An open-label pilot study of oral naltrexone-bupropion combination pharmacotherapy for the treatment of methamphetamine use disorder (the NABU trial)

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Presented by
Dr Krista Siefried
Associate Investigator
National Centre for Clinical Research on Emerging Drugs (NCCRED)
St Vincent's Hospital Sydney
National Drug and Alcohol Research Centre, University of New South Wales
NSW Drug and Alcohol Clinical Research and Improvement Network

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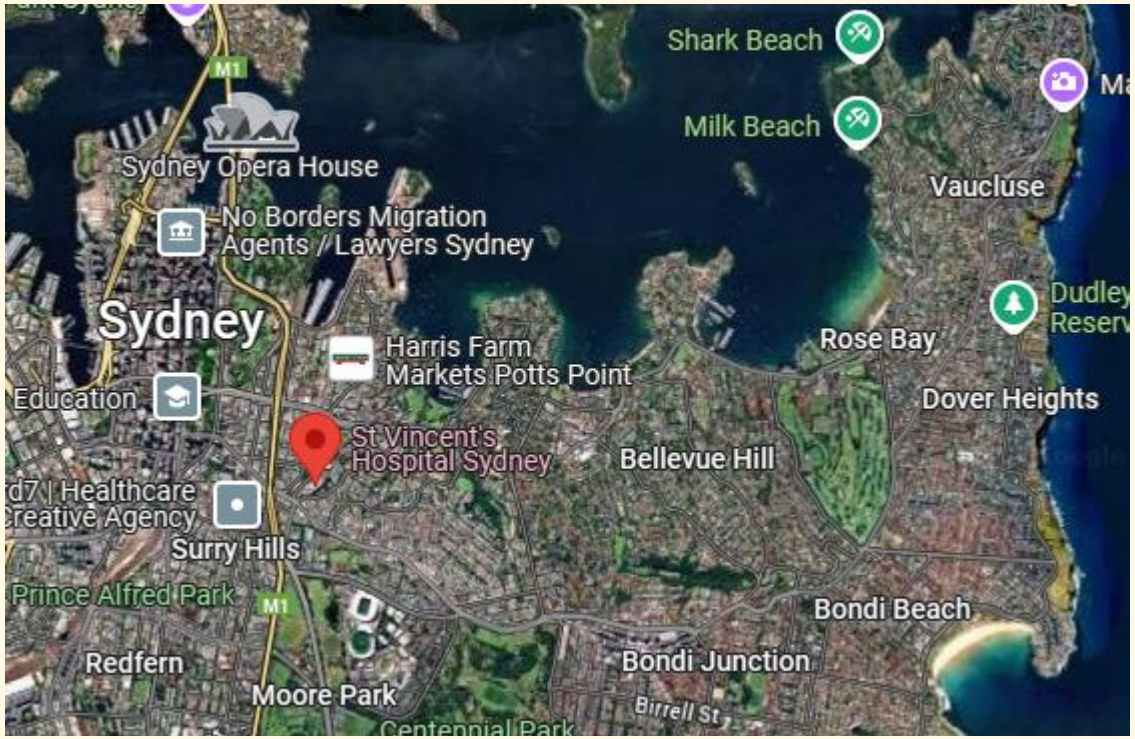
Study Team

Investigators

- Prof Nadine Ezard
- Dr Krista Siefried
- Dr Liam Acheson
- Prof Adrian Dunlop
- Prof Nicholas Lintzeris
- Prof Paul Haber
- Dr Brendan Clifford
- Dr Michael Christmass
- Prof Jonathan Brett
- Dr Carl Moller
- Prof Kirsten Morley
- A/Prof Didier Jutras-Aswad
- Prof Madhukar Trivedi
- Prof Steven Shoptaw

Study Coordinators

- Teodora Zanesheva-Karamanlieva
- Lucy Flood
- Arabella McMahon



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Funding and Conflicts

- The NABU trial was funded by the National Centre for Clinical Research on Emerging Drugs (NCCRED)

- NCCRED is funded by the Australian Department of Health, Disability and Aging

- KS is employed by UNSW and SVHS, and has received research funding from the National Health and Medical Research Council (NHMRC) Australia

Acknowledgement

Of Country

I acknowledge that the research that I am presenting took place on Gadigal land of the Eora nations, and recognise the strength and resilience of those people who maintain a continuing connection to the lands and waters in that region – a right and responsibility that was never ceded

Of Lived and Living Experience

I acknowledge the contributions of people with lived and living experience to this project. Through focus group participation, as a consumer investigator, as participants in the trial, and in qualitative interviews, they brought knowledge and wisdom along with a commitment to altruism through research

Study design

- **PRIMARY AIM**
  - To determine safety and feasibility of orally administered naltrexone-bupropion combination pharmacotherapy over 12 weeks in adults seeking treatment for methamphetamine use disorder

Feasibility

- Time taken to recruit sample
  - March – August 2024: 20 weeks
  - Including screen fails >1 participant per week
  - Comparable to other study enrolment rates[1]
- Proportion ineligible
  - 183 expressions of interest
  - 74 individuals pre-screened by telephone
  - 24 individuals formally screened for eligibility = 83% eligible to enrol
    - Screen failures included one individual not proceeding, all others (3/4, 75%) were drug use related (too little methamphetamine, too much (any!) opioids)
- Retention in study
  - 15 (75%) received all study medication to primary endpoint
  - 13 (65%) completed follow-up visit at Day 112 (week 16)
- Medication adherence
  - Pill counts were nearly impossible to assess – due to lack of returns; however for those that returned webster packs adherence ranged from 65% to 100% by pill count
  - SMAQ adherence averaged 34% across study visits; however on the single item *days missed* adherence was >80% among more than 60% across all study visits

1. Siefried et al, CNS Drugs 2020

Safety

- Treatment emergent adverse events
  - There were 93 AE's reported in 19 participants (95%)
  - One (1.1%) was classified serious
    - Hospitalisation for methamphetamine withdrawal, unrelated to study medication
  - One AE resulted in a participant withdrawing from the study medication
    - Participant reported that the study medication resulted in lethargy, and that when the medication was ceased the lethargy resolved
  - Most commonly reported AE's across the study
    - Nausea (reported by n=14 [70%])
    - Vivid dreams (reported by n=4 [20%])
  - Only n=1 (5%) had an adverse event of weight loss

1. Siefried et al, CNS Drugs 2020

Discussion

1. Naltrexone and bupropion were safe in this population
   - While one AE (lethargy) led to withdrawal from study medication, the IP was largely tolerated by participants
2. The study procedures were feasible
   - However, adherence data are unreliable given the missed opportunities for pill counts (not returning webster packs) and incomplete SMAQ data across study visits
   - EMA data collected by smartphone are pending, and may provide further adherence data from daily measures
   - Adherence was greater in the US RCT, ? given that one agent was given by 3-weekly injections
3. The study was small
   - While pilot study implementation is useful to evaluate study design including outcomes and measures they are unable to provide signals for efficacy or effectiveness
   - Further, randomised controlled data would be required
4. Future work required
   - Should take into account the qualitative data participants provided in this study, under analysis

Thank You

krista.siefried@svha.org.au

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