

Uzmah Sabar,¹ Catherine Rycroft,¹ Naoko Ronquest,² Vijay Nadipelli,² Bernd Wollschlaeger³ and Ron Akehurst.¹

¹BresMed Health Solutions, Sheffield, UK; ²Indivior Inc, Richmond, VA, USA; ³Aventura Family Health Center, North Miami Beach, FL, USA.

Background and Study Objective

- Opioid use disorder (OUD) is a chronic and relapsing medical illness characterized by repeated and compulsive use of an opioid despite adverse social, psychological, and/or physical consequences.¹
- OUD is associated with a high cost to individuals, families, and society, largely due to the high costs of criminal justice and productivity loss among untreated OUD patients.²
- Several studies have reported a concurrence of untreated OUD and infectious diseases such as HIV and hepatitis C.^{2,3}
- To understand the overall global economic burden of OUD and to identify evidence gaps, the current literature was evaluated and relevant published data were summarized.

Methods

Searches in literature databases

- The MEDLINE and MEDLINE In-Process databases were searched to identify relevant articles describing the burden of disease and treatment landscape associated with OUD.
- Articles reporting on patients with opioid abuse, and/or addiction, and/or dependence were identified.† All included publications were grouped as reporting on patients with OUD.
- Associated disorders, such as delirium due to opiates, were not specifically targeted in this review, however, the search likely captured studies reporting on other related/associated disorders due to the broad search terms used.
- The search strategy used both MeSH and free-text terms for OUD (Table 1).

Table 1. Search strategy

Text and MeSH terms
Text words: "substance abuse" and "substance withdrawal" and MeSH terms for "substance-related disorders"[Majr]; "substance withdrawal syndrome"[Majr]; and "substance abuse, intravenous"[Majr], all combined with terms for "opioid", "opiate", "heroin", "narcotic"
MeSH term: "opioid-related disorders"[Majr]
Text words for: opioid abuse ("opioid dependence", "opioid addiction", "opioid abuse"); opiate abuse ("opiate dependence", "opiate addiction", "opiate abuse"); narcotic abuse ("narcotic dependence", "narcotic addiction", "narcotic abuse"); heroin abuse ("heroin dependence", "heroin addiction", "heroin abuse")
Terms combined with the following
Risk factors; patient characteristics and comorbidities; epidemiology, humanistic and economic burden; employment and crime; treatment options; and current clinical guidelines.

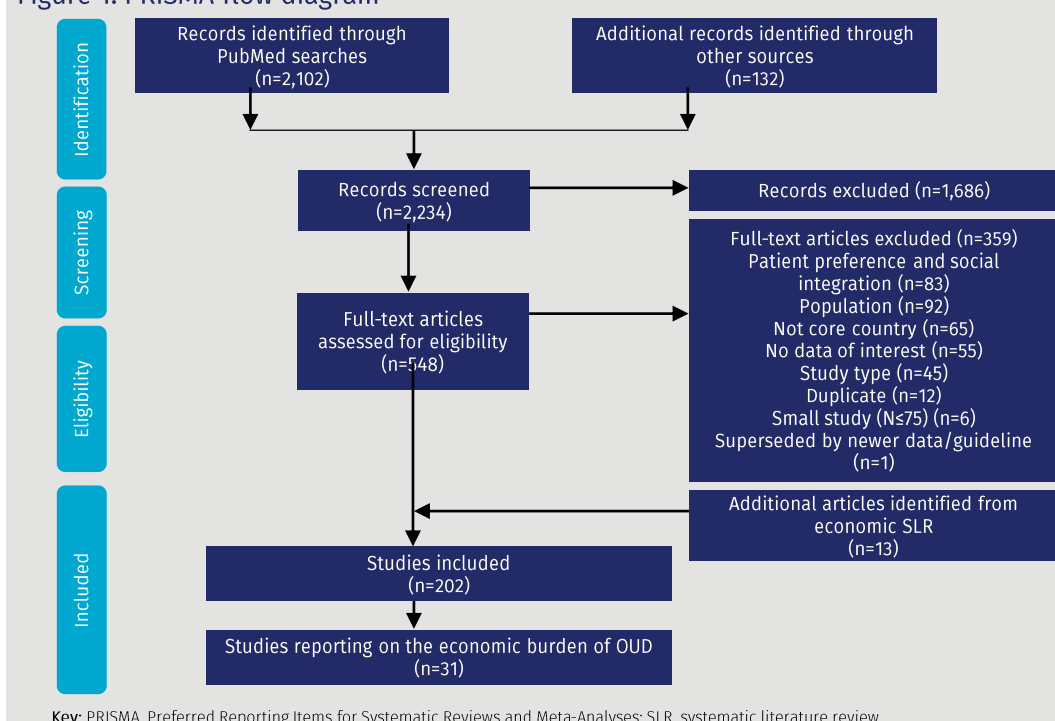
- Searches included articles published between 2000 and 2015 and were restricted to studies conducted in humans. Searches excluded comments, letters, news articles, editorials, and *in vitro* studies. Articles were not restricted by language.
- Additional websites were searched for further information on burden and clinical guidelines (details presented in ISPOR 2017 Poster PMH47).
- Titles, abstracts and full-text articles were screened for relevance against pre-defined inclusion/exclusion criteria. Inclusion criteria were:
 - Patients with OUD (opioid abuse, and/or addiction, and/or dependence);
 - Presented information on at least one of the following: risk factors, patient characteristics and comorbidities, epidemiology, humanistic and economic burden, employment and crime, treatment options, or current clinical guidelines;
 - Studies located in one of the countries of interest, i.e. EU5 (UK, France, Germany, Italy and Spain), USA, Canada, or Australia.
- Data were extracted from all included publications.

Results

Overall results of the literature review

- 2,234 citations retrieved; 202 met the pre-defined inclusion criteria (Figure 1).
- 31 reported on the economic burden and resource use associated with OUD; USA (20), Australia (7), Canada (3), and the UK (1).

Figure 1. PRISMA flow diagram



Cost of untreated opioid dependence in daily opioid users

- One study (cost-of-illness) from Canada reported on the economic burden of untreated heroin dependence and prescription opioids; the authors used data from 114 daily opiate users who were not receiving or seeking treatment between June 1996 and March 1997.⁴
- The total economic burden (in 1996) associated with untreated opioid dependence was CAD\$5.086 million/year; total costs were attributed to crime victimization (44.6%), law enforcement (42.4%), productivity losses (7%), and healthcare (6.1%).

Economic burden of heroin addiction: problem users and heroin-dependent people

- One study (cost-of-illness) from the USA reported that the total economic cost of heroin addiction was US\$21.9 billion/year (1996). The main contributors to cost were loss of productivity (52.6%), crime costs (23.9%), and medical care costs (23.0%).⁵

Economic burden of prescription OUD

- Ten studies from the USA reported on prescription opioid abuse, dependence, and misuse (Table 2). No data for prescription opioid abuse were identified in any other country.
- These publications used administrative claims data from beneficiaries covered by Medicaid, Medicare, or from privately insured populations.
- A study of privately insured patients who were opioid abusers reported that the mean annual direct healthcare costs for prescription opioid abusers were significantly higher than for non-abusers (US\$15,884 vs US\$1,830; $P < 0.01$ [US\$ 2003]).⁶
- Another study that included patients who had a mix of insurance programs (including commercial plans, Medicaid, Medicare, and the uninsured) and who were diagnosed with prescription opioid abuse reported that the annual per-patient excess medical costs associated with diagnosed abuse ranged from US\$9,456 to \$11,501 (US\$ 2011).⁷

- The total societal cost of prescription opioid abuse, dependence, and misuse ranged from US\$53.4 billion (2006)⁸ to US\$55.7 billion (2007).⁹
 - Studies highlight a variation in the component costs, with workplace and healthcare costs being higher than criminal justice costs.
 - Where healthcare costs were the major component, the cost of opioid dependence treatment was a small fraction of the total cost.
- Literature published since the original search indicates the total economic burden of prescription opioid overdose, abuse, and dependence stood at \$78.5 billion in the USA in 2013.¹⁰

Table 2. Publications reporting on prescription OUD^a in the USA

Reference	Study objective	Costs and author findings
Birnbaum et al. 2011 ⁸	To evaluate the societal costs associated with prescription opioid abuse in the USA	Total USA societal costs of prescription opioid abuse: \$55.7 billion in 2007 (US\$ 2009) Cost breakdown Workplace costs: \$25.6 billion (46%) Health care costs: \$25.0 billion (45%) Criminal justice costs: \$5.1 billion (9%)
Kirson et al. 2014 ¹¹	To calculate the percent reduction in abuse-related total annual medical costs associated with reformulated extended-release oxycodone	Annual societal costs of prescription opioid abuse in the USA: \$58.4 billion (US\$ 2011; adjusted from \$55.7 billion [US\$ 2009]) Of these: Excess medical and drug costs: \$24.2 billion (41.4%) Criminal justice costs: \$5.4 billion (9.2%) Lost workplace productivity: \$26.8 billion (45.9%)
Ghate et al. 2010 ¹²	To determine the associations between opioid abuse, dependence, and poisonings on costs and comorbidities in a Medicaid population	Annual medical costs (US\$ 2002–2003) Opioid abusers: \$14,054 to \$6,650 higher than non-abusers in patients with private insurance or Medicaid beneficiaries, respectively ($P < 0.01$ for both) Annual costs were similar for abusers with private insurance (\$15,884) or Medicaid beneficiaries (\$13,658)
Hansen et al. 2011 ⁹	To estimate current economic burden of nonmedical use of prescription opioids in the USA	Estimated cost of non-medical use of prescription opioids: Total: \$53.4 billion in 2006 Lost productivity: \$42 billion (79%) Criminal justice costs: \$8.2 billion (15%) Misuse treatment: \$2.2 billion (4%) Medical complications: \$944 million (2%)
Leider et al. 2011 ¹³	To assess the costs and utilization of chronic opioid users relative to similar patients without evidence of chronic pain	Healthcare utilization and costs (US\$ 2009): Chronic opioid users: \$23,049 Matched non-users: \$4975; $P < 0.001$ Total healthcare costs: Adherent patients (n=442): \$23,160 Non-adherent patients (n=1,658): \$26,433; $P = 0.036$
Michna et al. 2013 ¹⁴	To examine the payer-specific excess medical costs of diagnosed opioid abuse among commercially-insured, Medicaid and Medicare patients with recent prescription opioid use	Annual per-patient excess medical costs associated with opioid abuse compared with matched non-abusers (US\$ 2011) Commercially-insured patients: \$9,456 ($P < 0.001$) Medicaid patients: \$11,501 ($P < 0.001$) Medicare patients: \$10,046 ($P < 0.001$)
Rossiter et al. 2014 ⁷	To estimate the excess medical costs associated with diagnosed prescription opioid abuse among continuous extended-release opioid users	Annual per-patient excess medical costs associated with diagnosed abuse: \$9,456 to \$11,501 depending on the payer (US\$ 2011)
Rice et al. 2014 ¹⁵	To estimate the economic burden of prescription opioid abuse/dependence to employers	Incremental annual healthcare costs per patient (US\$ 2006–2012), compared with comparison patients: \$10,627 Excess annual work-loss costs in opioid abusers: \$1,244 Implied employer burden for diagnosed abuse: \$1.71 per member per month
White et al. 2005 ⁶	To calculate the mean annual per-patient total healthcare costs of opioid abusers from the perspective of a private payer	Mean annual direct health care costs (US\$ 2003) Opioid abusers: \$15,884 Non-abusers: \$1,830; $P < 0.01$
White et al. 2011 ¹⁶	To describe the prevalence and healthcare costs of opioid abuse during 2003–2007	Mean excess annual costs (US\$ 2009) per privately insured patient: \$20,546 Mean excess costs per Florida Medicaid patient: \$15,183

Note: ^aOUD refers to patients who are suffering from opioid abuse, and/or addiction, and/or dependence.

Resource use in select countries: USA, Australia, Canada and UK

- Nineteen articles focused on the resource use or on specific aspects of direct and indirect costs associated with heroin and/or prescription OUD (Table 3).
- Most articles in this group from Australia (5/7) and the USA (6/9) reported on resource use (use of opioid substitution treatment [OST] programs) and cost of treatment.
- Of the two articles from Canada, one reported on costs of OST programs and the second reported on crime-related costs.
- The single article from the UK reported on treatment costs.

Table 3. Publications reporting on resource use or specific aspects of direct and indirect costs of heroin and/or prescription OUD^a

Reference	Country	Patients	Type of costs reported
Stafford and Burns 2015 ¹⁷	Australia	People who regularly inject drugs: heroin and prescription opioids	Resource use – use of OST programs
Degenhardt et al. 2013 ¹⁸	Australia	Opioid-dependent people	Costs of court appearances and criminal justice
Gisev et al. 2014 ¹⁹	Australia	Opioid-dependent people	Costs of custody and criminal justice
Teesson et al. 2015 ²⁰	Australia	Heroin-dependent people	Resource use – use of OST programs
Hargreaves et al. 2002 ²¹	Australia	Patients with fatal heroin overdoses	Resource use – use of ambulances and the number of overdose calls made for an ambulance
Mills et al. 2005 ²²	Australia	Heroin-dependent people	Resource use – use of OST programs Comorbidity costs – impact of having PTSD on costs
Teesson et al. 2006 ²³	Australia	Heroin-dependent people	Resource use – use of OST programs
Fischer et al. 2005 ²⁴	Canada	Untreated illicit opioid users	Resource use – use of OST programs
Krebs et al. 2014 ²⁵	Canada	Opioid-dependent people	Crime-related costs
Mass et al. 2013 ²⁶	UK	Opioid-dependent people	Cost of treatment
Callahan et al. 2015 ²⁷	USA	Heroin users	Resource use and costs of welfare
Becker et al. 2008 ²⁸	USA	People with opioid use disorders	Resource use and costs of welfare
Hasegawa et al. 2014 ²⁹	USA	People with opioid overdose	Resource use – use of emergency department for opioid overdose
Hser et al. 2001 ³⁰	USA	Male heroin addicts	Resource use and costs of welfare
Inocencio et al. 2013 ³¹	USA	Patients with opioid poisoning	Costs of opioid poisoning and resource use
Lynch et al. 2014 ³²	USA	Opioid-dependent people	Resource use – use of counselling and addiction treatment
Baser et al. 2011 ³³	USA	Opioid-dependent people	Resource use – use of OST programs, treatment and healthcare costs
Clark et al. 2014 ³⁴	USA	Opioid-dependent people	Costs of comorbidities and healthcare costs
Clark et al. 2011 ³⁵	USA	Patients with opioid dependence	Treatment costs

Note: ^aOUD refers to patients who are suffering from opioid abuse, and/or addiction, and/or dependence.

Conclusions

- A substantial economic burden is associated with OUD.
- Most evidence is from studies restricted to OUD patient subgroups and only reports on specific elements of the total cost.
- Most identified studies were conducted in the USA, Australia and Canada, despite our review including 5 European countries.
- The available cost estimates are out of date and may significantly underestimate the current costs of OUD.
- Researchers quantifying the cost of OUD treatment need to be mindful of the lack of comprehensive reporting, and further research needs to be undertaken worldwide to better understand the comprehensive economic burden associated with OUD.

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