



TREATMENT INNOVATION

CHAIR: CAROLINE LONG

1. Guanfacine extended-release randomised controlled trial for adolescents with cannabis use: The GRACE study
2. Approach bias modification during alcohol withdrawal treatment increases duration of post-discharge abstinence
3. The Windana Health and Healing Program, a holistic complementary treatment approach, unique to Windana

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Guanfacine extended-release randomised controlled trial for adolescents with cannabis use: The GRACE study

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YSAS

YOUTH SUPPORT + ADVOCACY SERVICE



grace

Guanfacine extended-release Randomised controlled trial for Adolescents with Cannabis use: The GRACE Study

Emily Karanges, Aji Akintola, Andrew Bruun, Jacqui Sundbery, Gillinder Bedi

We acknowledge the Traditional Custodians of the land on which we meet today and pay our respects to Elders past and present. We extend that respect to Aboriginal and Torres Strait Islander peoples here today.



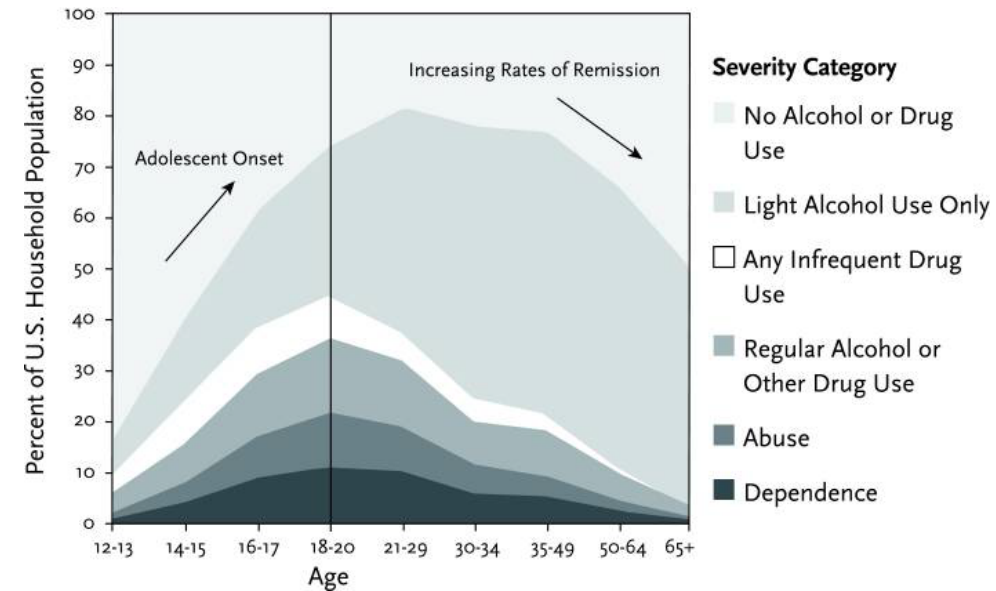
DISCLOSURE STATEMENT

The authors have no conflicts of interest to declare. No pharmaceutical grants were received towards development or implementation of this study.

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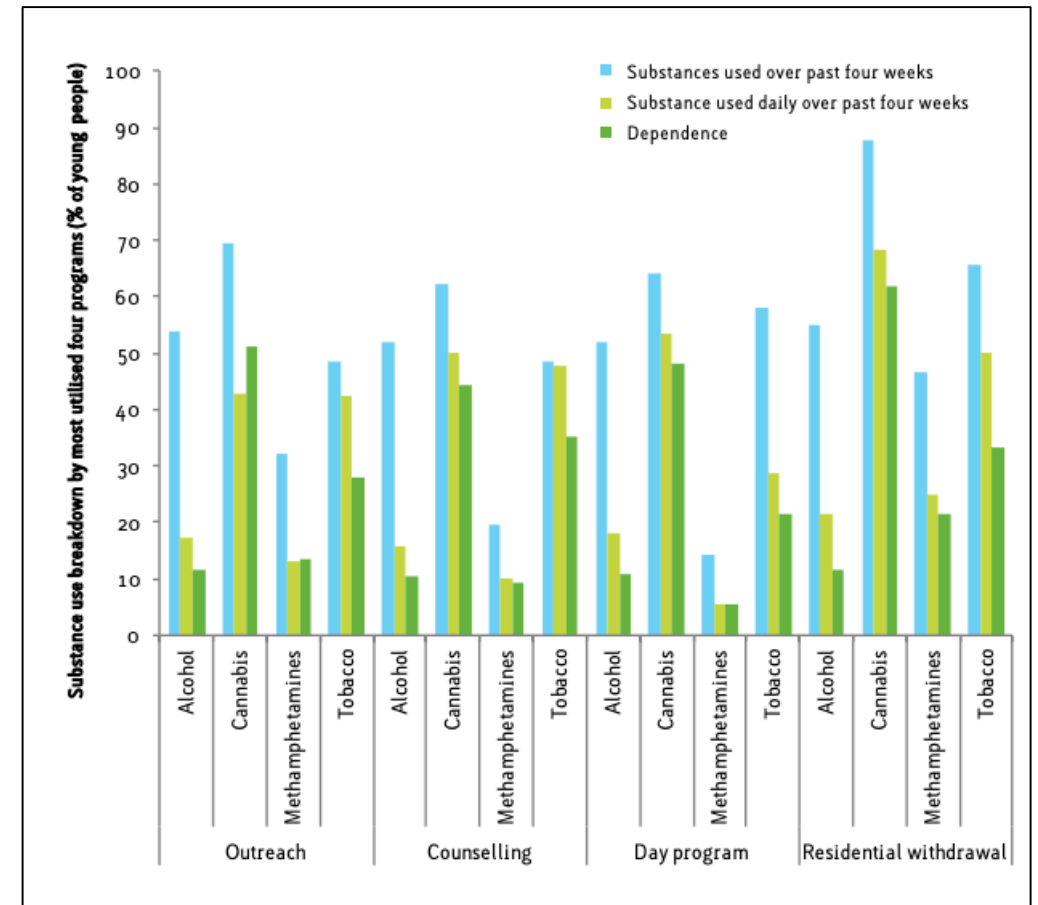
SUBSTANCE USE IN YOUTH

- Most substance use starts in adolescence
AIHW, 2017
- Peak onset of substance use disorders 18-20 years old
Dennis & Scott, 2007
- Some evidence outcomes improved by early treatment
Dennis et al, 2005
- Ideally, intervention at the earliest possible stage



CANNABIS USE IN YOUTH

- Cannabis – also onsets in adolescence
- Risk of harms to social & neurobiological development Hurd et al, 2014
- Early onset – marker for poor outcome Fischer et al, 2017
- 61% presentations to youth AOD services in Australia – cannabis use AIHW, 2020
- Most common substance used daily/dependence – all types of Victorian AOD services YSAS Youth Needs Census, 2018



CANNABIS USE DISORDER

- Cannabis use disorder (CUD):
 - Problems controlling use
 - Use despite negative consequences
 - Tolerance and/or withdrawal symptoms
- CUD – largest contributor to cannabis-attributable burden of disease

Imtiaz et al, 2016

- 9-30% of those who use cannabis develop CUD Hasin et al, 2015
- No approved pharmacotherapies Bedi et al, 2013

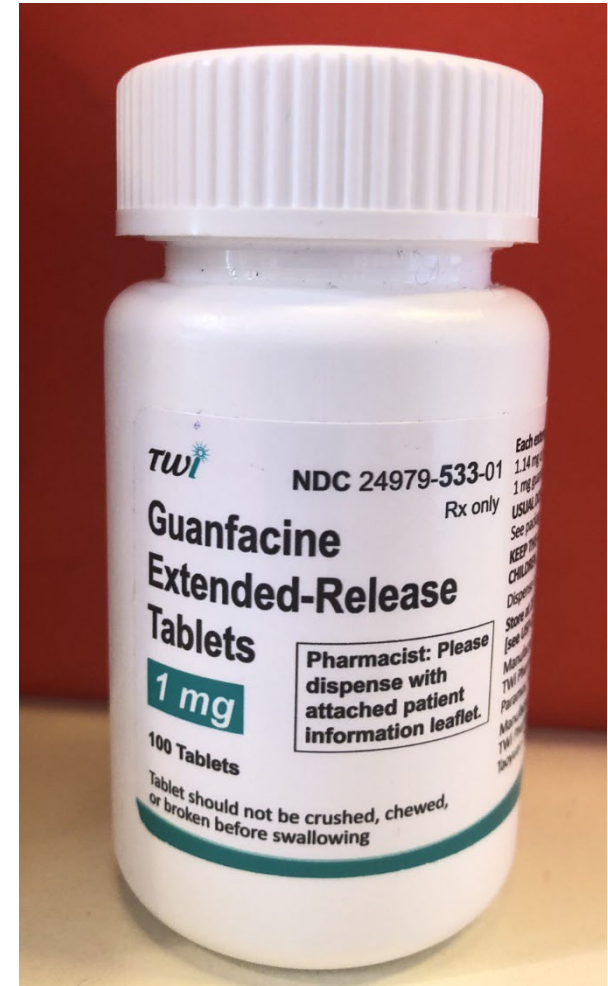
PHARMACOTHERAPY IN SUBSTANCE USE TREATMENT

- Opioid, alcohol, and nicotine use – key part of treatment Ray et al, 2020
- Best practice – combined pharmacotherapy & psychosocial where possible Ray et al, 2020
- Medications – bolster effects of, and engagement with psychosocial treatments – provide SPACE



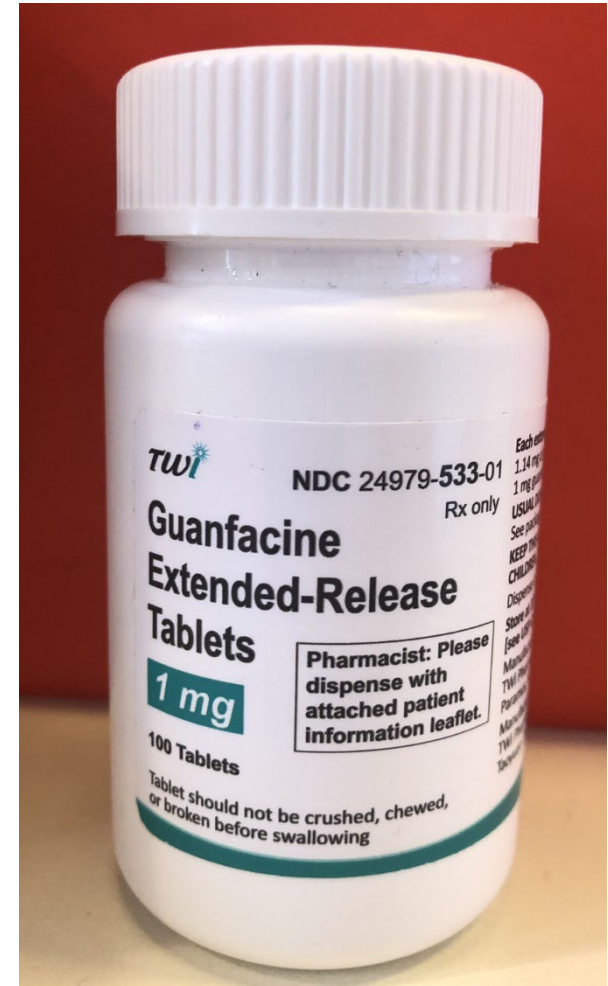
CANDIDATE FOR CANNABIS USE DISORDER

- Guanfacine extended-release (XR)
- Alpha 2A noradrenergic receptor agonist
- Guanfacine immediate-release (IR) – for hypertension
- Extended release – TGA registered in Australia for ADHD in children and adolescents
- Non-stimulant – 2nd line treatment for ADHD



NEW CANDIDATE FOR CANNABIS USE DISORDER

- ↑ attention and impulse control
- Well characterized and safe in young people
- IR – ↓ irritability and ↑ sleep during cannabis withdrawal Haney et al, 2019
- ER – 1 small open-label study in adults with CUD Dakwar et al 2019
- ER – never tested for CUD in young people



GRACE: Guanfacine extended-release Randomised controlled trial for Adolescents with Cannabis use

- Double-blind randomised controlled trial
- N = 100, young people (12-25 years old) with moderate to severe cannabis use disorder
- Recruited via YSAS AOD services

GRACE MEDICATION PROTOCOL

- Approx 12 Weeks Guanfacine XR or placebo plus Treatment As Usual

Week	A1	A2	A3	B1 - B2	C1	C2	C3	C4	C5	C6	C7
Phase	Phase A			Phase B	Phase C						
Description	Up-titration			Residential	Outpatient Maintenance and Main Endpoint				Taper		
Guanfacine XR dose†	1 mg	2 mg	3 mg	4 mg	4 mg				3 mg	2 mg	1 mg

GRACE

Primary Aim: Efficacy of guanfacine XR (4mg target dose)

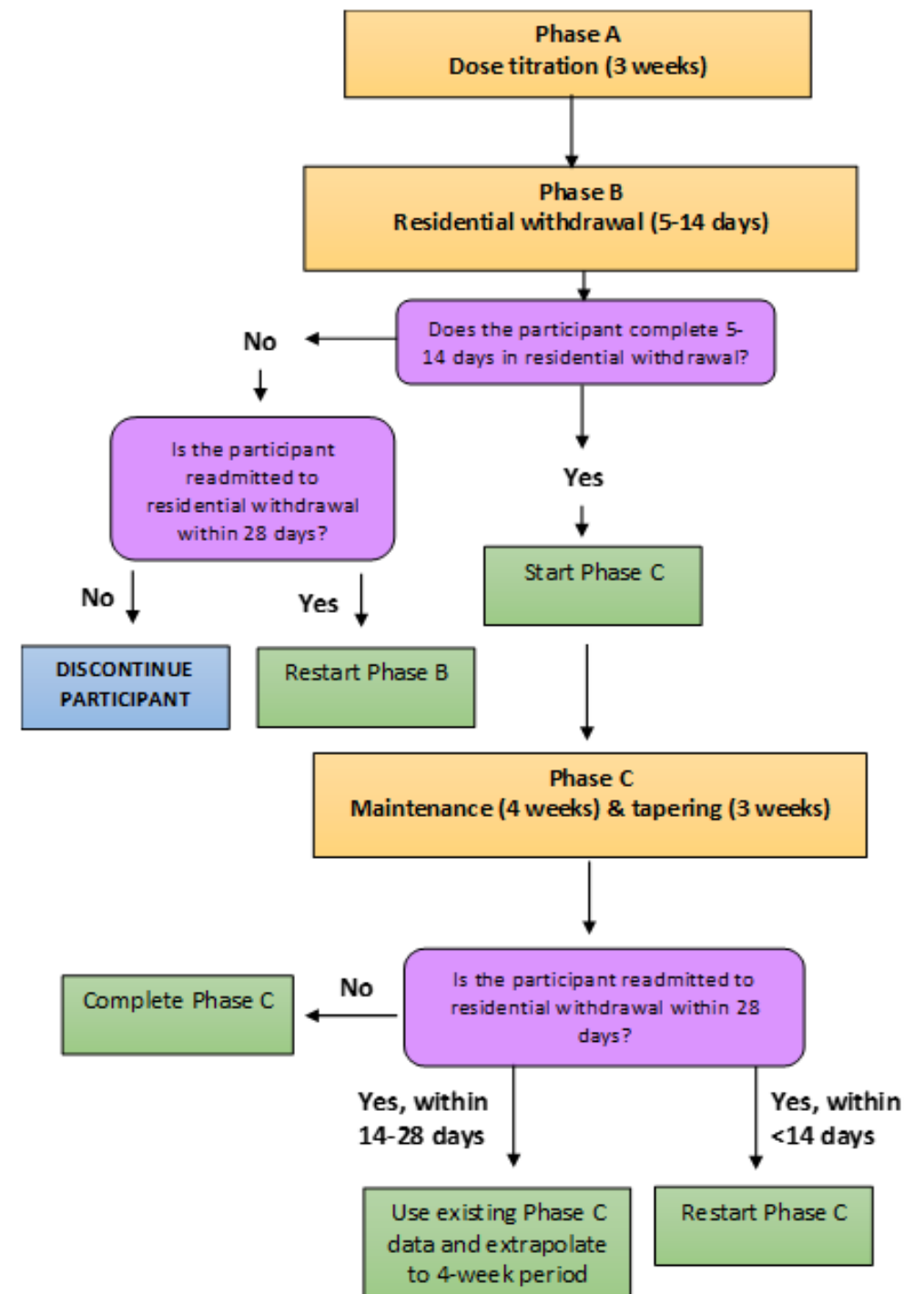
- Change from baseline in cannabis use frequency during 4-week period after from residential withdrawal (Phase C)

Secondary Aims:

- Withdrawal symptoms during residential treatment
- Change from baseline in cannabis use problems endorsed and daily function at end of treatment visit
- Number of positive weekly urine toxicology tests between Weeks 0 and end of treatment visit
- Treatment engagement – number of counselling sessions

FLEXIBLE DESIGN

- Young people have varying treatment needs
- GRACE can accommodate varying lengths of stay in the residential withdrawal unit (ranging from 5-14 days) and up to 2 admissions



SAFETY AND ETHICAL CONSIDERATIONS

- Previous pilot studies – reduction of cannabis withdrawal symptoms and supported tolerability, safety and efficacy Haney et al, 2019
- Guanfacine dosage is low and can be titrated up or down
- Regular reviews with study doctor to assess any issues with medication
- If not tolerated, stop before target dose
- Peer research assistant – resource for young people

PROGRESS – START-UP

- Staff hired
- IP contract signed, medication manufacture in progress
- Ethics pending
- Governance pending
- Extensive collaborative work – Orygen researchers and YSAS management and staff to plan implementation
- Recruitment start – early March

SUMMARY AND CONCLUSIONS

- Pharmacotherapies for CUD – needed
- Intervention in young people – reduce longer-term impacts
- Guanfacine XR – promising candidate
- GRACE – example of collaborative process between treatment and research organisations
- Watch this space!

**REVOLUTION
IN MIND** *ory
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THANK YOU

