

EVALUATING THE EFFECTIVENESS OF TREATMENTS FOR OPIOID USE DISORDER BASED ON RECOVERY OUTCOMES

HOW TO BRIDGE THE DISCONNECT BETWEEN CLINICAL TRIAL AND RECOVERY OUTCOMES?

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OBJECTIVES

Opioid use disorder (OUD) is a chronic illness, and the ultimate treatment goal is recovery. However, evaluating the effectiveness of OUD treatment is a challenge, as clinical trials typically do not follow patients long enough to capture important recovery outcomes. This research aimed to synthesise published evidence on the relationship between short-term outcomes measured in OUD clinical trials and long-term recovery outcomes.

METHODS

A systematic review of studies investigating the relationship between short- and long-term outcomes of patients with OUD (identified by search terms including OUD, opioid dependence/abuse to reflect diagnoses based on both DSM-5 and DSM-IV) was conducted. The search for studies was not restricted by country or year (up to September 2015) and was performed using the PubMed database and the following conference proceedings: The College on Problems of Drug Dependence¹; Global Addiction Conference²; The International Council on Alcohol, Drugs and Traffic Safety Conference³, International Society for Pharmacoeconomics and Outcomes Research⁴ and The Academy of Managed Care and Pharmacy.⁵

We pre-defined treatment retention, level of illicit opioid use (on-top use), abstinence, cravings and withdrawal, and outcomes that have been used often to demonstrate treatment efficacy in trials as short-term outcomes. The pre-defined long-term recovery outcomes of interest included relapse, mortality, comorbidity, quality of life, crime, diversion, misuse, absenteeism, employment, social integration, caregiver impact and impact on family.

RESULTS

Out of 1,220 relevant records, 89 studies met our criteria for data extraction (Figure 1). These studies covered three short-term outcomes: 1) treatment retention (under a year), 2) on-top use of illicit drugs and 3) abstinence.

There were three outcomes that were part of the screening inclusion criteria but were not identified due to lack of data: 'use of government-provided benefits' (long-term), cravings (short-term) and withdrawal symptoms (short-term). Extracted articles that linked treatment received to a long-term outcome, but did not compare different treatments, were included to gain insight into outcomes studied regardless of whether short-term and long-term outcomes were linked in the study.

As presented in Table 1, many of the studies reviewed followed a sizable population for multiple years (up to 15 years).

Figure 1: PRISMA flow diagram

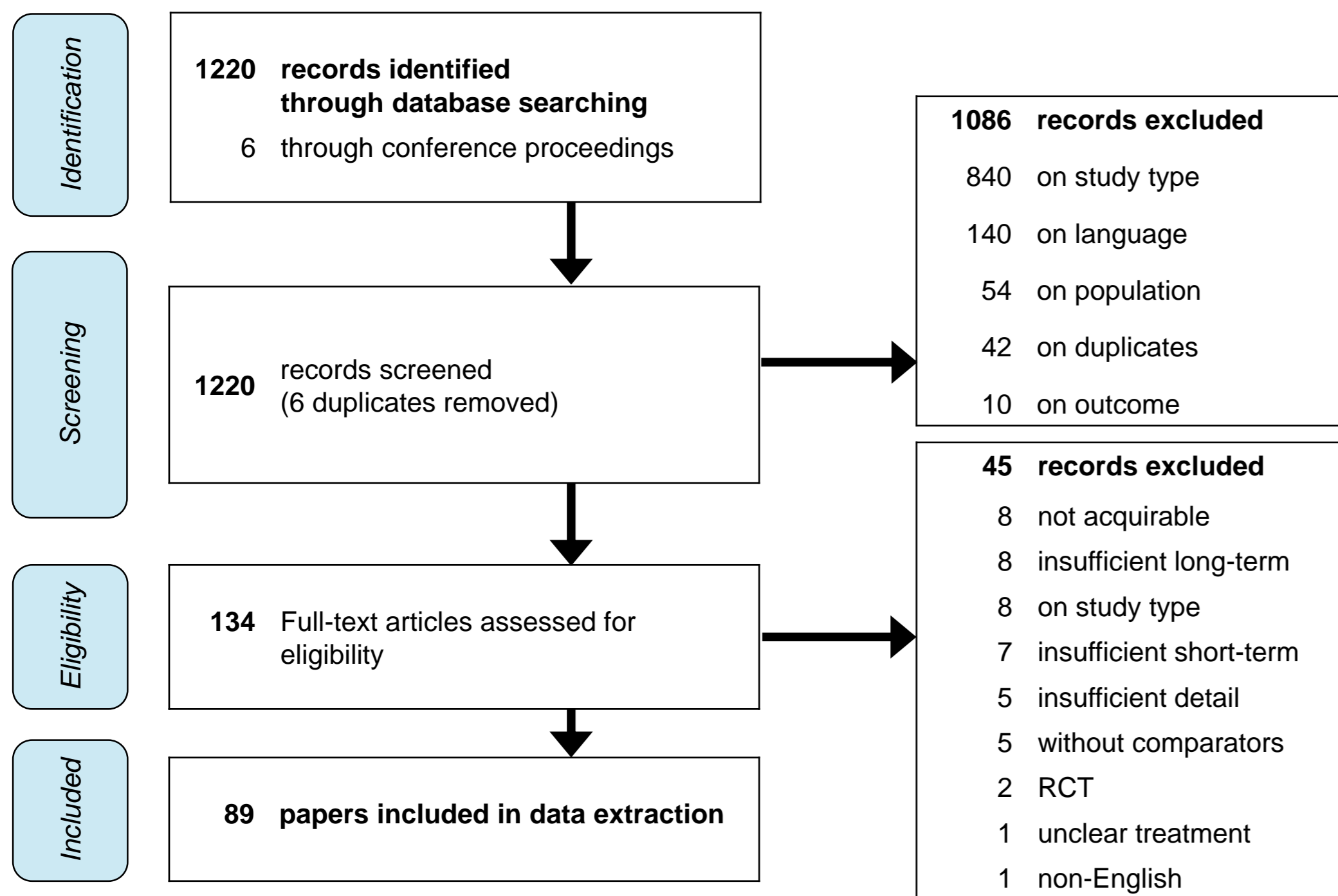


Table 1: Key articles linking short- to long-term outcomes

| Reference | Location | Treatment | Short-term outcome | Long-term outcome | Sample size | Follow-up (months) | Design |
|-------------------------------|----------|-------------------------|--------------------|---|-------------|--------------------|--------------|
| Bovasso 2003 ⁶ | USA | MMT | Illicit drug use | Criminal charges, employment, retention | 222 | 24 | LCS |
| Ohlin ⁷ 2015 | Sweden | BMT | Retention | Criminal convictions, productivity | 148 | 88 | LCS |
| Rounsaville ⁸ 1987 | USA | MMT, DTX, TC, NLX Dfp | Abstinence | Criminal activities, employment | 268 | 30 | LCS |
| Simpson ⁹ 1982 | USA | MMT, TC, Op DTX, Op Dfp | Abstinence | Criminality, productivity | 990 | 72 | LCS |
| Armstrong ¹⁰ 2010 | India | BMT | Retention | Relapse | 2,569 | 12 | LCS |
| Sørensen ¹¹ 2005 | Denmark | N/A | Abstinence | Mortality | 188 | 180 | Registry |
| Li ¹² 2014 | USA | Pharmaco therapies | Abstinence | Mortality | 20,408 | 60 | Data linkage |

Key: BMT, buprenorphine maintenance treatment; Dfp, drug-free program; DTX, detox; LCS, longitudinal cohort study; MMT, methadone maintenance treatment; NLX, naltrexone assisted; Op, outpatient; TC: therapeutic community.

As presented in Table 2, the reviewed studies covered 13 long-term outcomes of interest. The most reported ones in relationship to short-term outcomes are comorbidity, crime, employment, mortality and relapse. Specifically, retention was found to be associated with lower rates of relapse, death, criminal activities, HIV infection, severe depression and unemployment (accordingly, retention was also associated with better quality of life and interpersonal relationships). On-top use was linked to lower long-term retention and employment, increased crime rates, mortality, comorbidity and relapse, while no evidence was found to link cravings and withdrawal symptoms to long-term outcomes.

Table 2: Coverage of short- and long-term links

| Long-term outcomes | Treatment received | Short-term outcomes | | |
|-----------------------|--------------------|---------------------|--------------------|------------|
| | | Retention | Illicit opioid use | Abstinence |
| Mortality | 7 | 4 | 1 | 2 |
| Crime | | 6 | 1 | 3 |
| Comorbidity | 3 | 9 | 1 | 2 |
| Relapse | 2 | 4 | 2 | |
| Employment | | 4 | 1 | 2 |
| Retention (long-term) | 9 | N/A | 1 | |
| Impact on family | 7 | | | |
| Costs | 1 | 1 | | |
| Need for caregivers | 2 | | | |
| Quality of life | 1 | 1 | | |
| Overdose | 2 | | | |
| Social integration | | 1 | | |
| Diversion | 1 | | | |

Notes: 0 studies, white shading; 1 study, light shading; 2-4 studies, medium shading; 5-9 studies, dark shading.

DISCUSSION

Despite an increasing interest in understanding the effect of treatments on OUD patients' long-term recovery trajectory, the volume of studies that link short-term outcomes of OUD treatments to long-term outcomes was found to be small. Furthermore, the identified studies were conducted in a diverse group of countries with different patterns of treatment practices. Therefore, obtaining reliable quantitative estimates on the relationships is challenging.

However, this review yielded some evidence that is sufficiently strong to use in constructing cost-effectiveness models to demonstrate the long-term value of effective OUD treatments. Future research is desired to support qualitative arguments. The following findings are of note:

- Retention in a treatment programme is associated with better outcomes (quantified in a number of studies) for mortality, crime (and associated costs), quality of life, higher employment and better interpersonal relationships. The link with crime is complicated by the possibility that crime is a determinant of retention on programme. Research is needed to estimate the size of the effect while addressing this issue using suitable statistical approaches.
- There is some evidence that retention on buprenorphine maintenance therapy is more effective at reducing mortality than retention on methadone maintenance therapy.¹³
- The importance of supervision of patients on methadone maintenance therapy is highlighted in the literature. Studies demonstrate that both crime and diversion incidence rates are increased when methadone is taken home rather than administered in a supervised environment.
- A treatment that requires less-frequent administration may provide the prospect of direct savings to the healthcare system, but it is necessary for this type of treatment to be able to also ensure adherence to the treatment in order to avoid a higher rate of opioid abuse, crime and diversion.

CONCLUSION

This review identified published studies that confirmed longer treatment retention as being associated with various recovery outcomes. Further studies are warranted to validate such a link and to quantify the effect of OUD treatments on recovery.

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