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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
- Patients with OUD suffer from various symptoms including acute withdrawal syndromes and risk of overdose.²
- It is anticipated that there are a wide variety of instruments being used to assess health-related quality of life (HRQoL) and patient symptoms in OUD, likely for both patient-reported outcomes and instruments utilized by clinicians or caregivers.
- A comprehensive burden-of-illness literature review was performed, which included an evaluation of the types of instruments used to assess severity of patient symptoms and the impact of OUD on HRQoL.

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 (Table 2).

Table 2. Searches in websites

Category	Website
Epidemiology and treatment landscape	European Monitoring Centre for Drugs and Drug Addiction; Canadian Centre on Substance Abuse; National Drug and Alcohol Research Centre; American society of addiction medicine; Substance Abuse and Mental Health Services Administration; National Institute on Drug Abuse
Sites for epidemiology, diagnosis, definitions, classification and management guidelines	World Health Organization
Clinical Guidelines	TRIP database and AHRQ National Guideline Clearinghouse
Key international HTA assessment websites	CRD HTA database; National Institute for Health and Care Excellent; Scottish Medicines Consortium; All Wales Medicines Strategy Group; Federal Joint Committee, Institute for Quality and Efficiency in Health Care; Haute Autorité de Santé; Denmark's HTA-HSR/DHTA – HTA & Health Services Research; Dental and Pharmaceutical Benefits Agency; Finnish Office for Health Technology Assessment; Norwegian Knowledge Centre for the Health Services; Zorginstituut Nederland; Canadian Agency for Drugs and Technologies in Health; Pharmaceutical Benefits Advisory Committee; International Network of Agencies for Health Technology Assessment
Regulatory websites for approved treatments in the EU5, Canada, Australia and the US	US Food and Drug Administration, European Medicines Agency, Therapeutic Goods Administration, Health Canada

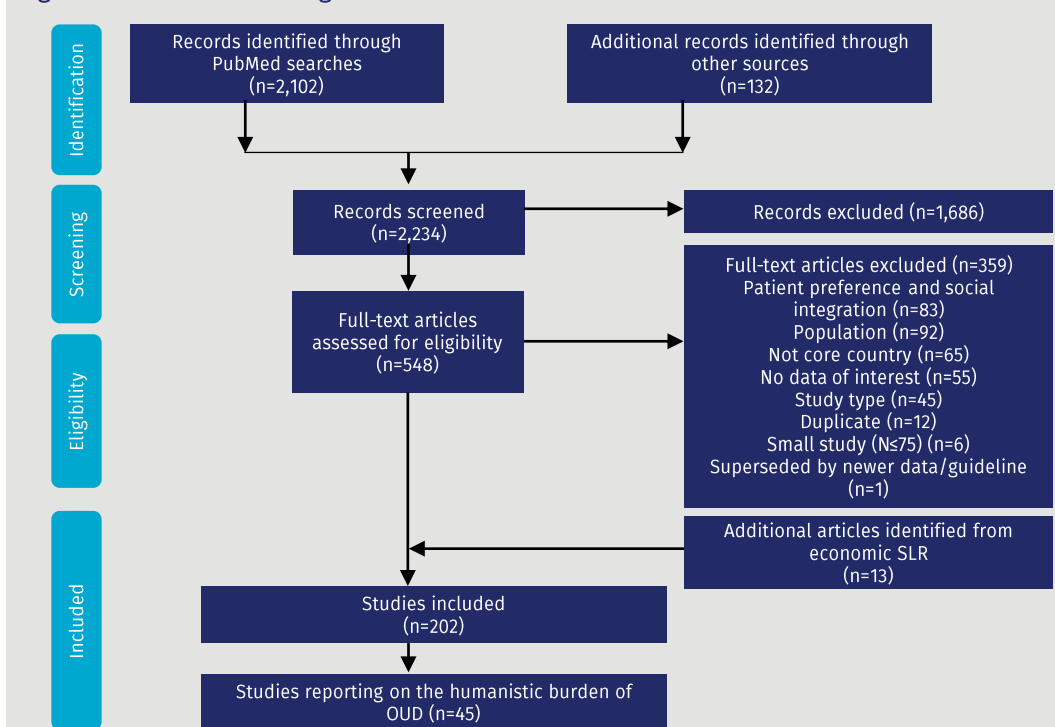
- Titles, abstracts and full-text articles were screened for relevance against pre-defined inclusion/exclusion criteria. Inclusion criteria were:
 - Patients with OUD (opioid abuse, and/or addiction, and/or dependence);
 - Presented information on at least one of the following: risk factors, patient 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.
- The current report describes instruments utilized to measure the humanistic burden of OUD as presented in the publications identified that met the inclusion criteria
 - Studies that examine humanistic burden typically aim to characterize the impact of illness on health and the consequences of treatment, including patient symptoms, HRQoL, patient functioning and activities, lost productivity and absenteeism, frequency of clinical events, and caregiver burden.

Results

Overall results of the literature review

- 2,234 citations retrieved; 202 met the pre-defined inclusion criteria and 45 articles reported on the humanistic burden of OUD (Figure 1).

Figure 1. PRISMA flow diagram



†The term OUD was introduced with the release of the Diagnostic and Statistical Manual (DSM) 5 criteria; as a result, some of the studies refer to opioid abuse and dependence, while others refer to OUD as a spectrum disorder.

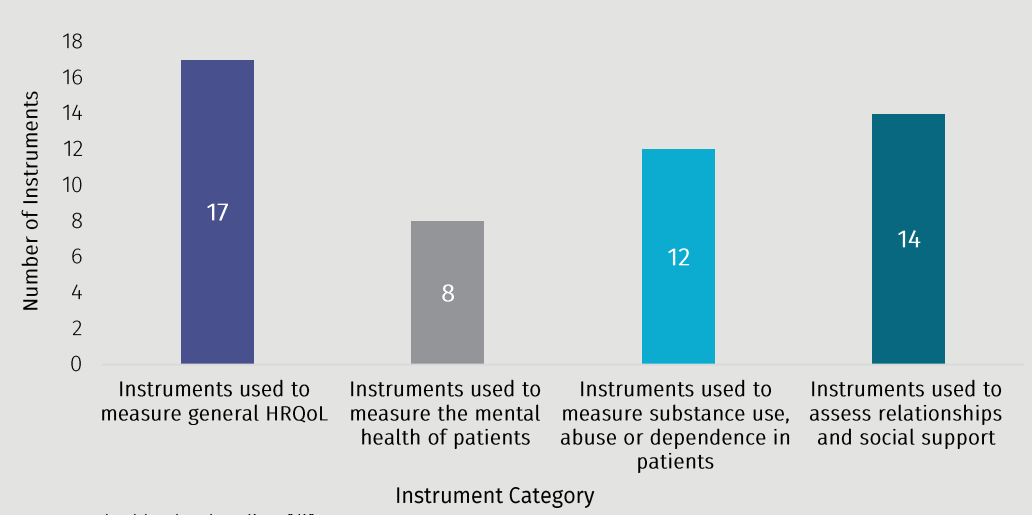
Brief overview of literature describing the humanistic burden of OUD

- Literature indicated that people with OUD have a reduced HRQoL when compared with the general population.³⁻⁵
- Most patients with OUD have ≥1 diagnoses of mental (including depression and mood disorders) or physical health problems, with greater detriments observed in the mental health than physical health components of generic instruments.⁶

Summary of the identified instruments

- From the 45 publications reporting on humanistic burden, 51 different instruments were identified that were used to measure the humanistic burden of OUD.
- These instruments were grouped into 4 categories based on the use of these instruments in the identified publications (Figure 2).

Figure 2. Number of instruments utilized by category



- Most of the instruments identified were classified as evaluating general HRQoL (17 instruments) or the wider impact of OUD on society (14 instruments) (Table 3).

Table 3. Identified instruments and the main aspects of humanistic burden in OUD measured in the reviewed studies

Instruments used to measure general HRQoL (n=17)	Instruments used to measure the mental health of patients (n=8)	Instruments used to measure substance use, abuse or dependence in patients (n=12)	Instruments used to assess relationships and social support (n=14)
General Health Questionnaire	Personality Diagnostic Questionnaire-Revised	Opiate Treatment Index Health Symptoms Scale	Adult attachment questionnaire
World Health Organisation Quality of Life Assessment	Internalised Stigma of Mental Illness Scale	Addiction Severity Index	Child behaviour checklist
Nottingham Health Profile	Italian version of the Temperament Evaluation of Memphis, Pisa, Paris and San Diego	Form-90	Significant others scale
Multidimensional Health Questionnaire	Beck Hopelessness Scale	Drug Addiction History Rating Scale	Multi-dimensional Scale of Perceived Social Support
EuroQoL EQ-5D Index Score	Kessler Psychological Distress Scale	ATOS structured interview	Experiences in close relationships- revised questionnaire
Short Form-36	Beck Depression Inventory	Severity of Dependence Scale	Social problems questionnaire
Short Form-12	Spielberger's State-Trait Anxiety Inventory	Adjective rating scale for withdrawal	Parental bonding instrument
Modular System for Quality of Life	Temperament and character inventory	Clinical opiate withdrawal scale	Duke-UNC Functional Social Support Questionnaire
German version of the Lancashire Quality of Life Profile		Readiness to change questionnaire	Parental warmth and control
Visual Analog Scale		Opioid drug use questionnaire	Observation of parent-child interaction
DSM-IV Global Assessment of Functioning scale		Minnesota student survey	Early adverse experiences index
Quality of Life Questionnaire		CAGE ^a questionnaire	Parent/child bonding child-report scale
McGill Quality of Life Questionnaire			Family management
Symptom Checklist 90			School engagement
Hopkins Symptom Checklist			
Clinical Global Impression			
The Satisfaction with Life Scale			

Key: ATOS, Australian Treatment Outcome Study; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; EQ-5D, EuroQoL 5 dimensions' questionnaire; HRQoL, health-related quality of life.
Note: ^aThe name CAGE is an acronym of the four questions in the survey.

- Most of the instruments identified were used only once, and 5 instruments were used in at least 4 articles each: World Health Organization Quality of Life Assessment, Short Form-12, Short Form-36, Opiate Treatment Index and Addiction Severity Index (Table 4).

Table 4. Overview of the most commonly used instruments for measuring humanistic burden in OUD (as reported in ≥4 publications)

Instrument	Overview of Instrument	Number of publications using instrument
Short Form-36	A 36-item self-rating scale. Summary scores range from 0 (worst health status) to 100 (best possible health status)	8
Opiate Treatment Index Health Symptoms Scale	A 50-item interviewer administered scale that assesses the current physical health status of injecting drug users. In all of the scales, the higher the obtained score, the greater the degree of dysfunction	8
Addiction Severity Index	A standardized 45-minute clinical research instrument used to quantify functioning in seven different domains. The instrument yields a composite score in each area from 0 to 1 based on responses to specific items covering the 30 days prior to the interview	8
Short Form-12	Measures generic health concepts relevant across age, disease, and treatment groups from the patient's point of view by scoring standardized responses to standard questions. Designed for self-administration	5
World Health Organization Quality of Life Assessment	A self-reported instrument measuring perceived HRQoL of patients in four areas: physical health, psychological health, social relationships, and environment	4

Key: DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; HRQoL, health-related quality of life; OUD, opioid use disorder.

- Many of the instruments identified are not validated or widely used, and have not yet been translated to multiple languages.

Conclusions

- A variety of instruments are used to measure the humanistic burden of OUD; they are heterogeneous and examine specific elements of OUD.
- When examined by category, most instruments identified fell under the category of general HRQoL instruments.
- There is an unmet need for the development of validated OUD-disease-specific HRQoL instruments that are both efficient and generalizable across regions.

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