A STUDY PROTOCOL FOR THE N-ICE TRIAL: A RANDOMISED DOUBLE-BLIND PLACEBO-CONTROLLED STUDY OF THE SAFETY AND EFFICACY OF N-ACETYL-CYSTEINE (NAC) AS A PHARMACOTHERAPY FOR METHAMPHETAMINE ("ICE") DEPENDENCE

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Introduction and Aims: There are currently no approved pharmacotherapies to manage methamphetamine dependence. N-acetyl-cysteine (NAC) has been found to reduce craving for methamphetamine and other drugs, but effects on methamphetamine use and other clinically related endpoints are uncertain. The N-ICE trial is evaluating the safety and efficacy of NAC as a take-home pharmacotherapy for methamphetamine dependence.

Design and Methods: This is a two-arm, parallel, double-blind, placebo-controlled, three-site, randomised (ratio 1:1) trial being conducted in Melbourne, Geelong and Wollongong. Participants (N = 180; 60 per site) will receive either 2,400 mg oral NAC or matched placebo, delivered as a take-home medication for 12 weeks (2 x 600 mg capsules, taken morning and evening). Adherence is being monitored using eCAP™ medication bottle lids which record the date and time of bottle opening. The primary outcome measure is methamphetamine use during the 12-week trial medication period measured as (a) days of use, assessed using the Timeline Followback, and (b) methamphetamine-positive saliva tests, taken weekly. Secondary measures include methamphetamine craving, severity of dependence, withdrawal symptoms, and psychiatric symptoms (depression, suicidality, psychotic symptoms and hostility).

Results: 81 participants have been randomised as at May 2019.

Discussions and Conclusions: The N-ICE trial is the first controlled clinical trial to assess whether NAC can reduce methamphetamine use. It will provide a platform for understanding

the potential utility of NAC in managing methamphetamine dependence and clinically related outcomes. If found to be effective, take-home NAC could provide a potentially scalable and affordable pharmacotherapy option for methamphetamine dependence.

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