

Treatment Outcomes and Measures in Clinical Trials of Pharmacotherapy for Methamphetamine Dependence

Krista J Siefried^{1,2,3}; Liam Acheson^{1,2,3}; Nick Lintzeris^{4,5,6};
Nadine Ezard^{1,2,3,6}

¹ National Centre for Clinical Research on Emerging Drugs (NCCRED); ² National Centre for Drug and Alcohol Research (NDARC); ³ St Vincent's Hospital Drug and Alcohol Service; ⁴ South Eastern Sydney Local Health District (SESLHD); ⁵ University of Sydney Central Clinical School Department of Addiction Medicine; ⁶ Drug and Alcohol Clinical Research and Improvement Network (DACRIN)

Conflicts of Interest

- KJS has no competing interests to declare
- LA is an NDARC Scholarship holder; and recipient of a Government of Australia RTP
- NL has received research funding from Camurus, and has served on Advisory Boards for Mundipharma, Camurus and Indivior
- NE has no competing interests to declare
- This study was funded by NCCRED, NCCRED is funded by the Australian Department of Health

NCCRED

Background

- A health outcome is a 'change in the health of an individual or group of people which is attributable to an intervention or series of interventions' ^{1,2}
- The ICHOM Standard Set for Addiction was only recently developed, listing outcomes and measures – very broad focus; various SUD's and other (e.g. gambling, internet) ³
- The US National Institute on Drug Abuse (NIDA) Clinical Trials Network has a list of Common Data Elements ⁴
- The use of consistent outcomes and measures could increase data sharing, capacity to meta-analyse across datasets, improving study power and generalisability



Methods

- We conducted a **systematic review** of studies examining a **pharmacotherapy** of **amphetamine/methamphetamine** use disorder / dependence
 - Studies from all time points to June 2019, published in English
 - RCTs of at least one pharmacotherapy
 - Studies were evaluated for design, methodology, eligibility criteria, sample size, pharmacological and if included psychosocial interventions, length of follow-up and follow-up schedules, outcome variables and measures, results, overall conclusions and risk of bias
 - **Outcomes** were any reported impact of treatment related to amphetamine/methamphetamine use (**measures** were how the study assessed outcomes)

Results

Studies included:

- 43 studies
- Collectively enrolled 4,065 participants
- Reported on 23 pharmacotherapies (alone / combination)

Outcomes and Measures

- 55 primary outcome measures were used 93 times
 - Some studies included multiple primary outcomes
- Disparate outcomes prevented meta-analyses
- 75 distinct secondary outcomes (inclusive of variations)
 - Used 158 times
 - Often used/defined differently to the primary outcomes of the same domain

Results

The most common primary outcome measures reported were:

- **Abstinence (51 times, 55%)**
 - Urine drug screens (UDS) (41 times, 80%)
 - UDS were analysed or results defined 16 different ways
 - Most commonly: weekly proportion of AMPH/MA-free UDS; or overall proportion of AMPH/MA-free UDS
- **Craving (10 times, 11%)**
 - Predominantly measured using a visual analogue scale (VAS)
 - Craving was also the most commonly measured secondary outcome

Results

Example of an outcome - adherence to study drug - and the various ways of measuring:

- Self-report
- Pill count
 - Direct counts or averages
- Staff administered doses
- MEMS caps
- Study drug / metabolite in urine or blood

In studies using more than one method of measurement, low concordance in results

NCCRED

Discussion

- In the studies reviewed, completion rates were low
 - Proportion of participants who did not complete the protocol was 38.4% of those randomised
- Lack of consistent outcomes or measurement methods prevented meta-analyses of results
 - And, no standardized approach meant important results such as safety were sporadically reported
- Outcomes were not always patient-centered
 - Abstinence versus reduction in use
- Disparate outcomes/measures also used to determine eligibility
- Current program of work attempting to include some of the most common outcomes and measures (see *Acheson et al*)
- Study published, table presented on the NCCRED website

Conclusions

- Harmonisation of outcomes / measures to produce results that can be synthesised by meta-analyses should be a sector-wide imperative, to ensure better research synthesis
- Reduction in MA/AMPH use should be required for assessment of efficacy (e.g. moving away from binary abstinence definitions)
- Reliance on extended periods of 'abstinence' as a primary endpoint does not always reflect participant treatment goals and is a somewhat insensitive marker of clinically meaningful change in substance use
- Further work is required to determine outcomes that are both clinically meaningful and meaningful to consumers

Thank You

For further information:

Siefried KJ, Acheson LS, Lintzeris N, Ezard N. *Pharmacological treatment of methamphetamine/amphetamine dependence: a systematic review*. CNS Drugs (2020) 34:337-365

<https://nccred.org.au/translate/methamphetamine-clinical-resources/outcome-measures/>

+61 9065 7808

Krista.Siefried@svha.org.au