

Quality of life as an outcome of opioid use disorder treatment: A systematic review

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Abstract:

Background and aims: The recent opioid epidemic has prompted renewed interest in opioid use disorder treatment, but there is little evidence regarding health-related quality-of-life (HRQoL) outcomes in treatment programs. Measuring HRQoL represents an opportunity to consider outcomes of opioid use disorder treatment that are more patient-centered and more relevant to overall health than abstinence alone. We conducted a systematic literature review to explore the extent to which the collection of HRQoL by opioid treatment programs is documented in the treatment program literature. **Materials and methods:** We searched PubMed, Embase PsycINFO and Web of Science for papers published between 1965 and 2015 that reported HRQoL outcome measures from substance abuse treatment programs. **Results:** Of the 3014 unduplicated articles initially identified for screening, 99 articles met criteria for further review. Of those articles, 7 were unavailable in English; therefore 92 articles were reviewed. Of these articles, 44 included any quality-of-life measure, 17 of which included validated HRQoL measures, and 10 supported derivation of quality-adjusted life year utility weights. The most frequently used validated measure was the Addiction Severity Index (ASI). Non-U.S. and more recent studies were more likely to include a measure of HRQoL. **Conclusions:** HRQoL measures are rarely used as outcomes in opioid treatment programs. The field should incorporate HRQoL measures as standard practice, especially measures that can be used to derive utility weights, such as the SF-12 or EQ-5D. These instruments provide policy makers with evidence on the impact of programs on patients' lives and with data to quantify the value of investing in opioid use disorder treatments.

Keywords: opioid use disorder treatment | health-related quality-of-life | systematic review

Article:

1. Introduction

Opioid misuse and opioid use disorders are pervasive public health problems globally. Worldwide, an estimated 28.6–38.0 million people used heroin or prescription opioids in the past year (United Nations Office on Drugs and Crime, 2015) and approximately 69,000 died from

opioid-related overdose in 2012 (World Health Organization, 2014). In the US, the rate of opioid overdose death in the US increased 200% from 2000 to 2014 and opioids killed an estimated 47,000 people in 2014 (Rudd, Aleshire, Zibbell, & Gladden, 2016). As a result, new policy efforts are being directed towards opioid use disorders (Blendon et al., 2016, Office of the Press Secretary, 2016) and the number of evidence-based therapies to address opioid use disorders is increasing (Amato et al., 2005, Brooks et al., 2010, Campbell et al., 2012, Carpenter et al., 2009, Mattick et al., 2014, Sullivan et al., 2006). Treatment programs are increasingly adopting many of these therapies (Andrews, D'Aunno, Pollack, & Friedmann, 2014) and program evaluations suggest they are effective in helping clients achieve and maintain abstinence (Sheehan et al., 1993, Wittchen et al., 2008).

Yet abstinence from opioids is not the only relevant outcome of opioid use disorder treatment. Many policy makers view health-related quality-of-life (HRQoL) and quality adjusted life years (QALYs) as important treatment outcomes and as critical inputs for decision-making, particularly for economic evaluations such as cost-effectiveness analyses (CEAs). The US Food and Drug Administration encourages the use of patient-reported outcome measures, a group of outcomes that includes validated HRQoL measures. Several non-profit organizations and professional societies in the US have recently introduced initiatives to measure the value of prescription drugs via CEAs that use QALYs (Neumann & Cohen, 2015). Despite controversy in the US surrounding the use of QALYs in economic evaluations (Neumann & Weinstein, 2010), the US Preventive Services Task Force (USPSTF) is charged with reviewing "...the scientific evidence related to the effectiveness, appropriateness, and *cost-effectiveness* of clinical preventive services... [emphasis added]" when it ranks preventive services (U.S. Preventive Services Task Force, 2015). Furthermore, the USPSTF lists HRQoL as a relevant health outcome and QALYs as a measure of disease burden (U.S. Preventive Services Task Force, 2015). The US Medicare program also considers CEA evidence when determining coverage for preventive services (Chambers, Cangelosi, & Neumann, 2015).

In the UK, the National Institute for Health and Care Excellence (NICE) explicitly includes CEA considerations in its development of clinical guidelines and requires the use of QALYs in CEA (National Institute for Health and Care Excellence, 2013). NICE also requires that the evidence is relevant to the patient populations that will be treated, which supports the need for treatment programs to collect HRQoL. For example, in its review of CEA evidence in support of methadone and buprenorphine for the management of opioid dependence, NICE states that "Although most of the included papers were considered to be of high quality, none used all of the appropriate parameters, effectiveness data, perspectives and comparators required to make their results generalisable to the NHS and personal social services (PSS)" (National Institute for Health and Care Excellence, 2007).

In light of the increased policy focus on opioid use disorder treatment and the importance to policy makers of HRQoL as a health outcome measure, we contend that opioid treatment programs should routinely collect HRQoL as a standard measure of treatment outcome, and should use an HRQoL measure that can be used to calculate QALYs. Measuring HRQoL in opioid use disorder treatment programs represents an opportunity to consider outcomes that are more patient-centered and more relevant to overall health than abstinence alone, and to expand the definition of treatment benefits. Some clinical trials of opioid use disorder therapies measure

HRQoL outcomes, and in particular QALYs, so that economic outcomes can be compared to those from studies of other health conditions (Byford et al., 2013, Campbell et al., 2012, Nosyk et al., 2011, Polsky et al., 2010). Measurement of these patient-centered and economic outcomes in “real world” program settings is also needed to support greater adoption of evidence-based services.

We conducted a systematic review of the opioid use disorder treatment program literature to explore the extent to which the reporting of HRQoL and/or QALYs by treatment programs is documented in the literature. We therefore focused our review on studies reporting data collected from extant, fully operational opioid treatment programs. Given the current opioid epidemic and resulting policy attention, we focus our review solely on opioids and do not consider other substances to better inform the responses to the current opioid-related public health crisis. We report the results of this systematic review and conclude with a discussion of how HRQoL and QALYs can be effectively incorporated into treatment program quality metrics.

2. Materials & methods

We conducted a systematic review to identify published studies that reported any quality of life (QoL) measure (encompassing but broader than HRQoL measures) as an outcome of substance abuse treatment programs. Systematic review procedures were conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher, Liberati, Tetzlaff, Altman, & Group, 2009).

We searched PubMed, Embase PsycINFO and Web of Science between June 2014 and July 2015 for published papers reporting QoL outcome measures of substance abuse treatment programs. To capture grey literature such as government reports, working papers, and presentations, we searched conferences and meetings in Web of Science and we searched the New York Academy of Medicine's Grey Lit Report. We identified the broadest search terms relevant to our goals and used database-specific search terms reflecting the search term mapping of each database. PubMed MeSH terms and Boolean connectors included ‘opioid-related disorders OR drug users’ AND ‘substance abuse treatment centers OR community health centers OR therapeutic community’ AND ‘incidence OR follow-up studies OR mortality’. Embase Thesaurus descriptors used included: ‘opiate addiction OR drug dependence’ AND ‘rehabilitation centers OR therapeutic community’ AND ‘incidence OR follow-up OR mortality’. PsycINFO Thesaurus descriptors used included: ‘drug usage OR drug addiction OR opiates’ AND ‘rehabilitation centers OR therapeutic community’ AND ‘followup studies OR prediction OR mortality’. Natural language searching in Web of Science consisted of the following: ‘opiate addiction or drug addict or drug dependence’ AND ‘drug rehab center OR rehabilitation center OR community health center OR therapeutic community’ AND ‘incidence OR follow up studies OR follow up OR prediction OR (prediction AND forecasting) OR mortality.’

Articles were screened by one co-author and review-relevant information on each was entered into a spreadsheet (Microsoft Excel 2013). Information collected on screened articles included: country in which the treatment program was located; type of study (e.g., observational); primary substance studied (e.g., heroin); type of substance use disorder treatment, classified as methadone, buprenorphine (Subutex), buprenorphine/naloxone (Suboxone), medical or

psychiatric care, and behavioral therapies including counseling and group therapy; HRQoL outcome measures reported, including reporting of QALYs or health utilities; additional treatment-related outcomes reported (e.g., abstinence); and any other social or psychosocial well-being measures reported (e.g. family support status, mental health status, housing status, etc.).

Articles were included in full-text review if they described heroin, prescription opioid, or a combination of heroin and prescription opioid use and described QoL measures as a treatment program outcome. The review of full-text articles was conducted by three co-authors: one co-author reviewed all articles and two co-authors each reviewed one-half of all articles. Articles selected for full-text review were subsequently excluded if they did not report QoL results, did not have an abstract available in English, were a review article, or reported results from a randomized control trial. We excluded articles reporting trial results because these studies likely do not report data being collected routinely by the involved treatment programs.

Included articles were qualitatively analyzed for their use of HRQoL measures. Included articles were classified as including a validated non-health-related quality of life (QoL) measure or another HRQoL/QoL measure. Studies classified as using validated HRQoL measures were subclassified as to whether they used measures that can be transformed into QALYs (e.g., SF-12, SF-36, or EQ-5D) (Brazier et al., 2002, Brazier and Roberts, 2004, Shaw et al., 2005). We defined validated HRQoL/QoL measures as those that encompass multiple facets of an individual's perceived physical and mental health and have a peer-reviewed validation study that was published separately from the article under review.

3. Results

Fig. 1 shows the PRISMA flow diagram for our review. A total of 3731 papers were identified electronically. After removing duplicates, abstracts for 3014 articles were screened for inclusion. Of those, 99 articles were identified as potentially including QoL measures, 7 of which were excluded because they were not available in English. The full-text of the remaining 92 articles was reviewed. Of those, 39 were excluded because they did not include QoL as a treatment outcome measure, 7 were excluded that described clinical trial results only, and 2 were excluded that were review articles, leaving 44 articles included in the subsequent analysis.

Table 1 presents the characteristics of the included articles compared to the complete set of articles identified. Among the 3014 articles initially identified, more than two-thirds were published since 2000 and less than one-third were published between 1965 and 1999. Among articles that use a QoL measure, approximately 80% were published since 2000. Among all articles identified, nearly two-thirds were from the US or Canada, with another quarter coming from Europe. In comparison, well under half ($n = 17$) of treatment programs in the studies that included a QoL measure were located in the US or Canada. Europe was the next most frequent region with 11 articles, followed by Asia/Middle East with 9 articles, Australia/New Zealand with 6 articles and the Caribbean with 1 article.

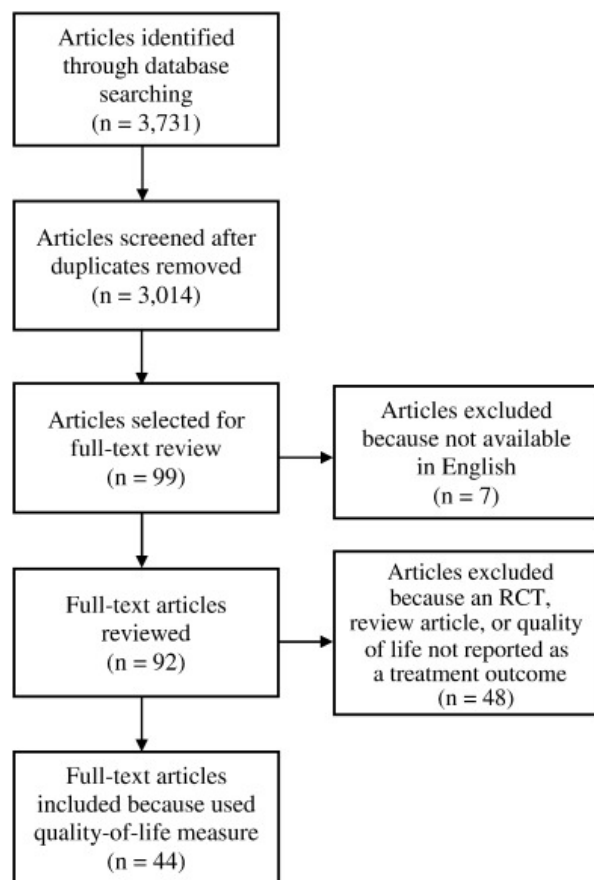


Fig. 1. PRISMA diagram.

Table 1. Characteristics of selected articles with quality of life measure compared to all articles.

Characteristic	Selected articles with quality of life measure (<i>n</i> = 44)			
	Literature review articles (<i>n</i> = 3014)		<i>n</i>	%
	<i>n</i>	%	<i>n</i>	%
Year of publication				
1965–1984	140	4.6	2	4.5
1985–1989	80	2.7	0	0
1990–1994	373	12.4	4	9.1
1995–1999	341	11.3	3	6.8
2000–2004	562	18.6	5	11.4
2005–2009	828	27.5	20	45.5
2010–2015	690	22.9	10	22.7
Origin of study				
US/Canada	1862	61.8	17	38.6
Europe	742	24.6	11	25.0
Asia/Middle East	170	5.6	9	20.5
Australia/New Zealand	161	0.4	6	13.6
South American/Caribbean/Mexico	28	5.3	1	2.3
Africa	12	0.9	0	0
Missing	39	1.3	0	0

Table 2 summarizes the use of QoL measures among the 44 included articles and presents the primary author, the year of publication, country of the opioid treatment program under study, and whether the treatment program included opioid substitution treatment (OST; including methadone, buprenorphine, or buprenorphine/naloxone). Thirty-two articles reported data on treatment programs that included OST. Seventeen of the articles used validated measures of HRQoL. Ten of these articles used HRQoL measures that can be used to derive QALYs. Of these, 8 used the SF-12 and 3 used the SF-36. None of these 10 articles reported QALY results. Only 3 of these articles were from the US, despite the US accounting for more than half of all articles screened. Other validated HRQoL measures used include the Q-LES-Q ($n = 2$), WHOQOL-BREF ($n = 1$), MSQoL ($n = 1$), McGill QOL ($n = 1$), HRQoLDA ($n = 1$) and a measure developed specifically to measure HRQoL among individuals with substance use disorders in China ($n = 2$). Additional QoL measures that did not specifically measure HRQoL include the Addiction Severity Index (ASI) (McLellan et al., 1992) or adaptations thereof ($n = 14$), Symptom Checklist-90 (SCL-90) (Derogatis, Lipman, & Covi, 1973) ($n = 6$), and a variety of QoL measures each used by a single article ($n = 7$). Half of all articles using the ASI were from the US ($n = 7$); all other QoL measures were relatively evenly spread across countries.

Table 2. Summary of articles with quality of life measure.

Authors (year)	Country	OST	HRQoL measure
HRQoL measures supporting utility analysis			
Astals et al. (2008)	Spain	Yes	SF-12
Darke et al. (2007)	Australia	Yes	SF-12
Havard, Teesson, Darke, and Ross (2006)	Australia	Yes	SF-12
Mills, Teesson, Ross, Darke, and Shanahan (2005)	Australia	Yes	SF-12
Mills, Teesson, Ross, and Darke (2007)	Australia	Yes	SF-12
Rosen, Smith, and Reynolds (2008)	USA	Yes	SF-12
Teesson, Havard, Ross, and Darke (2006)	Australia	Yes	SF-12
Williamson, Darke, Ross, and Teesson (2009)	Australia	Yes	SF-12
Kim et al. (2007)	USA	No	SF-36
Lofwall, Brooner, Bigelow, Kindbom, and Strain (2005)	USA	Yes	SF-36
Other HRQoL measures			
Ponizovsky and Grinshpoon (2007)	Israel	Yes	Q-LES-Q
Ponizovsky et al. (2010)	Israel	Yes	Q-LES-Q
Rao, Ambekar, Yadav, Sethi, and Dhawan (2012)	India	Yes	WHOQOL-BREF
Fassino, Daga, Delsedime, Rogna, and Boggio (2004)	Italy	No	McGill QOL (MQOL)
Gonzalez-Saiz, Gomez, Acedos, Rojas, and Ortega (2009)	Spain	Yes	HRQoLDA
Xiao, Wu, Wang, and Chen (2009)	China	Yes	Other
Xiao, Wu, Luo, and Wei (2010)	China	Yes	Other
QoL measures			
De Maeyer, Vanderplasschen, Lammertyn, van Nieuwenhuizen, and Broekaert (2011)	Belgium	Yes	ASI; LQOLP
Fareed, Casarella, Amar, Vayalapalli, and Drexler (2009)	USA	Yes	ASI
Hser, Kagihara, Huang, Evans, and Messina (2012)	USA	No	ASI
Kang, Deren, and Goldstein (2002)	USA	Yes	ASI
Lee, Bowen, Oei, and Yen (2012)	Taiwan	No	SCL-90
McLellan, Childress, Griffith, and Woody (1984)	USA	Yes	ASI
Meyer, Lin, and Brown (1996)	USA	Yes	ASI
Moylan, Jones, Haug, Kissin, and Svikis (2001)	USA	Yes	ASI

Authors (year)	Country	OST	HRQoL measure
Peles, Schreiber, and Adelson (2010)	Israel	Yes	ASI
Rajaratnam, Sivesind, Todman, Roane, and Seewald (2009)	USA	Yes	ASI
Ravndal, Vaglum, and Lauritzen (2005)	Norway	No	ASI
Ravndal and Amundsen (2010)	Norway	No	ASI
Soyka et al. (2012)	Germany	Yes	ASI
Verthein, Degkwitz, Haasen, and Krausz (2005)	Germany	No	ASI
Wittchen et al. (2008)	Germany	Yes	ASI
Jansson, Hesse, and Fridell (2008)	Sweden	No	SCL-90
Joe, Simpson, and Broome (1998)	USA	Yes	SCL-90; modified CMRS treatment motivation instrument
Rounsaville, Weissman, Crits-Christoph, Wilber, and Kleber (1982)	USA	Yes	SCL-90
Ravndal and Vaglum (1994)	Norway	No	SCL-90
Ravndal and Vaglum (1999)	Norway	No	SCL-90
Havassy, Hall, and Wasserman (1991)	USA	Yes	Social Support Questionnaire of Sarason
Ko et al. (2012)	Taiwan	Yes	Family APGAR Index
Lang and Belenko (2000)	USA	No	TCU Self-Rating Psychosocial Functioning Tool
Resnick, Resnick, and Galanter (1991)	USA	Yes	Unspecified
Rowan-Szal, Chatham, Joe, and Simpson (2000)	USA	Yes	TCU Self-Rating Psychosocial Functioning Tool
Skinner, Haggerty, Fleming, Catalano, and Gainey (2011)	USA	Yes	CIDI
Sheehan et al. (1993)	UK	No	BDI

ASI = Addiction Severity Index; HRQoL = health-related quality-of-life; OST = opioid substitution treatment; QoL = quality of life.

4. Discussion

We conducted a systematic literature review of studies of opioid use disorder treatment programs and screened over 3000 English-language articles published between 1965 and 2015. We found that the use of validated HRQoL measures in published literature on opioid use disorder treatment programs is rare, and HRQoL measures that can be used to derive QALYs are almost never used. Of the articles that reported HRQoL measures that would support QALYs, most reported data from treatment programs not located in the US. The most frequently used validated measure was the ASI, which does not include a composite score for HRQoL (McLellan et al., 1992).

Our finding that assessments of HRQoL are rare in the opioid use disorder treatment literature is confirmed by a related systematic review that compared studies reporting the QoL of opiate-dependent individuals and assessed the QoL instruments used (De Maeyer, Vanderplasschen, & Broekaert, 2010). In their review, De Maeyer and colleagues retrieved only 127 articles, 38 of which met their review inclusion criteria, leading them to conclude that opioid research with a primary focus on QoL is limited. Although our review and that of De Maeyer and colleagues both examine QoL and opioid use disorders, they employed different objectives and search criteria resulting in little overlap in the articles identified by the two reviews (only 5 articles were

included in both). Nonetheless, the review by De Maeyer and colleagues supports our conclusion that the reporting of QoL in the opioid treatment literature is rare.

Despite our finding of little evidence that treatment programs collect HRQoL measures, we contend that collecting these measures is nonetheless feasible and practicable. Given the data collection burden associated with the lengthy ASI, a measure that was collected by far more treatment programs than were HRQoL measures, collecting short HRQoL measures such as the 12-item SF-12 or 6-item EQ-5D should be feasible for most treatment programs. Concerns that generic HRQoL measures may not be appropriate for opioid using populations are contradicted by findings that many such measures are sensitive to changes in opioid use (Nosyk et al., 2010) and that they capture treatment-related changes in HRQoL (De Maeyer et al., 2010, Nosyk et al., 2015). Given the growing importance of patient reported outcomes and cost-effectiveness analysis, the benefits of collecting such short instruments likely outweighs the costs for most opioid treatment programs.

Our review is subject to limitations. We purposely excluded publications reporting clinical trial results because our intent was to assess the extent to which extant treatment programs report HRQoL data—data that could provide evidence relevant to decision makers evaluating the effectiveness of treatment for specific populations. In our effort to focus on “real world” settings, we may have missed some studies that reported data from treatment programs but did not meet our search terms. In particular, we find it somewhat surprising that we found no studies reporting use of the GAIN, despite its widespread use in US adolescent treatment studies (Dennis, Titus, White, Unsicker, & Hodgkins, 2008).

We believe the opioid use disorder treatment field should incorporate HRQoL measures and the assessment of QALYs as standard practice, both to provide policy makers with evidence that supports the impact of programs on patients' lives and to provide data to support cost-effectiveness evaluations that quantify the value of investing in opioid use disorder treatments. A potential barrier to achieving this goal is that programs may be required to pay licensing fees to use some of the current standard measures, although fees may be discounted for non-commercial users. Alternative HRQoL measures are available without cost from the World Health Organization and the National Institutes of Health PROMIS initiative (Hays, Bjorner, Revicki, Spritzer, & Cella, 2009), but there is not yet an accepted approach to using these measures to calculate QALYs (Hanmer et al., 2015). The lack of HRQoL evidence prevents opioid treatment programs from assessing the full impact of treatment on patients' lives and limits their ability to fully capture the value of investments in opioid use disorder treatments. We advocate for the development of publicly available, validated HRQoL measures and associated health utilities that opioid use disorder treatment programs can routinely collect.

Adopting opioid use disorder treatment outcomes that extend beyond abstinence to assess HRQoL outcomes will require changing attitudes among treatment programs and the payers to whom they are accountable. The task will become easier as there is greater recognition that opioid use disorder is a chronic disease requiring continuing care, and as opioid use treatment programs are more fully integrated into healthcare delivery systems.

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