A consensus approach to opioid substitution treatment outcomes and how they are monitored

Lucas Wiessing PhD, EMCDDA, et al.
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Collaborators

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A public health perspective on OST outcome monitoring

• Opioid use is a main driver of drug-related disease and death globally (~75% of all drug-related Daly’s)

• OST (opioid substitution treatment) is highly effective at reducing health problems and mortality

• OST outcome monitoring should prominently include health and overdose/mortality indicators?
Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies

Luis Sordo,1,2,3 Gregorio Barrio,4 Maria J Bravo,1,2 Icici Indave,1,2 Louisa Degenhardt,5,6 Lucas Wiessing,7 Marica Ferri,7 Roberto Pastor-Barriuso1,2

ABSTRACT

OBJECTIVE
To compare the risk for all cause and overdose mortality in people with opioid dependence during and after substitution treatment with methadone or buprenorphine and to characterise trends in risk of mortality after initiation and cessation of treatment.

DESIGN
Systematic review and meta-analysis.

DATA SOURCES
Medline, Embase, PsycINFO, and LILACS to September 2016.

STUDY SELECTION
Prospective or retrospective cohort studies in people with opioid dependence that reported deaths from all causes or overdose during follow-up periods in and out of opioid substitution treatment with methadone or buprenorphine.

out of buprenorphine treatment (2.20, 1.34 to 3.61). In pooled trend analysis, all cause mortality dropped sharply over the first four weeks of methadone treatment and decreased gradually two weeks after leaving treatment. All cause mortality remained stable during induction and remaining time on buprenorphine treatment. Overdose mortality evolved similarly, with pooled overdose mortality rates of 2.6 and 12.7 per 1000 person years in and out of methadone treatment (unadjusted out-to-in rate ratio 4.80, 2.90 to 7.96) and 1.4 and 4.6 in and out of buprenorphine treatment.

CONCLUSIONS
Retention in methadone and buprenorphine treatment is associated with substantial reductions in the risk for all cause and overdose mortality in people dependent on opioids. The induction phase onto methadone treatment and the time immediately after leaving treatment with both drugs are periods of particularly increased mortality risk which should be dealt with by


Abstract

Our objective was to determine the prevalence and incidence of human immunodeficiency virus (HIV) infection and related risk behaviors among opiate-abusing intravenous drug users (IVDUs) either in or out of methadone treatment. The subjects, 152 in-treatment and 103 out-of-treatment intravenous opiate users, were followed prospectively for 18 months. Behavioral and serologic assessments were made at 6-month intervals, with complete information available on 89% of the sample. Subjects were recruited from a single methadone maintenance program and the surrounding neighborhood in north-central Philadelphia. At baseline, the HIV seroprevalence rate for the total sample was 12%; 10% for the methadone-maintained group and 16% for the out-of-treatment group. Out-of-treatment subjects were injecting drugs, sharing needles, visiting shooting galleries, and practicing unsafe sex at significantly higher rates than in-treatment subjects. Follow-up of HIV-negative subjects over the next 18 months showed conversion rates of 3.5% for those who remained in methadone maintenance versus 22% for those who remained out of treatment. The sixfold difference in rate of seroconversion between the two groups suggests that although rapid transmission of HIV still occurs, opiate-abusing IVDUs who enter methadone treatment are significantly less likely to become infected. In contrast, those opiate addicts who do not enter treatment are at significantly higher risk of contracting and spreading the disease. Implications for developing additional risk interventions for out-of-treatment IVDUs are discussed.

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[Indexed for MEDLINE]
"Healthy" years of life lost (DALYs) attributable to drug use disorders among men and women, 2005 and 2015

Source: Global Burden of Disease Data, Institute for Health Metrics and Evaluation.
Drugs and infectious diseases that produce the highest negative health impact of drug use

### Number of deaths and “healthy” years of life lost (DALYs) attributable to drug use, 2015

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of deaths (thousands) attributable to drug use, 2015</th>
<th>“Healthy” years of life lost (DALYs) (millions) attributable to drug use, 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV/AIDS—tuberculosis</td>
<td></td>
<td>-25.7</td>
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<tr>
<td>HIV/AIDS resulting in other diseases</td>
<td></td>
<td>-3.6</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td></td>
<td>-12.0</td>
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<tr>
<td>Liver cancer resulting from hepatitis C</td>
<td></td>
<td>39.0</td>
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<tr>
<td>Cirrhosis and other chronic liver diseases</td>
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<td>19.0</td>
</tr>
<tr>
<td>resulting from hepatitis C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioid use disorders</td>
<td></td>
<td>29.6</td>
</tr>
<tr>
<td>Cocaine use disorders</td>
<td></td>
<td>49.7</td>
</tr>
<tr>
<td>Amphetamine use disorders</td>
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<td>67.5</td>
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<tr>
<td>Cannabis use disorders</td>
<td></td>
<td></td>
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<tr>
<td>Other drug use disorders</td>
<td></td>
<td>23.0</td>
</tr>
<tr>
<td>Self-harm</td>
<td></td>
<td>2.6</td>
</tr>
</tbody>
</table>

Percentage change from 2005


World Drug Report 2017
SYSTEMATIC REVIEW OF OBSERVATIONAL OST STUDIES
Large variation in measures used to assess outcomes of opioid dependence treatment: A systematic review of longitudinal observational studies

LUCAS WIESSENG, MARICA FERRI, SHANE DARKE, ROLAND SIMON & PAUL GRIFFITHS

European Monitoring Centre for Drugs and Drug Addiction, Lisbon, Portugal, and National Drug & Alcohol Research Centre, University of New South Wales, Sydney, Australia

Abstract

Issues. Treatment outcomes for drug users are critical for informing policy and therapeutic practice. The coherence of outcomes, changes and drug use measures from observational studies on opioid use treatment were reviewed. Approach. Systematic review of the literature for longitudinal observational studies, from 1980 through November 2015, in all languages, with data on treated opioid users, using Pubmed, the Cochrane Library and additional strategies (e.g. Pubmed function ‘related citations’ and checking reference lists of eligible studies). Key Findings. Twenty-seven studies were included (11 countries, 85 publications, recruitment 1962–2009). Baseline n was >65,686 and median follow-up 34.5 months (21 studies) or 51.4 person-months (10 studies). Eight outcome domains were identified: ‘drug use’ (21/27 studies), ‘crime’ (13), ‘health’ (13), ‘treatment-related’ outcomes (16), ‘social functionings’ (13), ‘harms’ (8), ‘mortality’ (13) and ‘economic estimates’ (2 stud-
Figure 1. Flow-diagram of the selection of studies in a systematic review of 27 longitudinal observational opioid treatment studies.
Two main problems in the literature on observational OST outcome studies

1. Large variation in outcome domains and indicators used (8 domains identified, few of which used by more than 50% of studies)

2. Few studies include key public health problems among PUO as part of outcome evaluation (e.g. non-fatal overdose, infectious diseases, injecting and sexual risks)
Figure 2. Outcome domains identified in a systematic review of 27 longitudinal observational opioid treatment studies.

Wiessing et al. DAR 2017
Limited focus on key health problems among people who use opioids (27 studies)

2 /27 HIV or hepatitis C virus status
7 / 27 injection drug use

8 / 27 ‘Harms’ (here defined as ‘physical injury or behaviour posing a risk of adverse health consequences’)

Of which
5 / 27 needle sharing
4 / 27 sexual risk
5 / 27 overdose
Implications of systematic review

• Need for a minimum set of consensus outcome indicators to evaluate OST results

• Need to prioritise (public) health domains when constructing these indicators

• Difficult to rely on the literature to achieve a consensus set of indicators with a public health focus (few studies have such a focus)
EMCDDA OST OUTCOMES MONITORING PROJECT
EMCDDA project to develop guidance for OST outcomes monitoring

• EMCDDA started process to develop guidance (agreed indicators, methods) to monitor OST (and other treatment) outcomes in Europe (and elsewhere?)

• This guidance should include the key public health priorities (e.g. infectious diseases and overdose/mortality)

-> (Public) Health Perspective
Methods

- **Workshop** with representatives from 17 European countries in October 2018 during TDI meeting
- **Expert group** formed and 2-day meeting early 2019
- **Domains prioritisation**, draft indicators asked in both meetings. At expert group meeting also: format of guidance and process (Delphi study)
- **Wider panel for Delphi study** in 2020 (60 experts, different professions, 10 countries?)
- **Pilot implementation** of guidance in 2021-22
- **Final guidance** 2022?
7 responses received on set of questions prior to workshop (from 17 countries)

- **Estonia**: Tx interruptions, Work/education, Crime, Tx duration, Relapse
- **Croatia**: Tx plan, Health, Infectious Diseases, Risk behaviour, Mortality
- **Hungary**: CAST+SDS, Health locus of control, Life management, Self reflection, self-reported abstinence
- **Kazachstan**: Mortality, Life expectancy, Social /work adaptation
- **Luxembourg**: Current use of drugs, addiction level, craving, social cognitive factors such as (abstinence & relapse) self-efficacy and attitude towards abstinence, social support and social norms, intrinsic and extrinsic motivation, intention to remain abstinent, level of depression/anxiety, period of abstinence, relapse & lapses, crime, quality of life, co-morbidity/health, socio-economic factors (social and professional re-integration), infectious diseases (notably HCV re-infections), health-related problems related with IDU
- **Latvia**: Substance use outside Tx, Mortality
- **Netherlands**: Always combination of indicators, Quality of Life and Social functioning and client satisfaction (+ longer list)
Summary country responses

• Few countries seem to have Tx outcome monitoring in place, and some report serious problems in data quality (e.g. only positive outcomes being recorded)

• Many different indicators, no common core set visible, variation between more medical or more social indicators

• Indicators were generally thought to also apply for other opioid treatment, or other drugs

• Countries were missing e.g. UK - has outcome monitoring
Workshop results, 3 working groups

1\textsuperscript{st} priority OST health impact indicators (by all 3 w.groups):
• Overdose and mortality /causes (results indicator)
• Infectious diseases (hepatitis C) test and treat (results/process)
• OST waiting time and coverage /treatment participation (affordable and including prisons) (results)

2\textsuperscript{nd} priority OST health impact indicators (2/3 w.groups):
• Retention (results/process)
• NSP coverage of PWID population including in prisons (process)
• Quality of life /health (results)

Workshop country representatives during 2018
EMCDDA Treatment Demand Indicator expert meeting
Workshop results continued

Additional (3rd) priority health impact indicators (1/3 w.groups):

• Healthcare contact /discharge reasons (results)
• Use of non-prescribed drugs (results)
• Arrest /crime (results)
• Job /education (results)
• Economic analyses (process)
• (Psychiatric disorders) (process)

Workshop country representatives during 2018
EMCDDA Treatment Demand Indicator expert meeting
EMCDDA EXPERT GROUP & MEETING
(31 JAN – 1 FEB 2019)
EMCDDA expert group and meeting  
(31 Jan – 1 Feb 2019)

<table>
<thead>
<tr>
<th>Present</th>
<th>María Gabriela Barbaglia (Barcelona, ES), Gregorio Barrio (Madrid, ES), Peter Blanken (Rotterdam, NL), Esther Croes (Utrecht, NL), Geert Dom (Antwerp, BE), Patrizia Carrieri (Marseille, FR), Catherine Comiskey (Dublin, IE), Hugo Faria (Lisbon, PT), Dave Liddell (Glasgow, UK), Viktor Mravčík (Prague, CZ), Carlos Nordt (Zurich, CH), Bernd Schulte (Hamburg, DE), Luis Sordo (Madrid, ES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not present but participating by email</td>
<td>EMCDDA: Lucas Wiessing, Marica Ferri, Linda Montanari, Klaudia Kępa, Antón Gomez-Escolar, Julián Vicente</td>
</tr>
<tr>
<td></td>
<td>Tim Millar, Barbara Broers, Luís Mendão, Vendula Belackova, Rodrigo Coutinho, Gianni Morandi, Mads Uffe Pedersen, Emilis Subata</td>
</tr>
</tbody>
</table>
Expert meeting main results

- Treatment outcomes monitoring should cover both **result** and **process** indicators.
- OST outcome domains prioritised as:
  1. Continuity of OST care
  2. Overdose and mortality
  3. Somatic care (incl. HIV, hepatitis, STIs, Strep A etc.)
  4. Mental health
  5. Quality of life
  6. Control over substance use
  7. Criminality (arrest /jail)*

*There was no consensus on including crime data as these can form a danger for the patient.*
Indicators

• Detailed outcome indicators being currently discussed per domain (about 6 indicators per domain, to reduce during Delphi study)
• 14 indicators preliminary considered “core”, others to be flexibly used according to need
• Additional aggregate (system) level indicators were also proposed, e.g. coverage, retention rate, waiting time /access, dosage distribution...
Delphi study (in preparation)

• To try to achieve consensus with a wider group of stakeholders (including people who use drugs)

• Panel would likely include:
  o “Addiction specialists” (Psychiatrists, General practitioners, Addiction doctors, Psychologists, Social (care) workers, Nurses, Counsellors, Outreach workers, Service managers, Receptionists of services)
  o Prison medical staff
  o Reitox network of EMCDDA focal points
  o Public health professionals
  o Patients (and their family)
Delphi study

- 3 rounds, preceded by a test/pilot round using the tools just in our expert group. First round in January/February 2020, after recruitment of panel participants
- ~6 participants per country: 3 addiction specialists and 3 from the other categories
- Try to cover all addiction specialist groups including patients/family
- Aim at 10 countries to have a total panel size of 60?
Core indicators (draft)

• Domain 1 – Continuity of OST care
  1. To staff: “What % of clients starting OST remained in OST after X months”
  2. To staff: “What % of clients starting OST were linked to other services within X months”
  3. To patient: “How easy was it for you to get OST when you needed it?” (5 point scale)
  4. To patient: “How long did you have to wait to get OST when you asked for it” (in days /weeks /months /years)
Core indicators (draft)

• Domain 2 – **Overdose and mortality**
  5. To staff: “How many entered OST and how many died within X months?”
  6. To patient: “How many times did you have an overdose in the last X months?”

• Domain 3 – **Somatic care (incl. HIV, hepatitis etc.)**
  7. To patient: Injection and risk behaviour (needles, sex) *(format?)*
  8. To patient: Hepatitis C and HIV testing *(format?)*
  9. To patient: “How do you rate your physical health?” *(5 point scale)*
Core indicators (draft)

• Domain 4 – **Mental health**
  10. To patient: “How do you rate your mental health?” (5 point scale)
  11. To patient: Whenever you've needed treatment for your mental health problems, in the last X months, have you gotten it?” (yes /no /don’t know)

• Domain 5 – **Quality of life**
  12. To patient: “How do you rate your overall quality of life?” (5 point scale)
Core indicators (draft)

• Domain 6 – Control over substance use
  13. To patient: Frequency, quantity, include alcohol, benzo’s (prescribed or not) cannabis and tobacco (format?)

• Domain 7 – Criminality /arrest /jail
  14. To patient: “Have you been in prison / arrested in the last X months?” (yes /no /don’t know)
Aims of this workshop

• To test the idea of consensus indicators for OST outcome monitoring with the audience
• To see if the audience thinks they can potentially implement future guidance on OST outcome monitoring
• To get feedback and comments on work so far
• To include interested workshop participants in the 2020 Delphi panel or implementation pilot

(PLEASE EMAIL me at lucas.wiessing@emcdda.europa.eu)
Possible questions for discussion

- Is there a need for consensus OST outcome indicators?
- Is there a need for more focus on (public) health outcomes in OST outcome evaluation?
- Combine different levels: result and process indicators, individual level and aggregate level (system) indicators
- Has the Expert group chosen and prioritised the right outcome domains?
- Has the Expert group chosen feasible and important core outcome indicators?
- Is the Process right? (expert group -> Delphi panel -> pilot implementation -> final guidance)
- How to format future monitoring, can it be integrated into routine clinical practice?
Thanks for your attention!
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