiences

16-18 use high-potency cannabis (N=145)

Age 12-18

No psychotic experiences



16-18 use lower-potency cannabis (N=1415)

High-potency cannabis use associated with twice the likelihood of having incident psychotic experience (OR 2.38, 95% CI 1.30-4.38, P=0.005)

Adjusted for tobacco use age 16–18, social class, maternal education, sex and depression symptoms at age 16

Limitations

- Illegal market = self-reported potency
- Inferred use of potency – but we aren't aware of any other studies that have longitudinal measures of psychotic experiences and potency
- Study drop out means this sample is more likely to be white, female and more affluent than the general UK population

JAMA Psychiatry | Original Investigation

Association of High-Potency Cannabis Use With Mental Health and Substance Use in Adolescence

Lindsey A. Hines, PhD; Tom P. Freeman, PhD; Suzanne H. Gage, PhD; Stanley Zammit, PhD; Matthew Hickman, PhD; Mary Cannon, PhD; Marcus Munafo, PhD; John MacLeod, PhD; Jon Heron, PhD

JAMA Psychiatry. 2020;77(10):1044-1051. doi:10.1001/jamapsychiatry.2020.1035
Published online May 27, 2020.

https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2765973

JAMA Psychiatry | Original Investigation

Association of High-Potency Cannabis Use With Mental Health and Substance Use in Adolescence

Lindsey A. Hines, PhD; Tom P. Freeman, PhD; Suzanne H. Gage, PhD; Stanley Zammit, PhD; Matthew Hickman, PhD; Mary Cannon, PhD; Marcus Munafo, PhD; John MacLeod, PhD; Jon Heron, PhD

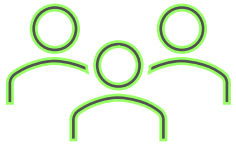
JAMA Psychiatry. 2020;77(10):1044-1051. doi:10.1001/jamapsychiatry.2020.1035
Published online May 27, 2020.

https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2765973

- First general population study of cannabis potency
- Same cohort, but only one time point (age 24)
- So associations are cross-sectional
- But we used *longitudinal confounders*

Results (1087 people)

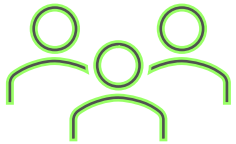
Age 24 mostly used high-potency cannabis in past year (N=141)



Age 24 mostly used lower-potency cannabis in past year(N=946)

Results (1087 people)

Age 24 mostly used high-potency cannabis in past year (N=141)



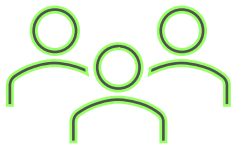
Age 24 mostly used lower-potency cannabis in past year(N=946)

People using high-potency cannabis **more likely** to report psychotic experiences
(OR 1.86, 95% CI 1.00-3.46, P=0.05)

Adjusted for sex, childhood socioeconomic position, and Psychotic Experiences at 12 years of age (to ensure mental health symptoms preceded onset of cannabis use)

Results (1087 people)

Age 24 mostly used high-potency cannabis in past year (N=141)



Age 24 mostly used lower-potency cannabis in past year(N=946)

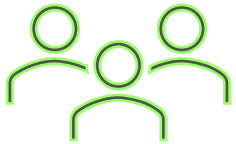
People using high-potency cannabis **four times** as likely to use cannabis at least once a week (frequent use) (OR 4.38, 95% CI 2.89-6.63, P<=0.01)

And **eight times** as likely to report problems from cannabis use (OR 8.45, 95% CI 23.04 – 23.50, P<=0.01)

Adjusted for sex, childhood socioeconomic position, and age of onset of cannabis use

Results (1087 people)

Age 24 mostly used high-potency cannabis in past year (N=141)



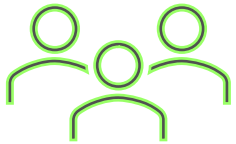
Age 24 mostly used lower-potency cannabis in past year(N=946)

People using high-potency cannabis **more likely** to report psychotic experiences
(OR 1.86, 95% CI 1.00-3.46, P=0.05)

Adjusted for sex, childhood socioeconomic position, and Psychotic Experiences at 12 years of age (to ensure mental health symptoms preceded onset of cannabis use)

Results (1087 people)

Age 24 mostly used high-potency cannabis in past year (N=141)

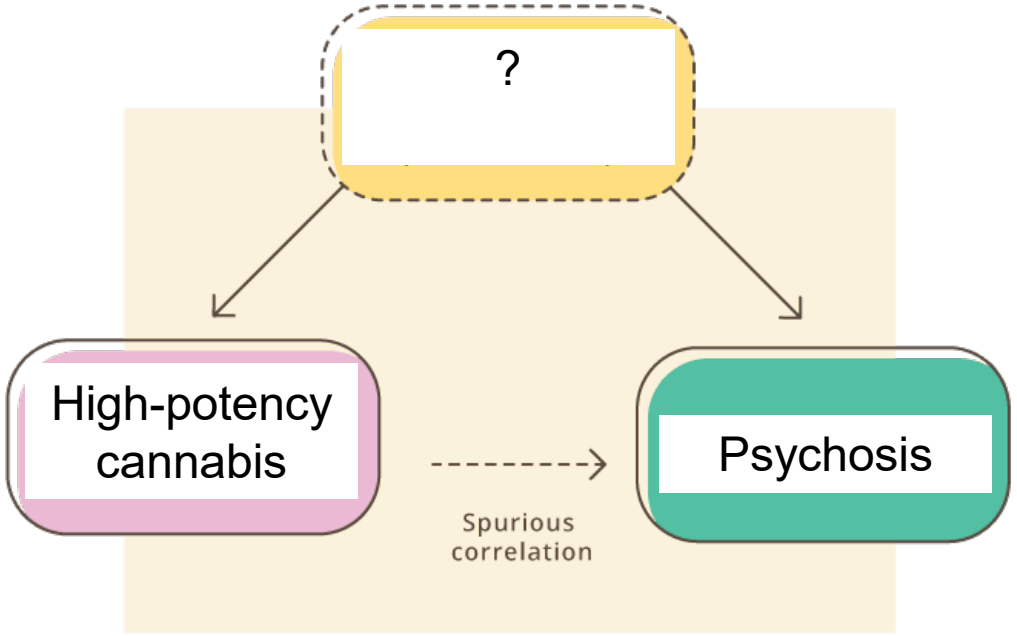


Age 24 mostly used lower-potency cannabis in past year(N=946)

When we adjusted for frequency of use, this association for psychotic experiences **did not** remain (OR 1.29, 95% CI 0.67-2.50, P=0.45)

Adjusted for sex, childhood socioeconomic position, and Psychotic Experiences at 12 years of age (to ensure mental health symptoms preceded onset of cannabis use) and frequency of cannabis use age 24

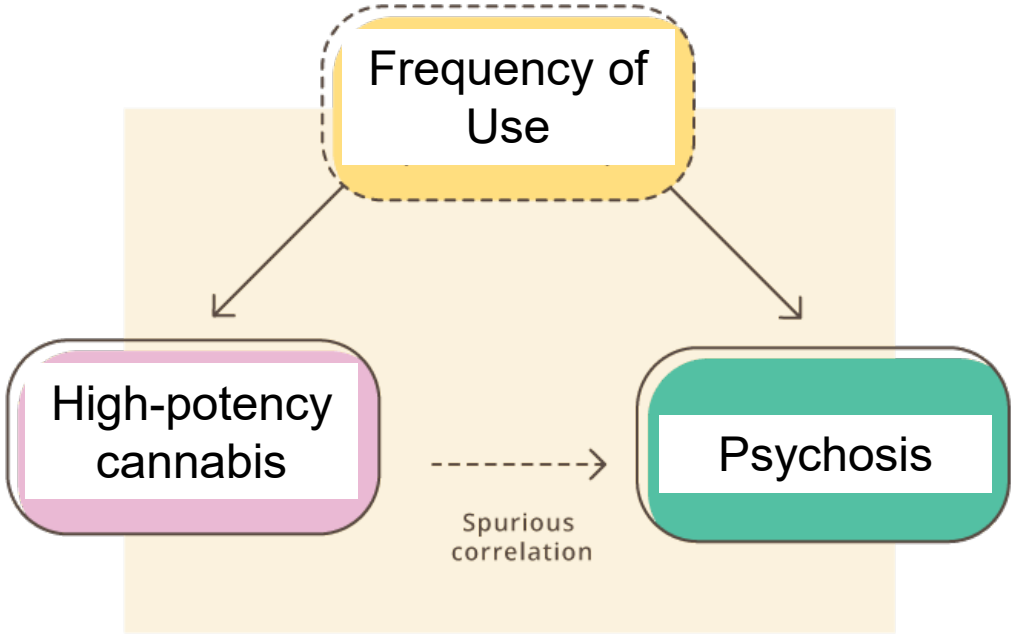
What about confounding?



What at first looks like a causal relationship between IV and DV is ultimately spurious. The confounding variable is the hidden explanation.

From https://explorable.com/confounding-variables/discuss/

What about confounding?



What at first looks like a causal relationship between IV and DV is ultimately spurious. The confounding variable is the hidden explanation.

From https://explorable.com/confounding-variables/discuss/

Cannabis use behaviours and potency

Which comes first…?

High potency cannabis use → Frequent cannabis use/ Cannabis use disorder

Frequent cannabis use/ Cannabis use disorder → Tolerance → High potency cannabis use

Cannabis use behaviours and potency

Which comes first…?

Cannabis use behaviours and potency

Which comes first…?

Policy: regulate potency

High potency cannabis use → Frequent cannabis use/ Cannabis use disorder

High potency cannabis use → Psychotic experiences/ Clinical psychosis

Frequent cannabis use/ Cannabis use disorder → Tolerance → High potency cannabis use

Cannabis use behaviours and potency

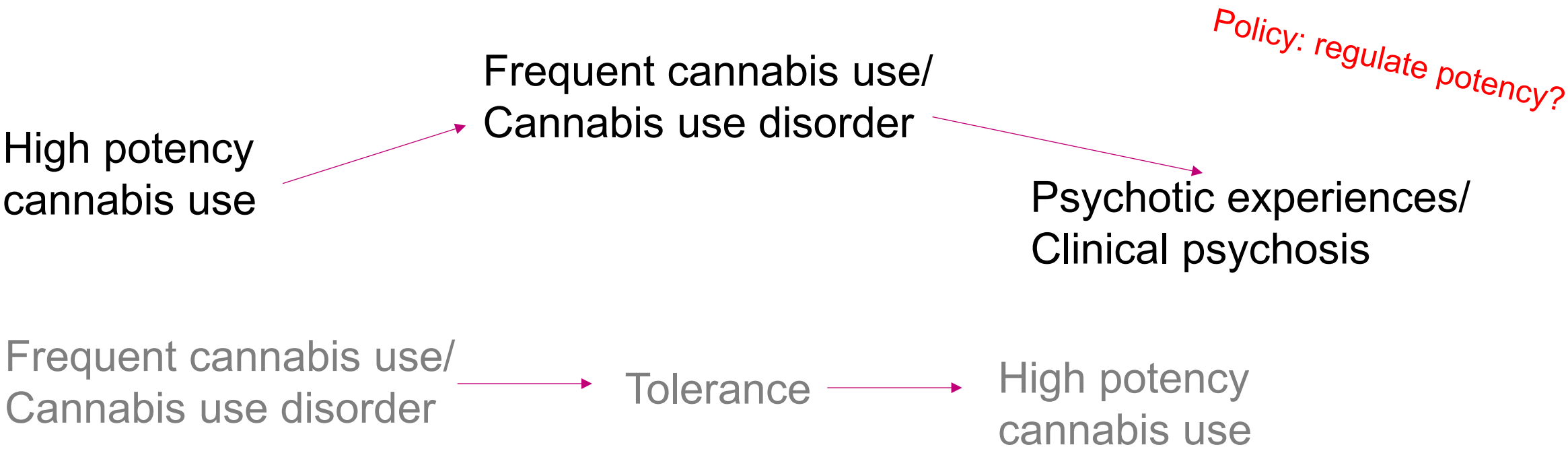
Which comes first…?

High potency cannabis use → Frequent cannabis use/ Cannabis use disorder → Psychotic experiences/ Clinical psychosis

Frequent cannabis use/ Cannabis use disorder → Tolerance → High potency cannabis use

Cannabis use behaviours and potency

Which comes first…?



Cannabis use behaviours and potency

Which comes first…?

High potency cannabis use → Frequent cannabis use/ Cannabis use disorder

Frequent cannabis use/ Cannabis use disorder → Tolerance → High potency cannabis use

Frequent cannabis use/ Cannabis use disorder → Psychotic experiences/ Clinical psychosis

Cannabis use behaviours and potency

Which comes first…?

Policy: focus on availability/frequency

High potency cannabis use → Frequent cannabis use/ Cannabis use disorder

Frequent cannabis use/ Cannabis use disorder → Tolerance → High potency cannabis use

Frequent cannabis use/ Cannabis use disorder → Psychotic experiences/ Clinical psychosis

Conclusions

- Previous epidemiological work indicates use of high-potency cannabis increases risks of psychosis
- When we consider timing of use in study design, there are still increased risks of incident psychotic experiences
- Relationship also remains after adjustment for early life psychotic experiences (preceding cannabis use)
- Points towards a rationale for policy limits on potency
- But role of frequency still under explored

Acknowledgements

Professor Stanley Zammit

Dr Jon Heron

Prof Matt Hickman

Dr Tom Freeman

Dr Suzanne Gage

Prof Mary Cannon

Prof Marcus Munafo

Prof John MacLeod

The participants and study teams of ALSPAC

The MRC & The Wellcome Trust (ALSPAC funding)

The Wellcome Trust (Postdoctoral Fellowship)