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## Background

Methamphetamine use disorder is a significant public health concern in Australia and internationally. There are no TGA approved pharmacotherapies for methamphetamine use disorder.

The Tina Trial is testing whether mirtazapine, an antidepressant medication, will help people reduce their methamphetamine use.

## Aim

The aim of this clinical trial is to assess whether take-home oral mirtazapine can be used safely and effectively in routine clinical care to help people with a methamphetamine use disorder reduce their methamphetamine use.

We hypothesise that 12 weeks of take-home oral mirtazapine treatment (30 mg/day) will reduce methamphetamine use, reduce depressive symptoms, improve sleep, improve quality of life, and reduce HIV risk, relative to placebo.

## Methods

**Design:** A multi-site randomised double-blind placebo-controlled trial (Figure 1).

**Registration:** ACTRN12622000235707

**Target population:** 340 participants aged 18-65 years, who are currently using methamphetamine and meet DSM 5 criteria for a moderate to severe methamphetamine use disorder.

**Exclusions:** Taking antidepressants, pregnancy, a past year suicide attempt, contraindications for mirtazapine.

**Setting:** Alcohol and other drug services in Geelong, Wollongong, Brisbane, Perth, Adelaide and Townsville.

**Intervention:** Participants will be randomly assigned to receive either 12 weeks of take-home oral mirtazapine (30 mg/day) or equivalent placebo.



Figure 2: Medication bottles with MEMS Smartcaps®

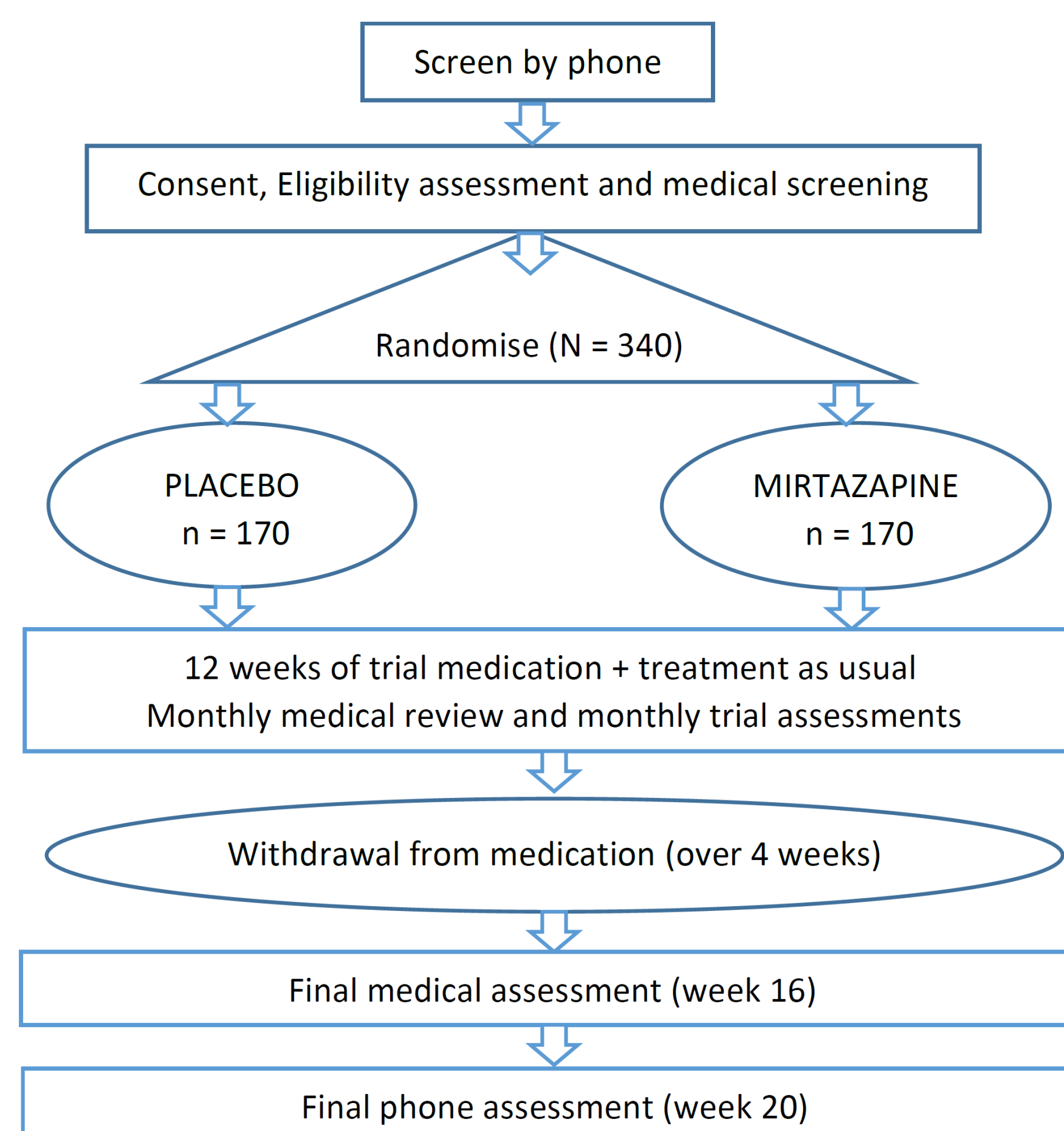


Figure 1: Flow diagram for trial assessments

## Measures

### Primary endpoint:

Self-reported days of methamphetamine use in the 4 weeks prior to week 12, assessed using the Timeline Followback.

### Secondary endpoints:

**Abstinence:** Methamphetamine negative oral fluid samples

**Depression:** Patient Health Questionnaire - 9

**Sleep:** Athens Insomnia Scale

**HIV Risk:** HIV Risk-Taking Behaviour Scale from the Opiate Treatment Index.

**Quality of life:** EuroQOL-5D

### Tertiary endpoints:

Other substance use, suicidality, anxiety, patient impression, medication tolerability, medication adherence (using MEMS Smartcaps®, Figure 2), work productivity, health service use and contact with the criminal justice system.

## Progress

Recruitment for the Tina Trial commenced in November 2022. As of July 31, 2024, 267 participants had been randomised. The follow-up rate over all 10 assessments was 89% (with a follow up rate at week 12 of 87%).

Randomised participants had used methamphetamine on a median of 24 days in the past 4 weeks (IQR 17-28), 45% reported injecting methamphetamine, and 56% had not previously received drug treatment for their methamphetamine use. Almost half (48%) had screened positive for major depression on the PHQ-9 (score of 10 or greater).

## Implications

If mirtazapine is found to be safe and effective, the trial will provide evidence to support methamphetamine use disorder being included as one of the indicated uses for mirtazapine. This may allow mirtazapine to be prescribed as a PBS Schedule 4 medication for methamphetamine use disorder, providing a potentially scalable and relatively low-cost intervention



## References

- [1] Colfax GN, Santos GM, Das M, Santos DM, Matheson T, Gasper J, Shoptaw S, Vittinghoff E. Mirtazapine to reduce methamphetamine use: A randomized controlled trial. *Archives of General Psychiatry* 2011;68:1168-75
- [2] Coffin PO, Santos GM, Hern J, Vittinghoff E, Walker JE, Matheson T, Santos D, Colfax G, Batki SL. Effects of Mirtazapine for Methamphetamine Use Disorder Among Cisgender Men and Transgender Women Who Have Sex With Men: A Placebo-Controlled Randomized Clinical Trial. *JAMA psychiatry* 2019