

Understanding the mechanisms that link childhood stress with risk of addiction

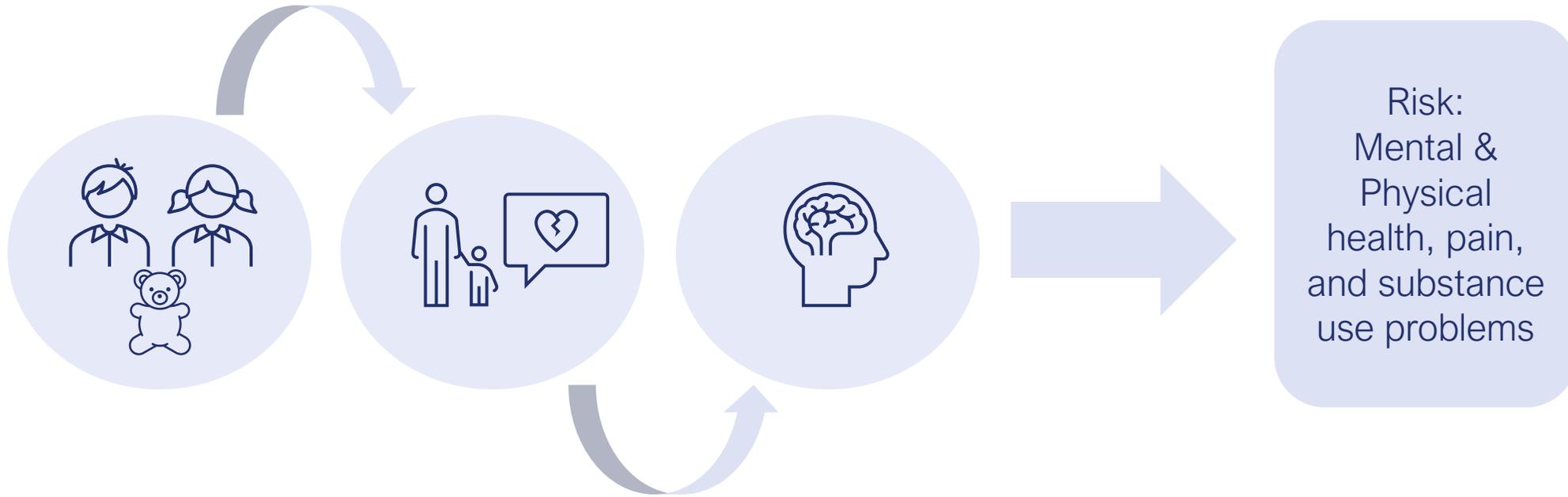
Dr Molly Carlyle

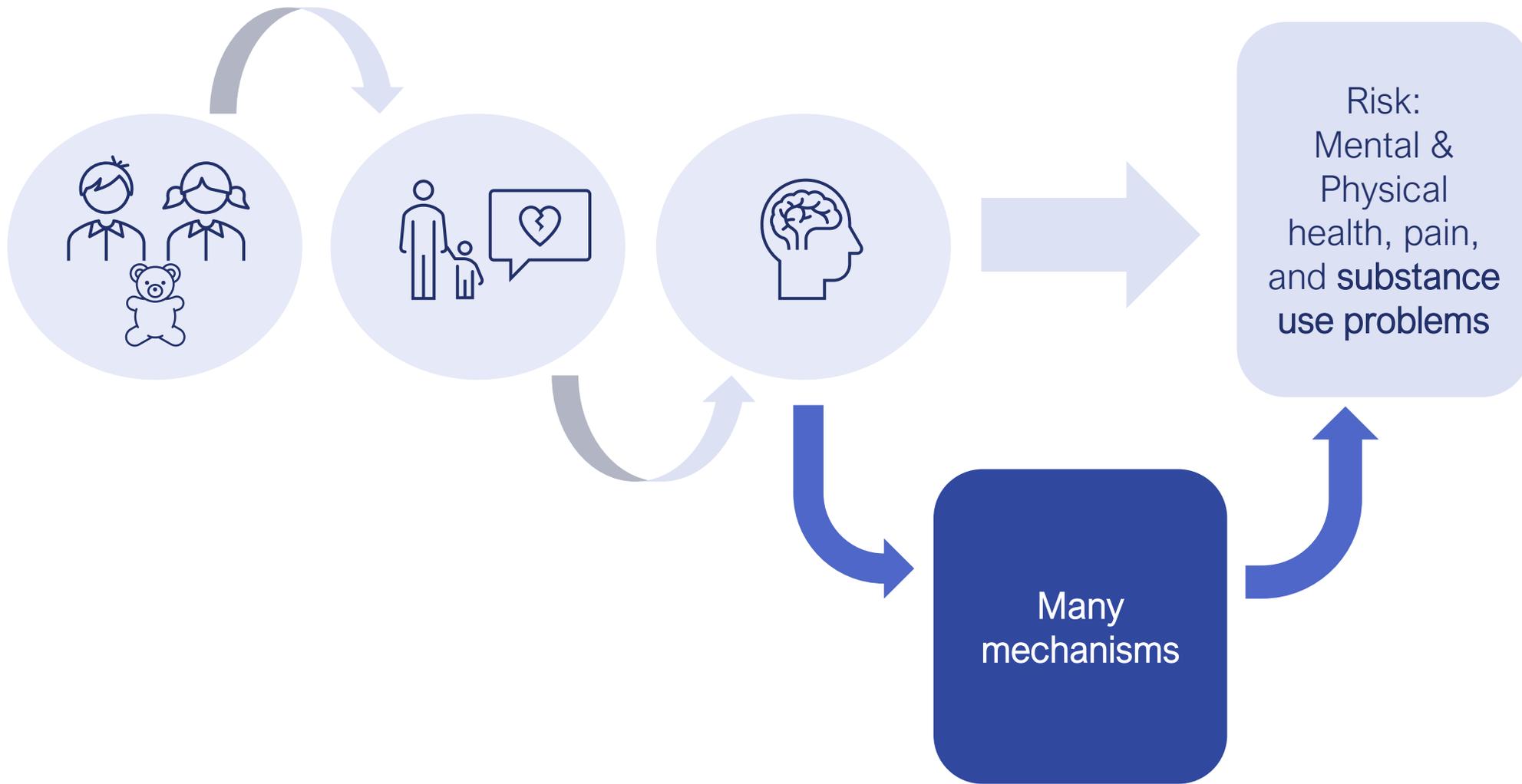
Postdoctoral Research Fellow, Leknes Affective Brain Lab, University of Oslo

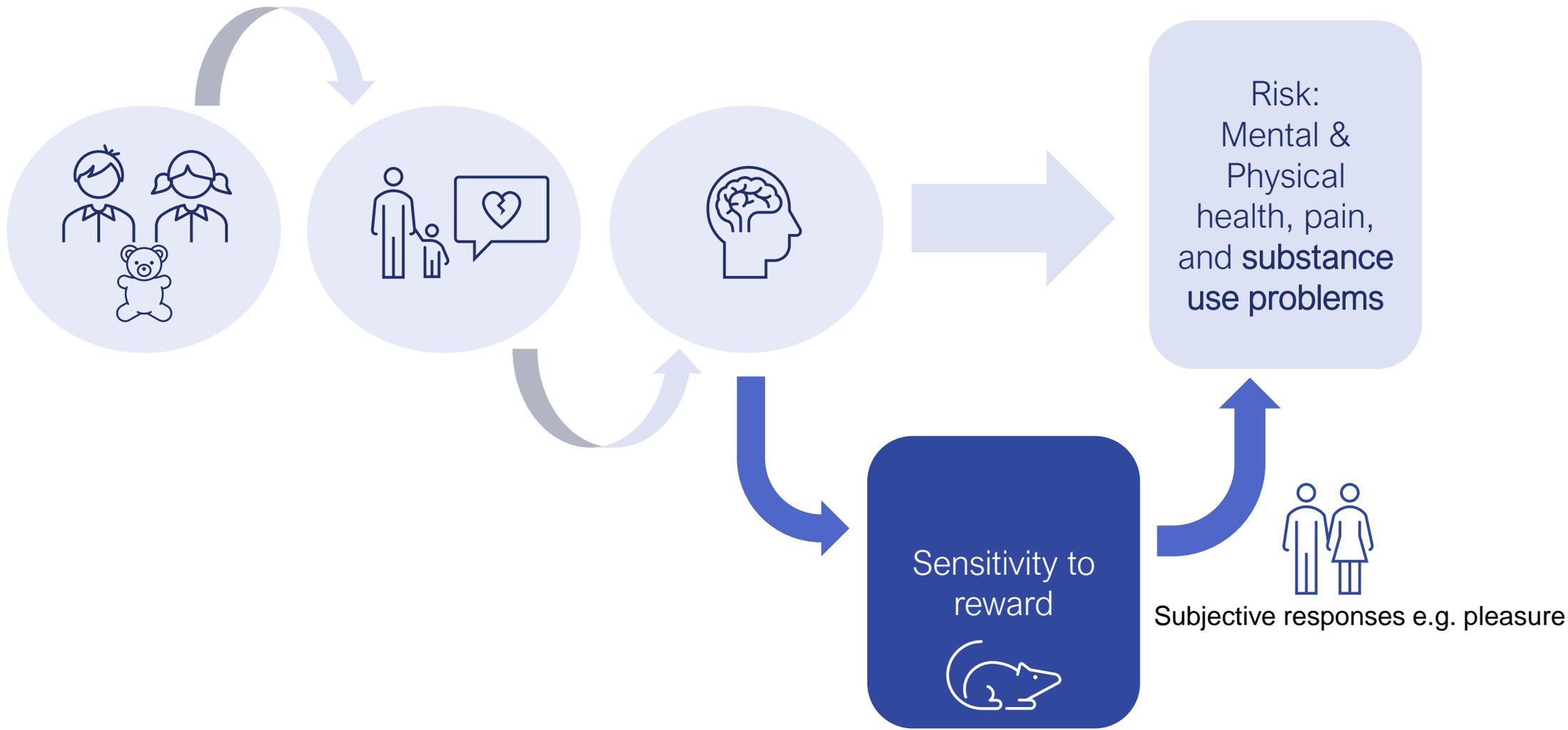


UiO : **University of Oslo**









Overview:

Study 1

- Does childhood trauma alter subjective drug reward for opioids?



Study 2

- Does this translate clinically to medically prescribed opioids?



Study 3

- Does this apply to other drug groups, like stimulants?



Study 4

- Is this seen in people with substance use problems?



Experimental Study 1

Addiction Biology

SSA SOCIETY FOR THE
STUDY OF
ADDICTION

ORIGINAL ARTICLE |  Open Access

A randomised, double-blind study investigating the relationship between early childhood trauma and the rewarding effects of morphine

Molly Carlyle , Rupert Broomby, Graham Simpson, Rachel Hannon, Leah Fawaz, O Merve Mollaahmetoglu, Jade Drain, Mohammod Mostazir, Celia J. A. Morgan

First published: 21 June 2021 | <https://doi.org/10.1111/adb.13047> | Citations: 2

UNIVERSITY OF
EXETER

PARC
Psychopharmacology and
Addiction Research Centre

NHS
Royal Devon and Exeter
NHS Foundation Trust

NIHR | Exeter Clinical
Research Facility

Study 1: Methods

Participants & Design

Double-blind, placebo controlled, counterbalanced design

2 sessions: Morphine or low dose control (repeated)

2 groups: childhood trauma (n=27) or no trauma control (n=25) (between-groups)

Healthy volunteers:

- No history of addiction or severe mental health problems.
- Selected on childhood trauma history.

Administration procedure

Intramuscular dose of either

1. Morphine (0.15mg/kg; max of 10mg), or
2. Low dose control (saline containing miniscule dose of morphine 0.01mg/kg)

Measures

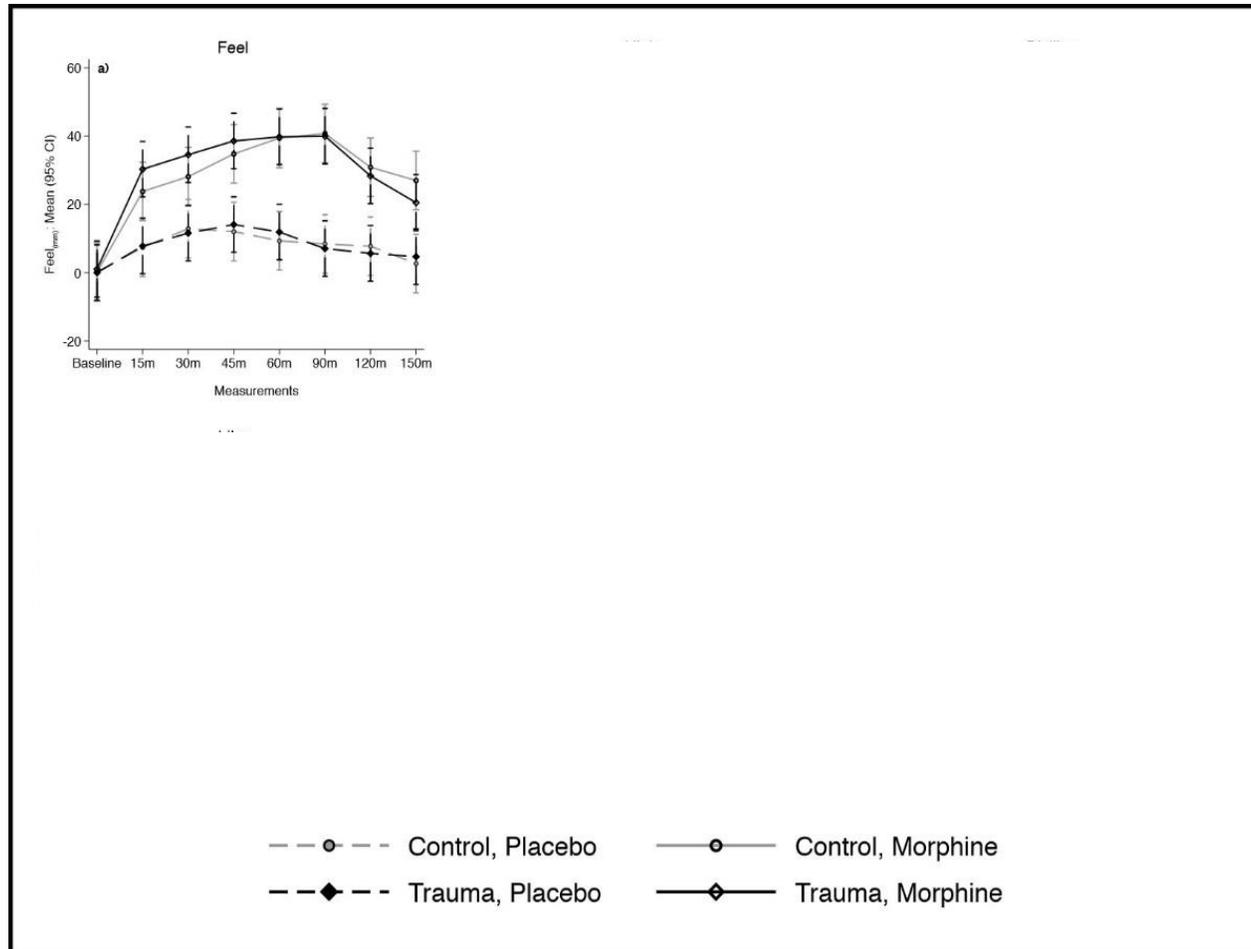
Subjective opioid effects

- Drug effects questionnaire (DEQ) for feel, liking, disliking, high, more
- Additional opioid-specific effects

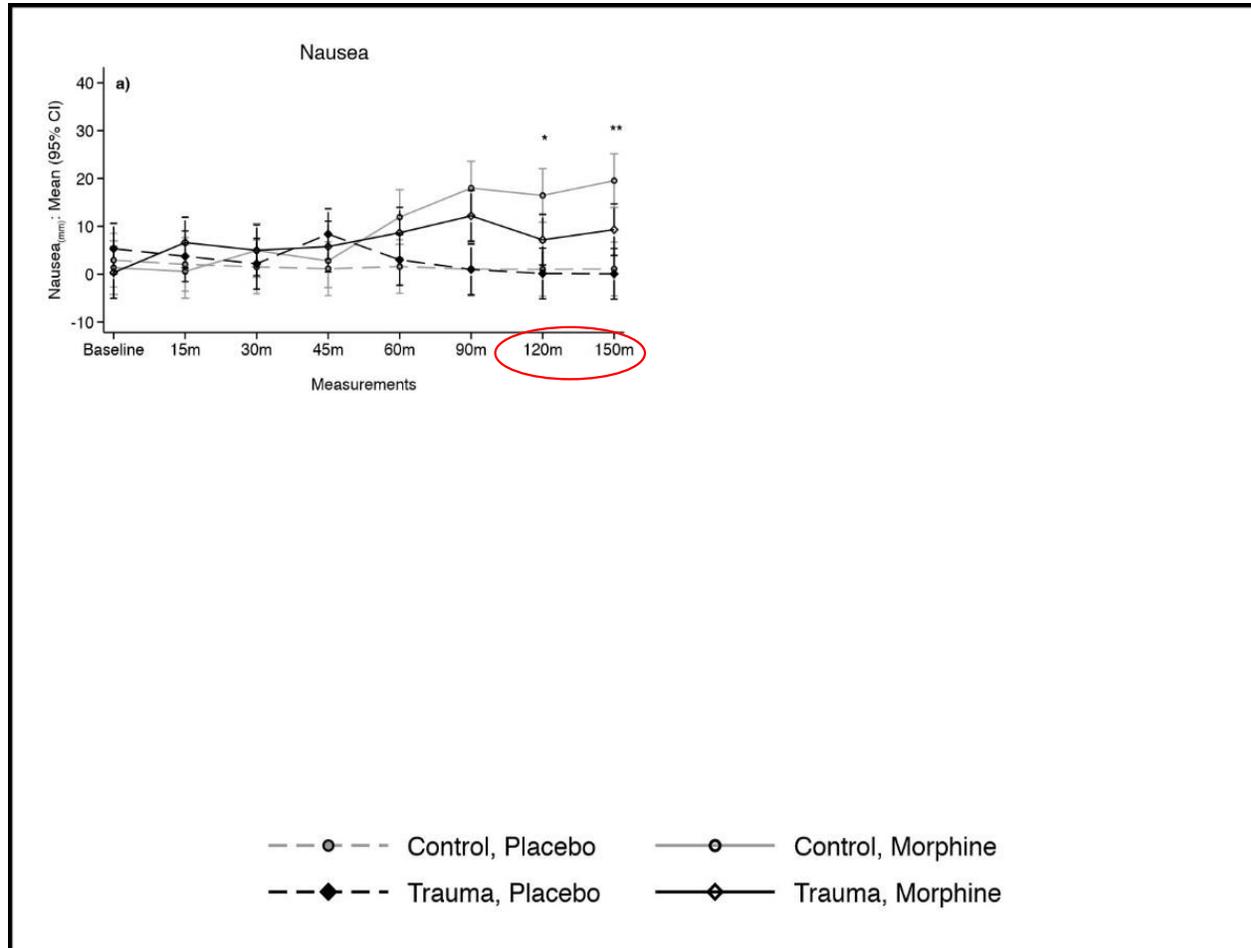
Question to answer:

Do people with childhood trauma have more pleasurable effects of opioids?

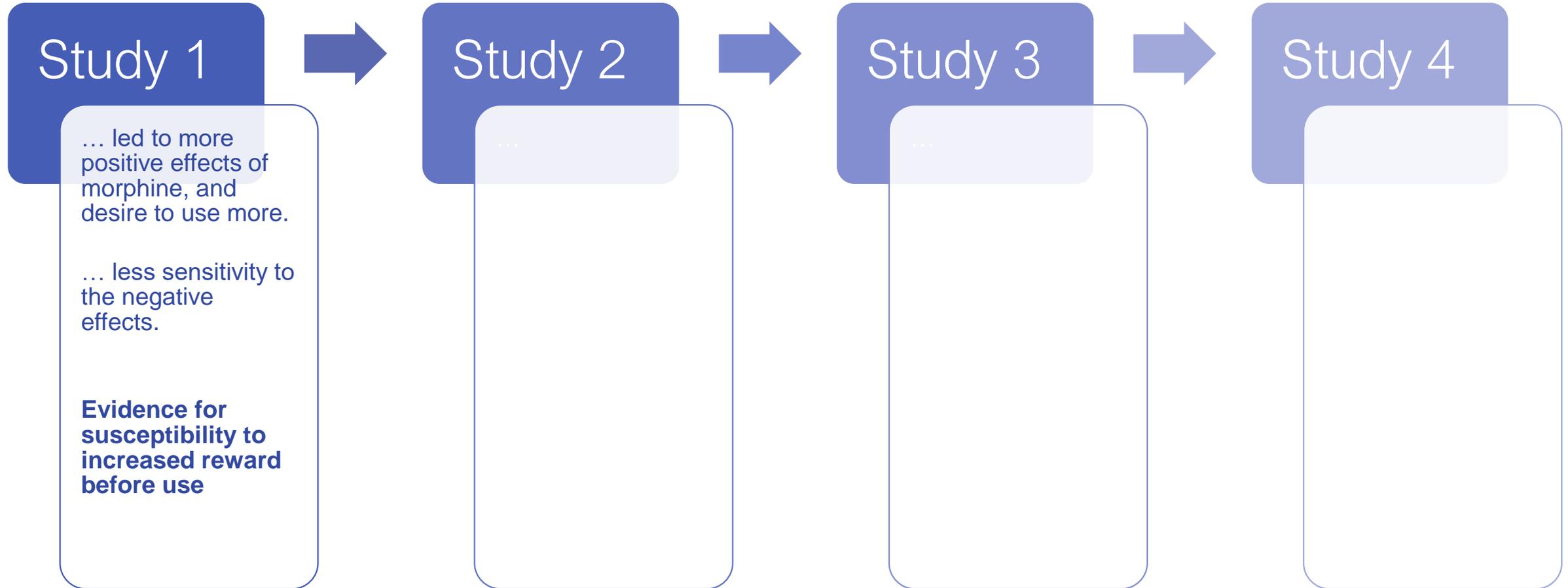
Study 1: Results - reward



Study 1: Results - reward



Implications: childhood trauma...



Overview:

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Study 4

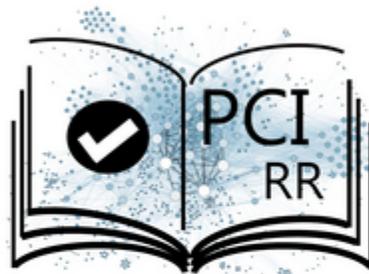
- Is this also observed in people with substance use problems?



Naturalistic Study 2

A recommendation of:

STAGE 1



Does childhood adversity alter opioid drug reward? A conceptual replication in outpatients before surgery

Molly Carlyle*, Malin Kvande*, Siri Leknes, Isabell Meier, Kaja Buen, Eira Nordeng Jensen, Gernot Ernst, Marie Eikemo. *denotes equal contribution.
https://osf.io/qcj5m?view_only=4238d2ee3d654c4f908a94efea82a027
version v4

READ REPORT ON SERVER

Abstract

Submission: posted 15 March 2022
Recommendation: posted 24 October 2022

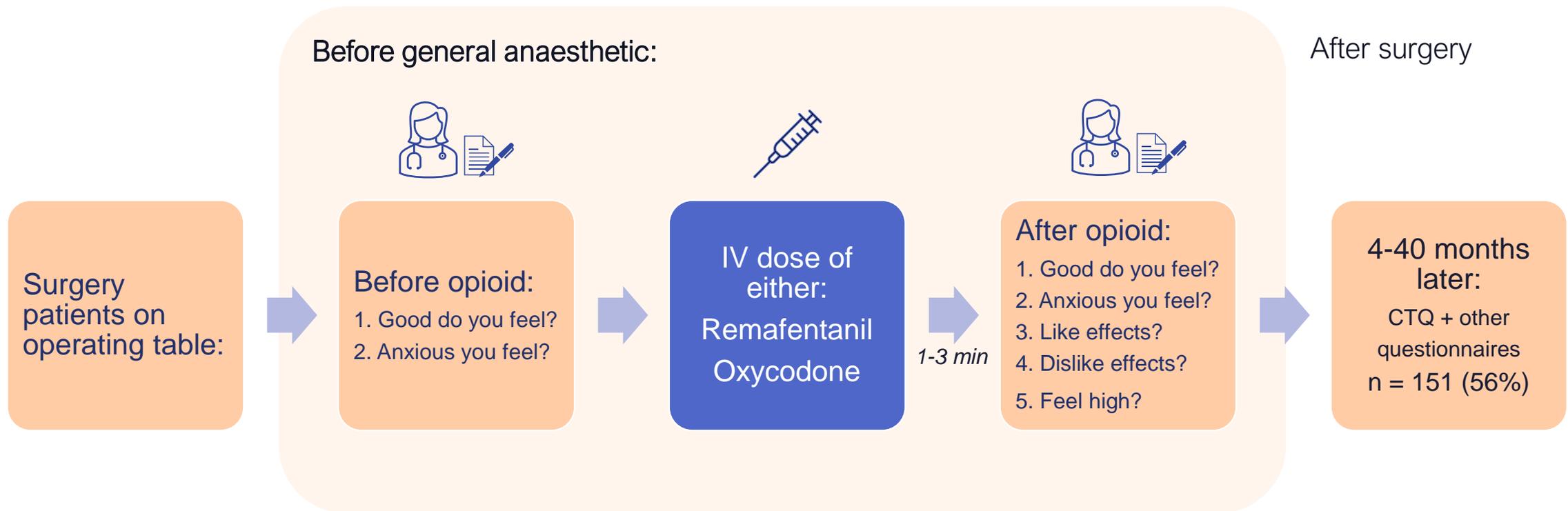


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Study 2: Methods

A prospective observational study of acute preoperative opioid effects
Day surgery patients (n=269)



Question to answer:

Do people with more childhood trauma have more pleasurable effects (liking + feel good) of pre-surgical opioids?

Study 2: Results

Primary results:

No significant effects of CTQ total score on

- post-opioid liking: (b = -0.06, 95%CIs [-0.12 – -0.01], p = 0.062)
- feeling good: (b = 0.01, 95%CIs [- 0.03 – 0.04], p = 0.660)

Exploratory results:

Significant associations between CTQ and:

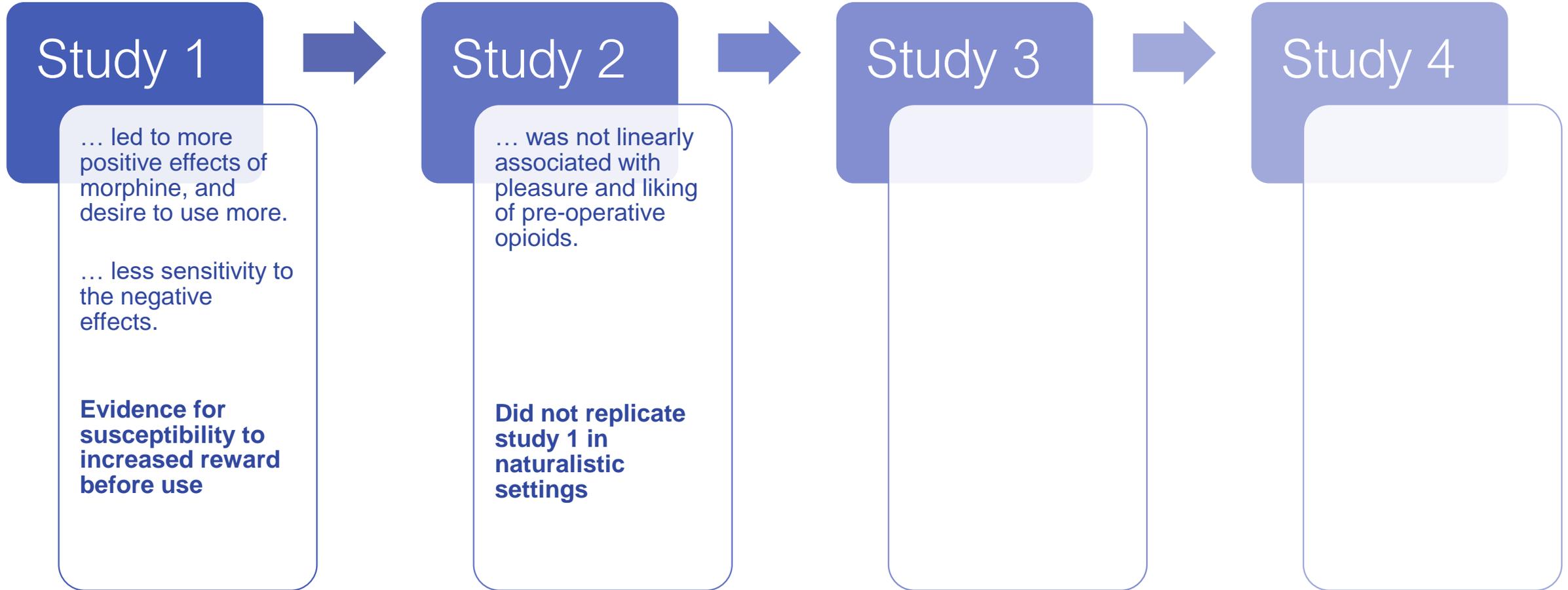
- Childhood & adulthood SES
- Loneliness
- Anxiety
- Pain catastrophising

None with alcohol or other drug use scores (AUDIT & DUDIT)



Did not
conceptually
replicate
previous study

Implications: childhood trauma...



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- Is this also observed in people with substance use problems?



Experimental Study 3

Does childhood trauma alter subjective responses to stimulants? Secondary analyses of two placebo-controlled, double-blind studies

Molly Carlyle, Siri Leknes, Harriet de Wit et al.



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Study 3: Methods

Secondary data analysis

Screening data

- Routine screening questionnaire across many studies

Childhood trauma questionnaire

Experimental data

- Placebo-controlled double blind drug administration
- 2 studies, 4 sessions

d-amphetamine,
20mg

Methamphetamine
20mg

Pooled dataset

- 'Stimulants'

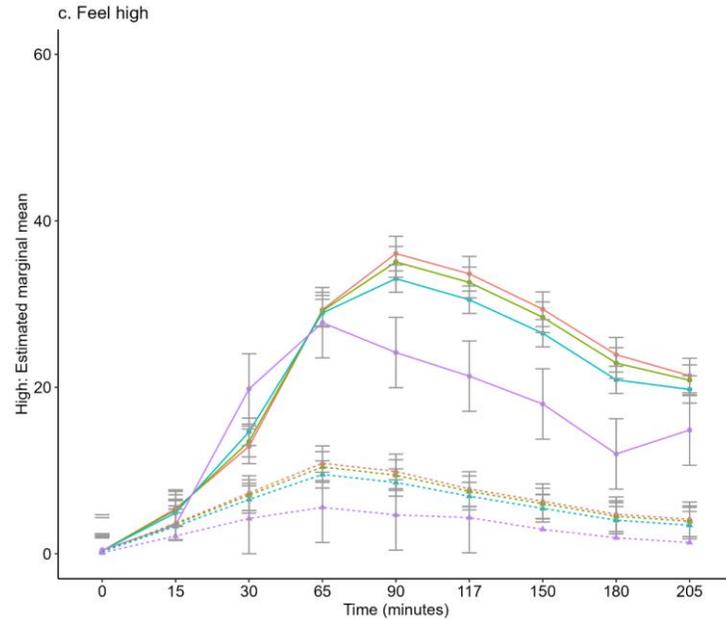
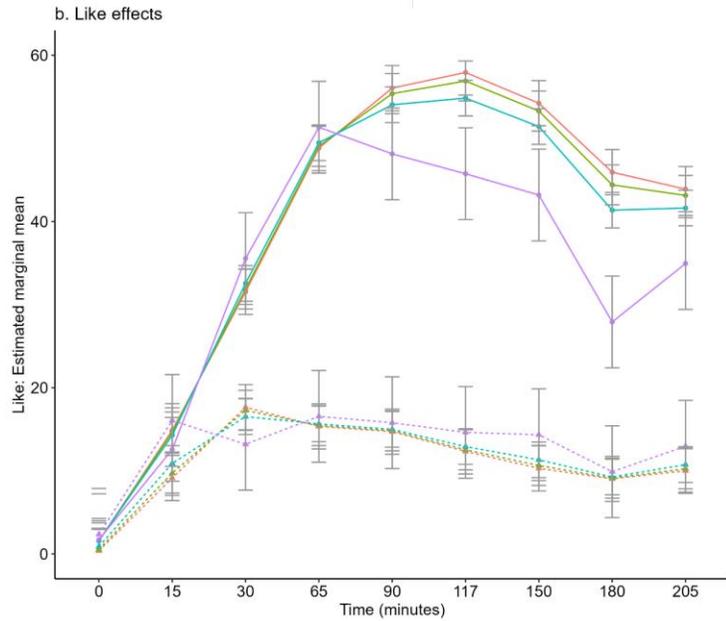
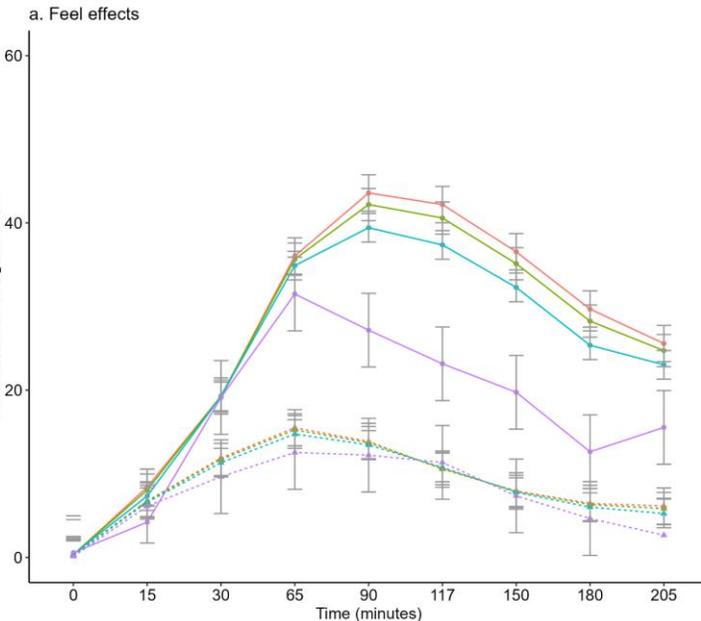
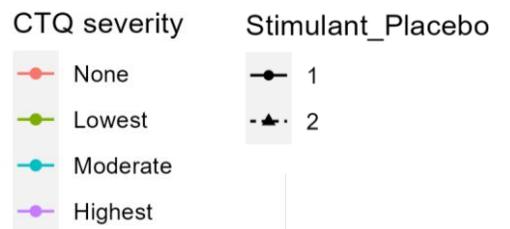
N = 84 (with CTQ)
Drug effects: Feel, like, dislike,
more, high

Question to answer:

Do people with greater childhood trauma have more pleasurable responses to stimulants?

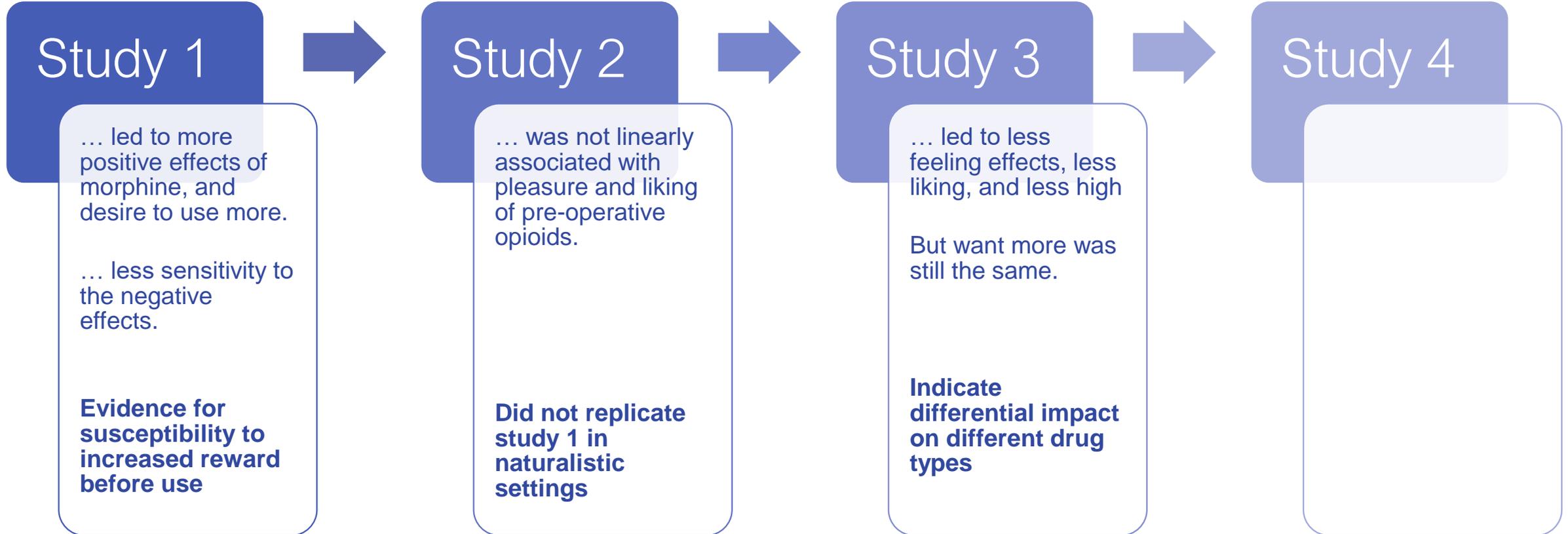
Study 3: Results

Sig 3 x interaction for:



No interaction with CTQ for dislike, or want more

Implications: childhood trauma...



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Clinical study 4



Contents lists available at [ScienceDirect](#)

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres



Cannabis-induced dysphoria/paranoia mediates the link between childhood trauma and psychotic-like experiences in young cannabis users

Molly Carlyle^{a,b,*}, Toby Constable^a, Zoe C Walter^{a,b}, Joanna Wilson^a, Grace Newland^{a,b},
Leanne Hides^{a,b}

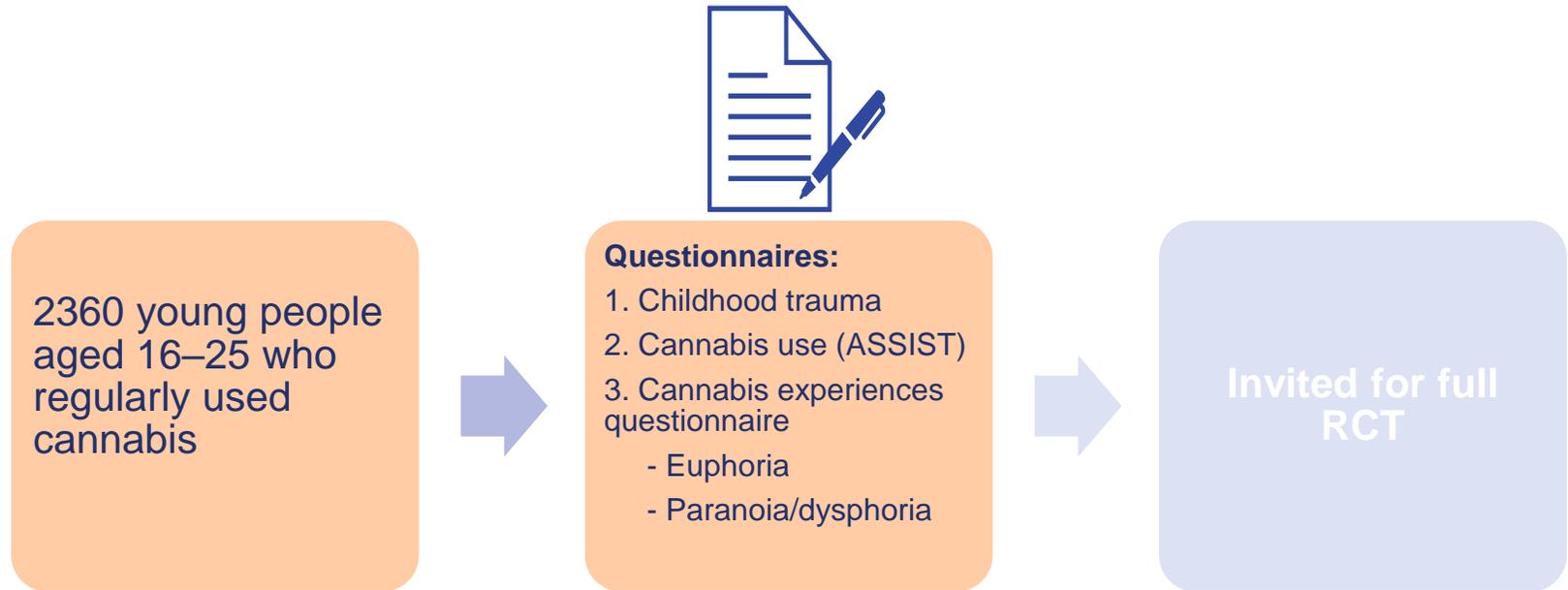
^a Lives Lived Well research group, School of Psychology, Faculty of Health and Behavioural Sciences, University of Queensland, Brisbane, Australia

^b National Centre for Youth Substance Use Research, Faculty of Health and Behavioural Sciences, University of Queensland, Brisbane, Australia

A Web-Based Program for Cannabis Use and Psychotic Experiences in Young People (Keep It Real): Protocol for a Randomized Controlled Trial

Leanne Hides¹ ; Amanda Baker² ; Melissa Norberg³ ;
Jan Copeland⁴ ; Catherine Quinn¹ ; Zoe Walter¹ ; Janni Leung¹ ;
Stoyan R Stoyanov¹ ; David Kavanagh^{5,6} 

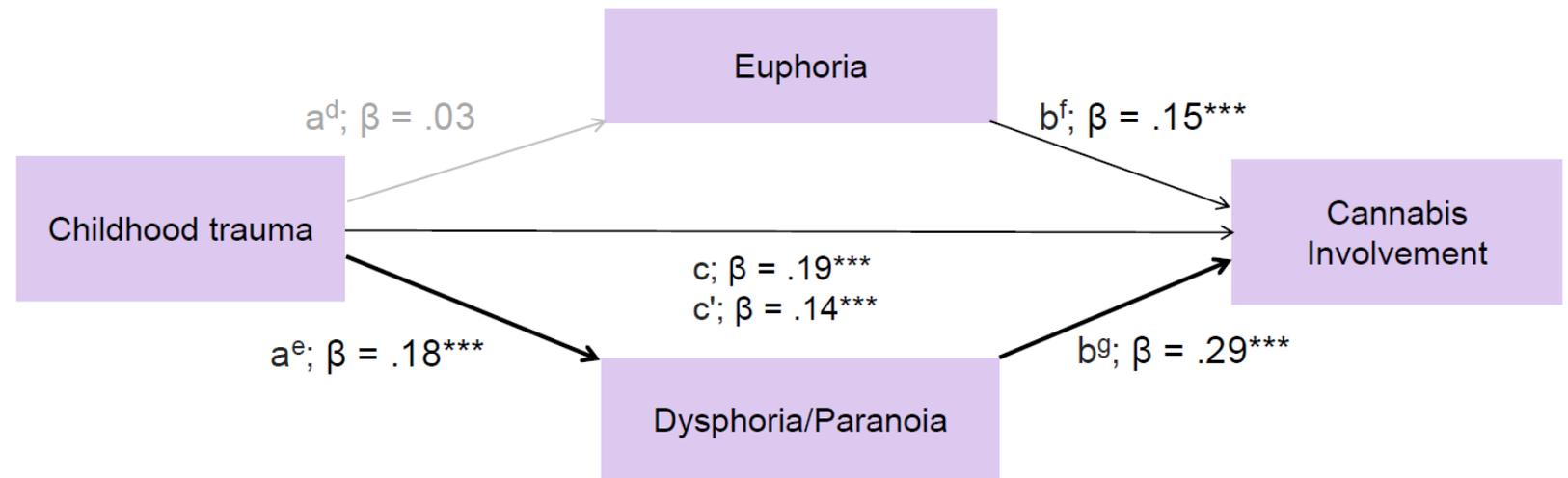
Study 4 methods



Questions:

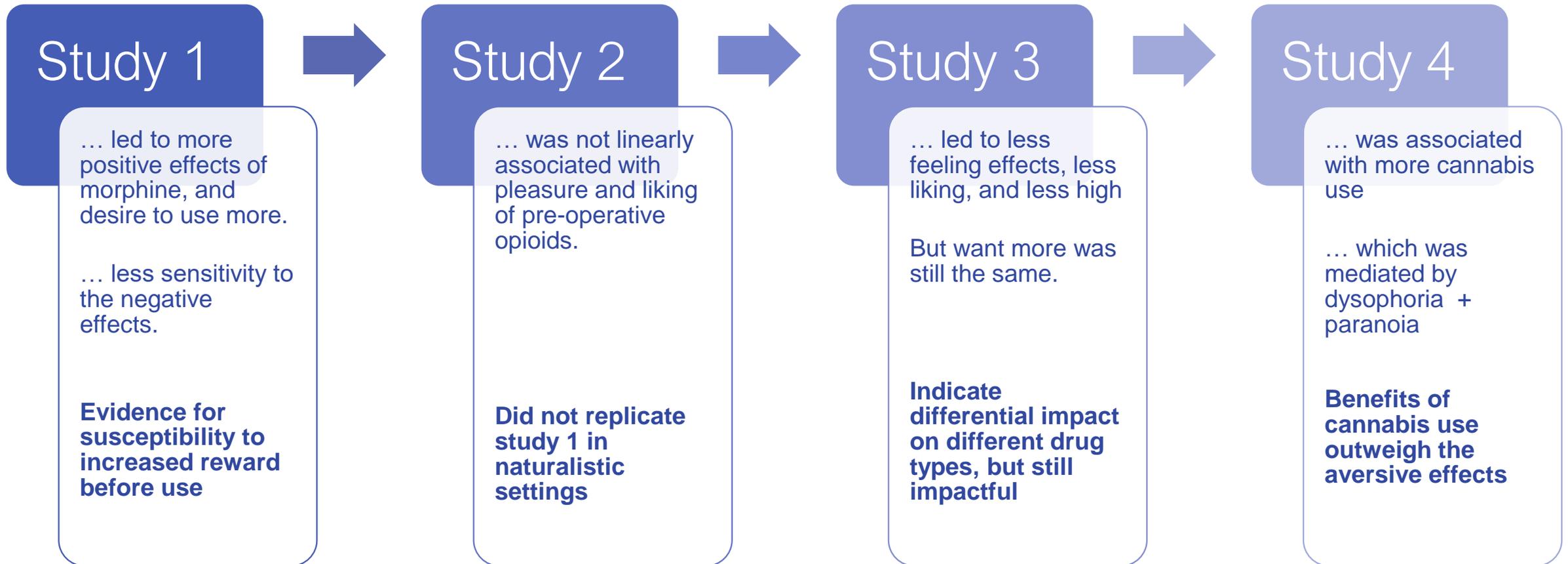
1. Is childhood trauma associated with more cannabis use?
2. Is this mediated by more positive subjective effects (i.e. euphoria)?

Findings: Subjective effects



- Age M = 19.24 years, 1332 (50.6%) female
- Cannabis involvement M = 16.95 (10.42) (moderate risk)
- Moderate risk for tobacco (low for all other drugs)
- Depression avg 9.10 (7.46) - (mild)
- Anxiety avg. 6.35 (5.91) - (mild)

Implications: childhood trauma...



Why is this all important?

Theoretical + clinical contributions

Supports childhood trauma as aetiological risk

Targeted transdiagnostically in preventions and interventions

Treatments that focus on increasing other pleasurable experiences e.g., social connection?

Provides important link between preclinical and clinical research

Medically – possible intersection with acute stress?

Destigmatizing for people with substance use problems

Considerations:

- Participants in these studies + resilience
- Whether this longitudinally is linked to use
- Associations with other outcomes

Study 1

University of Exeter

Prof Celia Morgan
Dr Rupert Broomby
Dr Graham Simpson

PARC and CRF research teams



Funding: University of Exeter

Study 2

University of Oslo

Prof Siri Leknes
Ms Malin Kvande
Dr Marie Eikemo
Dr Isabell Meier
Dr Gernot Ernst
Ms Kaja Buen

Rest of LABlab team

Funding: Norwegian Health Authority and European Research Council under the European Union's Horizon 2020 research and innovation programme

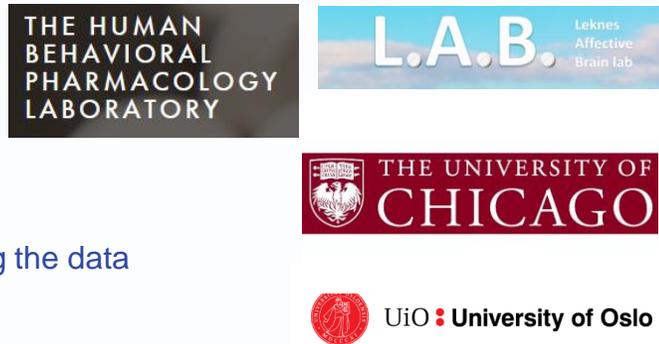


Study 3

University of Oslo & University of Chicago

Prof Harriet de Wit
Prof Siri Leknes

HBPL team involved in collecting the data



Funding: No specific for this secondary analysis (funding was connected to each individual study). M Carlyle's position (who is conducting the analyses) is funded on the ERC grant awarded to LABlab at UiO.

Study 4

University of Queensland

Prof Leanne Hides
Dr Zoe Walter

UQ Lives Lived Well team

Funding: the Australian Government Department of Health awarded to the National Centre for Youth Substance Use Research (NCYSUR) under the Drug and Alcohol Prevention Program.



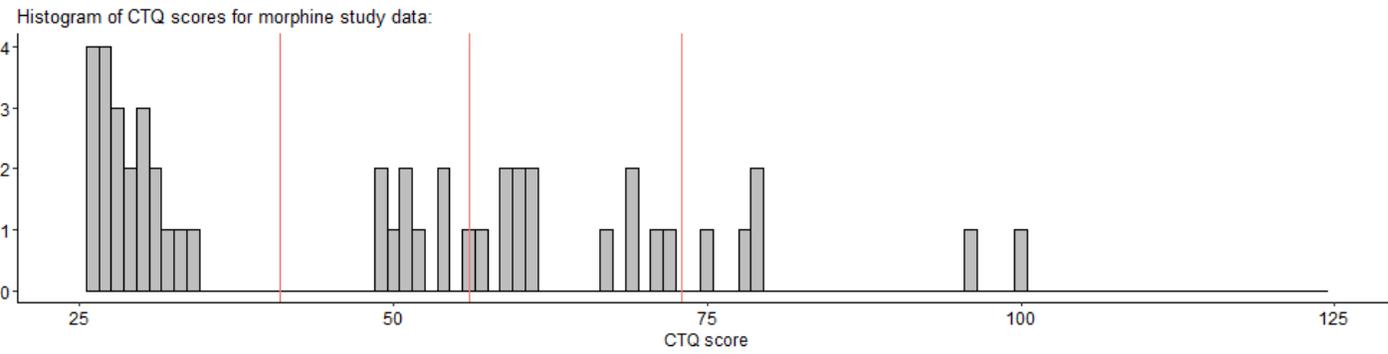


Thank you

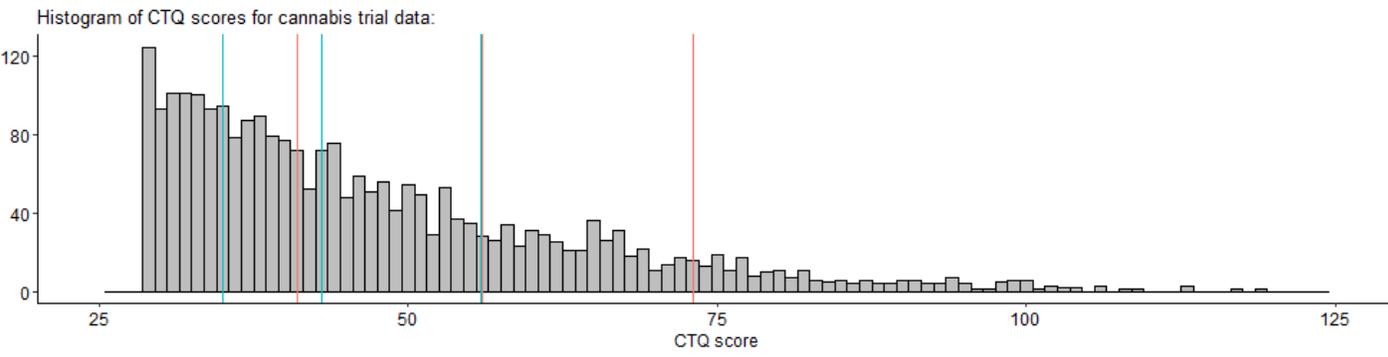
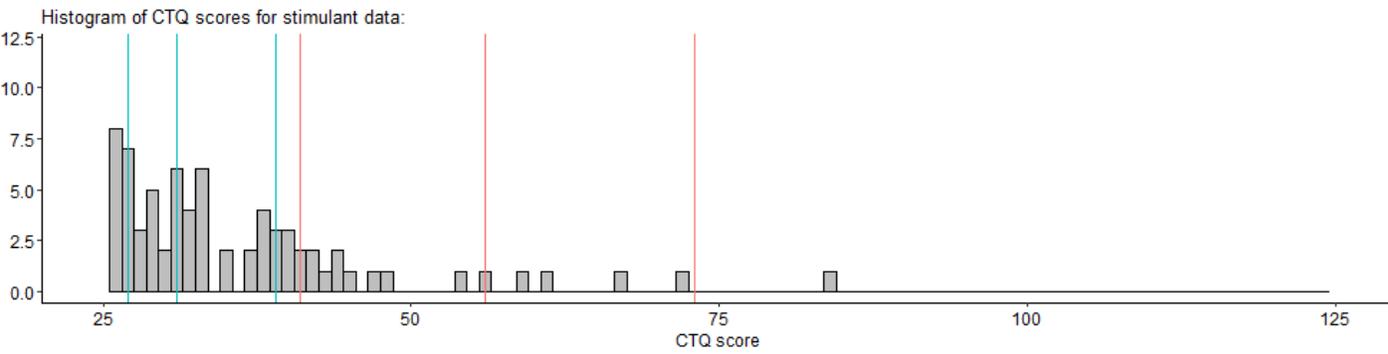
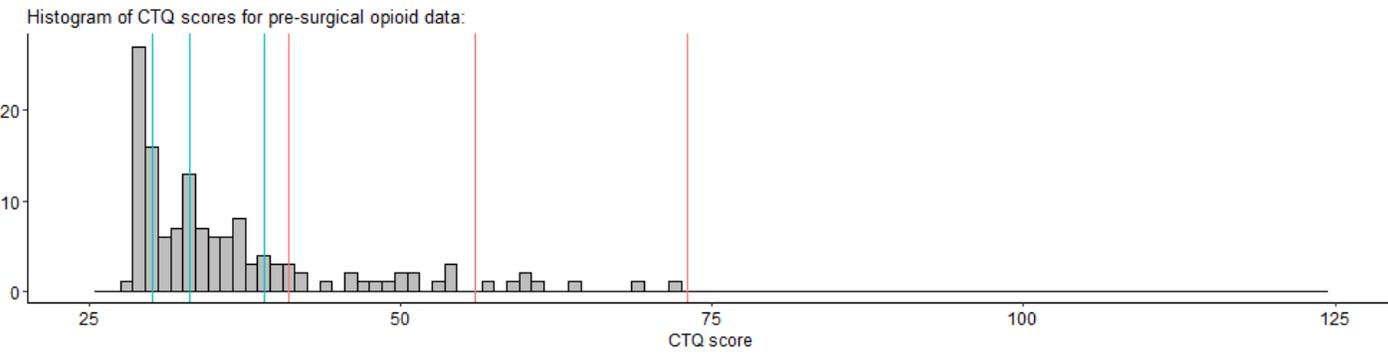
Molly Carlyle

molly.carlyle@psykologi.uio.no

Twitter: @drmollycarlyle



None: 25 – 40
 Low: 41 – 55
 Moderate: 56 – 72
 Severe: 73 – 125



Implications: childhood trauma...

Study 1

... led to more positive effects of morphine, and desire to use more.

... less sensitivity to the negative effects.

Evidence for susceptibility to increased reward before use

Experimental settings, healthy volunteers.

Stratified by trauma history (none, severe).

Study 2

No linear relationship between childhood trauma with pleasure and liking of pre-operative opioids.

Did not replicate study 1 in naturalistic settings

Only for none, low, and moderate childhood trauma.

Naturalistic study in patients, with opioids delivered as routine care.

CTQ on a continuous scale.

Study 3

Greater childhood trauma – less feeling effects of stimulants, less liking, and less high

But want more is still the same.

Greater mood fluctuations, or ADHD symptoms

Experimental settings, healthy volunteers.

CTQ continuously measured.

Study 4

Childhood trauma associated with more adverse effects, which in turn was associated with more use

No association with CTQ and positive effects.

Benefits of cannabis use after trauma outweigh the aversive subjective effects?

Retrospective and cross sectional.