Review Article

PALLIATIVE MEDICINE

Palliative Medicine
2021, Vol. 35(7) 1295–1322

DOI: 10.1177/02692163211015567
journals.sagepub.com/home/pmj
SAGE

Assessment tools for problematic opioid use in palliative care: A scoping review

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Abstract

Background: Screening for problematic opioid use is increasingly recommended in patients receiving palliative care.

Aim: To identify tools used to assess for the presence or risk of problematic opioid use in palliative care.

Design: Scoping review.

Data sources: Bibliographic databases (inception to January 31, 2020), reference lists, and grey literature were searched to find primary studies reporting on adults receiving palliative care and prescription opioids to manage symptoms from advanced cancer, neurodegenerative diseases, or end-stage organ diseases; and included tools to assess for problematic opioid use. There were no restrictions based on study design, location, or language.

Results: We identified 42 observational studies (total 14,431 participants) published between 2009 and 2020 that used questionnaires ($n = 32$) and urine drug tests ($n = 21$) to assess for problematic opioid use in palliative care, primarily in US ($n = 38$) and outpatient palliative care settings ($n = 36$). The questionnaires were Cut down, Annoyed, Guilty, and Eye-opener (CAGE, $n = 8$), CAGE-Adapted to Include Drugs (CAGE-AID, $n = 6$), Opioid Risk Tool ($n = 9$), Screener and Opioid Assessment for Patients with Pain (SOAPP; $n = 3$), SOAPP-Revised ($n = 2$), and SOAPP-Short Form ($n = 5$). Only two studies' primary objectives were to evaluate a questionnaire's psychometric properties in patients receiving palliative care. There was wide variation in how urine drug tests were incorporated into palliative care; frequency of abnormal urine drug test results ranged from 8.6% to 70%.

Conclusion: Given the dearth of studies using tools developed or validated specifically for patients receiving palliative care, further research is needed to inform clinical practice and policy regarding problematic opioid use in palliative care.

Keywords

Adult, analgesics, opioids, mass screening, opioid-related disorders, palliative care, surveys and questionnaires, substance abuse detection

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What is known already about this topic?

- Prescription opioids are essential medications for symptom management in palliative care.
- Opioids can cause serious adverse effects, including problematic opioid use, overdose and death.
- In response to growing concerns about problematic opioid use, palliative care experts and organizations are recommending the use of tools to screen for problematic opioid use.

What this paper adds?

- This scoping review identified 42 observational studies reporting on tools used to assess for problematic opioid use in palliative care.
- The tools identified were urine drug tests and questionnaires (CAGE, CAGE-AID, ORT, SOAPP, SOAPP-SF, SOAPP-R), which reported mostly on research conducted in outpatient settings in the US.
- No studies identified in this review adequately evaluated the effectiveness of these tools to assess for problematic opioid use in palliative care.

Implications for practice, theory or policy

- There is a lack of tools to assess for problematic opioid use that are developed or validated specifically for palliative care populations.
- Research on development and validation of tools to assess for problematic opioid use in palliative care is urgently needed.

Introduction

Prescription opioids are essential medicines in palliative care because they effectively reduce pain and dyspnea.[1] There is likely no other class of drug that is as instrumental in reducing suffering at the end-of-life.[2–4] Guidelines for opioid use in palliative care have traditionally emphasized proactive treatment to prevent pain, and it has long been held that addiction is both extremely rare and irrelevant for those with a short life expectancy.[5–7] However, health care professionals and organizations are increasingly recognizing that a significant minority of patients receiving palliative care may demonstrate problematic opioid use, both relating to their own use and to diversion of these medications.[8–11] This is particularly relevant given the ongoing international crisis of opioid-related deaths.[12–16] As well, there is advocacy for and evidence supporting early involvement of palliative care in serious but not imminently life-threatening illnesses, which can lead to increased and prolonged exposure to opioids.[12,13,17–19]

Identification of patients who are at high risk and have problematic opioid use is an important step in measuring the extent of opioid-related harms. Tools have been developed for patients with chronic non-cancer pain, including questionnaires and urine drug tests.[20–22] In response to the growing concerns about problematic opioid use, experts and organizations are recommending the use of these tools in palliative care.[17,21,22] However, these tools may not be suitable for palliative care due to differences between palliative care and chronic non-cancer pain. Traditionally, all chronic pain disorders outside of pain related to cancer and end-of-life are known as "chronic non-cancer pain."[23] By definition, chronic non-cancer pain is present for longer than 3 months[24] but most patients will experience pain for years.[25] These patients can therefore receive chronic opioid therapy and be at risk of significant opioid-related harms, including problematic opioid use,[26,27] overdose,[28] and death.[29,30] In contrast, patients receiving palliative care have advanced, progressive illnesses that are usually associated with worsening symptoms and functional deterioration.[31,32] Opioids are titrated to balance pain control and adverse effects.[33] Opioid therapy duration and the development of opioid-related harms are naturally limited by patients' life-expectancy.[34] Given these significant differences, knowledge about the available evidence that supports the use of these tools in palliative care is critical before widespread adoption into clinical practice. Therefore, we conducted a scoping review to answer the research question, "what tools are used to assess the presence or risk of problematic opioid use in studies conducted in the palliative care context?"

Methods

The purpose of scoping reviews is to identify and map available evidence, rather than to produce critically appraised answers to research questions.[35] We used the Arksey and O'Malley methodological framework, which was enhanced by Levac et al. and the Joanna Briggs Institute, to conduct our scoping review.[36–39] Key stakeholders informed our research question and search strategy, provided input on the results and analysis, and helped formulate the key recommendations and messages. These partners were representatives from the Health Canada, Canadian Hospice Palliative Care Association (CHPCA),

Canadian Society of Palliative Care Physicians (CSPCP), Canadian Virtual Hospice (CVH) and the University of Toronto Safer Opioid Prescribing continuing professional development course.[40–43] The PRISMA extension for Scoping Reviews (PRISMA-Scr) was used as a guide for reporting this review.[44] Our review protocol was not registered online but is available upon reasonable request.

Study eligibility criteria

We used the Population, Intervention, Comparison/Control, Outcome, Study design (PICOS) framework to structure our eligibility criteria (Table 1).[45] We focused on patients who were receiving palliative care and were prescribed opioids for symptom management related to advanced cancers, neurodegenerative diseases, or end-stage organ failure. These three disease groups have been identified by CSPCP as needing palliative care.[46] There were no restrictions according to design, publication year, location, or language. Exclusion criteria included studies related to chronic non-cancer pain (such as from accidents or other non-life-threatening illnesses), chronic pain in survivors of adult cancers, and non-opioid substance use disorders as well as studies that used surrogate markers for opioid-related harms (e.g. alcohol use disorder).

Search strategy

In collaboration with an information specialist and our key stakeholders, we developed a comprehensive search strategy that involved searching bibliographic databases from inception to January 31, 2020 (Supplemental Appendix A: Bibliographic databases searched and Ovid Medline® search strategy). Where available, controlled vocabulary terms and text words were used to maximize the number of potentially relevant studies identified. The search strategies were limited to human studies and adult populations (age $\geqslant$ 18 years) where the limits were applicable. To identify additional relevant studies, we conducted hand searches of reference lists for all potentially eligible full text articles. Furthermore, we conducted a grey literature search using grey literature databases and websites of prominent health and medical organizations (Supplemental Appendix B: Grey literature search terms and sources).

Guiding definitions

The following established definitions were used to guide this review: *misuse* was defined as "opioid use not in accordance with prescribed directions, regardless of the presence or absence of harm resulting from use;"[47] *abuse* was "intentional opioid use for non-medical purposes;"[47] *diversion* was defined as "unlawful channeling of regulated pharmaceuticals from legal sources to the illicit marketplace;"[48] and, *problematic opioid use* was used to encompass the concepts of opioid misuse, abuse and diversion.[47,49] *Palliative care* was defined as "an approach that improves the quality of life of patients and their families facing the problem[s] associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual."[50]

Data management and synthesis

The information specialist in our team oversaw the information management process. We used EndNote X8.2™ bibliographic software to store the records retrieved from all literature searches and to remove duplicate entries.[51] We used Covidence, a web-based literature review software platform, to screen all records.[52]

Our PICOS criteria were applied in duplicate and independently to the titles and abstracts of the records (Table 1). For articles with no available abstracts, categorization was based on the title alone. If the two reviews conflicted, then a third review of the record was conducted to determine the final inclusion. This same screening process was applied to retrieved full texts. Eligible conference proceedings and abstracts were included in full-text review and we contacted study authors for additional information, as necessary. We expanded on the reasons for exclusion for each of the PICOS criteria and developed a hierarchy of importance for the identified reasons for exclusions (Supplemental Appendix C).

Each full text record was independently documented and coded using standardized forms in duplicate. The data extraction forms were piloted and revised throughout the review process. The following data were extracted: first author, title, publication year, record type (abstract or full text article), language, location, setting, study design, duration, population, inclusion/exclusion criteria, sample size, data collection methods, and comparison or control. Specific data related to measurement tools that were extracted were: administration of the tools, use of the tool, cut-off values, and results. Sources of evidence, key concepts and findings, and gaps in knowledge were synthesized and presented as narrative descriptions and tables.

Results

A total of 42,510 records were identified by bibliographic databases, grey literature, and hand searching of references (Figure 1 for PRISMA diagram). After removing duplicates and screening for relevance, we included 42 studies published between 2009 and 2020 with a total of 14,431 participants. The majority of the studies were published in the US (n = 38; 91%) and conducted in outpatient

Table 1. PICOS criteria.

PICOS category	Inclusion criteria	Exclusion criteria
Population	Adult (18 years or older) Receiving palliative care Using opioids Life threatening illnesses from one or more of these disease groups: advanced cancers, neurodegenerative diseases, end-stage organ diseases	Preclinical studies (i.e. cell studies) Non-life-threatening disease or cured disease (i.e. cancer survivor, chronic non-cancer pain) Non-opioid substance use disorders Non-patient populations (i.e. health care providers, caregivers) Clinically stable opioid use disorder
Intervention	Interventions that assess for presence or risk of problematic opioid including: • Diagnostic tools • Risk stratification tools	Interventions unrelated to problematic opioid use (i.e. methylnaltrexone for opioid induced constipation) Iatrogenic opioid-related harms
Comparator/control	Studies with comparison/control group (i.e. randomized control trial, quasi-experimental, before and after studies, observational studies) Studies without a control group (i.e. retrospective analysis of administrative databases, uncontrolled observational studies, cross-sectional surveys, qualitative studies)	None
Outcome	Quantitative and qualitative outcomes associated with use of tools and opioid prescription-related harms (i.e. prevalence of positive urine drug screen results, scores of risk, and diagnostic tools)	Opioid adverse effects unrelated to problematic opioid use (i.e. constipation, nausea, pruritus) Policy or prescriber errors that result in opioid adverse effects (i.e. intentional use of opioids to euthanize patients)
Study designs	Observational (i.e. case report, case-control, cohort) Experimental (i.e. randomized control trial)	None

palliative care clinics ($n = 36$; 86%). Of these studies, 15 (36%) were abstracts, and 27 (64%) were cross-sectional studies. Table 2 presents the general characteristics of included studies. The grey literature search did not yield any results that met our study eligibility criteria. We contacted authors of 13 studies[53–59,68–73] and received responses from six authors,[54,55,69–72] who provided additional data for four studies.[54,55,69,72]

We identified two types of tools used to assess for problematic opioid use in palliative care: questionnaires ($n = 32$, 76%)[53–55,57,58,61–63,65,66,68–89] and urine drug tests ($n = 21$, 50%),[17,53,55,56,57,59,60,63,64,67,68,70,71,81,82,85,89–93] with an overlap of both types in 11 studies (26%).[53,55,57,63,68,70,71,81,82,85,89] Two studies did not specify which questionnaire they used.[68,88] The primary study objective of 22 studies (52%) was to evaluate the use of one or more assessment tools in palliative care.[53–63,66,68–73,82,85,91,93] In the remaining studies, the primary objectives were to describe patients with problematic opioid use who were receiving palliative care ($n = 17$, 40%);[60,64,67,74–81,84,86–88,90,92] and to evaluate the impact of interventions related to problematic opioid use in palliative care ($n = 3$, 7%)[17,83,89] (Table 2). Though evaluation of the tools was not the primary objective in these studies, they reported on use of these tools to assess for problematic opioid use. Tables 3 and 4 present the reported characteristics and findings related to the use of these tools in palliative care.

*Problematic opioid use questionnaires (*n *= 32)*

The following questionnaires were used in the studies included in our review: Cut down, Annoyed, Guilty, and Eye-opener (CAGE, $n = 8$, 25%),[70,74–80] CAGE-Adapted to Include Drugs (CAGE-AID; $n = 6$, 28%),[62,69,81–83,89] Opioid Risk Tool (ORT) ($n = 9$, 28%),[53,54,57,58,61,71–73,85] Screener and Opioid Assessment for Patients with Pain (SOAPP) ($n = 3$, 9%),[65,66,69] SOAPP-Revised (SOAPP-R; $n = 2$, 6%),[55,87] and SOAPP-Short Form (SOAPP-SF; $n = 5$, 16%)[54,63,70,75,86] Four studies (13%) used two different questionnaires;[54,69,70,75] one study (3%) used a self-designed opioid dependence assessment;[88] one study (3%) used a 5-point Likert scale to measure opioid craving;[84] and one study (3%) did not specify the questionnaire that they used.[68] Supplemental Appendix D provides information about the development and validation studies for CAGE, CAGE-AID, ORT, SOAPP, SOAPP-SF, and SOAPP-R questionnaires.

Most studies ($n = 30$, 94%) were conducted in outpatient clinics[53–55,57,58,61–63,65,66,68–79,81–83,85–89] and in the US ($n = 28$, 88%),[53–55,57,58,61,62,63,65,66,69–79,81–83,85–87,89] and published between 2009 and 2020. The same tertiary cancer center conducted many of the studies ($n = 16$, 50%): CAGE ($n = 7$, 44%),[74–80] CAGE-AID ($n = 6$, 37.5%),[62,81–83,89,94] SOAPP ($n = 3$, 19%),[65,66,69] and SOAPP-SF ($n = 2$, 13%).[75,86] This cancer center refers to its palliative care service as

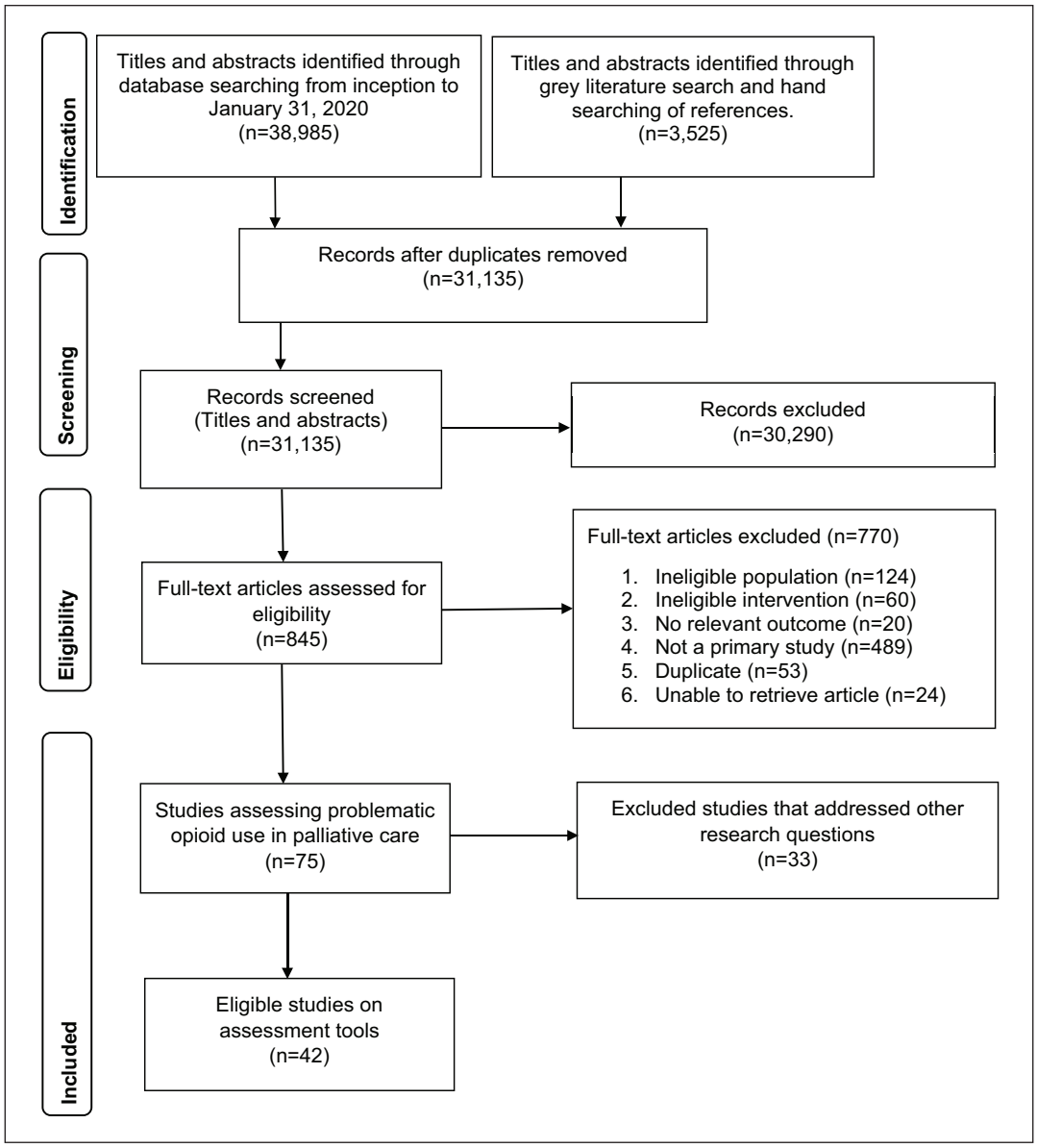

Figure 1. PRISMA flow diagram.

"supportive care."[95] All studies were observational study designs with the most common being cross-sectional studies ($n = 22$, 69%).[53–55,57,58,61,63,65,66,68–74,77–80,85,86] Most studies ($n = 30$, 94%) focused on patients with cancer, with reported proportion of participants with cancer ranging from 75% to 100%.[53,54,57,58,61–63,65,66,68–70,72–79,81–83,85–89] Of these studies, 10 studies (31%) reported that 7.6% to 46% of their participants had early stage or no evidence of cancer.[56,63,70,77,79,80,82,83,89,91] Fourteen studies (47%) did not report the stages of their patients' cancer diagnoses.[53,54,57,58,61–63,65,66,68,69,72,73,85] Regarding the two studies that did not focus primarily on cancer, one study did not provide information about their patients' diagnoses.[55] The other study reported only a small proportion (18%) of its patients had current or past history of cancer.[71] The diagnoses of the remaining patients were not reported in the article.[71]

Regarding assessment of the questionnaires, 13 studies (40%) only reported on use of the questionnaires in palliative care.[53,55,57,61,62,68,71,75,76,81,84,87,88] The remaining studies assessed the following: relationship between questionnaire results with patient characteristics ($n = 9$, 28%),[58,63,65,66,69,70,72,73,86] specific problematic opioid use ($n = 4$, 13%),[77–80] and urine drug tests ($n = 3$, 9%);[63,82,85] questionnaire results before and after implementing problematic opioid-use related interventions ($n = 2$, 6%);[83,89] comparison of characteristics of patients with normal and abnormal questionnaire ($n = 2$, 6%);[72,74] and,

Table 2. General characteristics of studies included in this review.

Author, year, reference type	Location, setting	Study design	Study duration (months)	Sample size population	Eligibility criteria	Comparator or control	Primary study objective	Assessment tools
Arthur et al., 2016[82] Full text	US, MD Anderson Cancer Centre, Supportive Care Clinic[a]	Case control	11	1058 (61 cases, 120 controls) Cancer (86% advanced, 14% early or no evidence of disease)	Age ⩾18 years, current or past cancer diagnosis, receiving chronic opioid therapy[b]; underwent urine drug tests	Patients who did not undergo urine drug tests	To determine factors associated with physicians ordering urine drug tests for patients who are receiving chronic opioid therapy	CAGE-AID, urine drug test
Arthur et al., 2016[81] Full text	US, MD Anderson Cancer Centre, Supportive Care Clinic[a]	Case series	NA	2 Advanced cancer	NA	NA	To report two patients with aberrant opioid use	CAGE-AID, urine drug test
Arthur et al., 2018[89] Full text	US, MD Anderson Cancer Centre, Supportive Care Clinic[a]	Case control	20	100 (30 cases, 70 controls) Cancer (82% advanced, 17% early or no evidence of disease, 1% data missing)	Age ⩾ 18 years, current or past cancer diagnosis, receiving chronic opioid therapy[b]; documented evidence of aberrant behavior and received intervention	Patients without aberrant behavior	To determine frequency and type of common aberrant behaviors; examine the changes in patient behaviors, symptoms and opioid use within 3 months following intervention; and identify predictors of aberrant behavior among patients receiving opioid therapy	CAGE-AID, urine drug test
Arthur et al., 2018[60] Abstract	US, MD Anderson Cancer Centre, Supportive Care Clinic[a]	Cross-sectional	NR	319 (212 random urine drug tests, 88 targeted urine drug tests) cancer	All patients were eligible for random urine drug tests. Target urine drug tests ordered based on MD's estimation of patient's risk for nonmedical opioid use	Targeted urine drug test	To describe the characteristics of patients who underwent random urine drug tests and a similar cohort who underwent targeted urine drug tests	Urine drug test
Barclay et al., 2014[85] Full text	US, Emily Couric Clinical Cancer Centre, Palliative Care Clinic	Cross-sectional	1	114 Cancer	Current or past cancer diagnosis	NA	To report results of a chart review that was looking for presence of risk factors for substance abuse and rates of abnormal urine drug tests	ORT, urine drug test
Boerstler et al., 2020[90] Full text	Canada, Providence Health Care, Palliative Care Clinic	Case report	NR	1 Neurodegenerative condition—muscular dystrophy	NA	NA	To report a case that demonstrates the balancing act between providing end-stage or chronic patients with pain relieving medications that they need while not contributing to the possibility of drug diversion	Urine drug test
Broglio et al., 2018[55] Abstract	US, Dartmouth-Hitchcock Medical Centre, Palliative care clinic	Cross-sectional	0.75[c]	68 Palliative care	NR	NA	To assess feasibility of implementing universal precautions for opioid prescribing	SOAPP-R,[e] urine drug test
Childers et al., 2015[70] Full text	US, Hillman Cancer Centre, Cancer Pain and Supportive Care Clinic	Cross-sectional	11	76 or 77[d] (57 SOAPP-SF, 32 CAGE) Palliative care (56% active treatment, 6% palliative only, 31% no evidence of disease)	NR	NA	To assess types of pain and risk of opioid misuse	CAGE, SOAPP-SF, urine drug test

(Continued)

Table 2. (Continued)

Author, year, reference type	Location, setting	Study design	Study duration (months)	Sample size population	Eligibility criteria	Comparator or control	Primary study objective	Assessment tools
Chua et al., 2019[61] Abstract	US, Dana-Farber Cancer Institute, Palliative Care Clinic	Cross-sectional	7	231 Cancer	New consults seen in the outpatient palliative care clinic prescribed opioids by their oncologist or palliative care provider	NA	To increase ORT completion rate from 0% to 70% for eligible new consults	ORT
De La Cruz et al., 2017[83] Full text	US, MD Anderson Cancer Centre, Palliative Care Clinic	Cohort, prospective	12	600 (300 cases, 300 control) Cancer (90.1% advanced)	Age ⩾18 years; received opioids for ⩾1 month, able to read, write and converse in English, no cognitive impairment, returning for follow-up visit, received opioid education; patients with acute symptom distress were excluded	Patients that completed survey before initiation of educational program	To determine whether an improvement occurred in the patterns of use, storage, and disposal of opioids after implementation of patient education program	CAGE-AID
Dev et al., 2011[74] Full text	US, MD Anderson Cancer Centre, Supportive Care Clinic[a]	Cross-sectional	NR "before Jan 2017"	665 (100 CAGE positive, 100 CAGE negative) Advanced cancer	CAGE positive	CAGE negative	To determine frequency of undiagnosed alcoholism and to study the correlation between CAGE positivity and history of smoking and use of illegal drugs and sedatives, hypnotics, anxiolytics	CAGE
Dev et al., 2019[86] Full text	US, MD Anderson Cancer Centre, Supportive Care Clinic[a]	Cross-sectional	12	490 (399 participated) Advanced cancer	Age ⩾18 years; attended at least one follow up visit in outpatient supportive care clinic; seen in supportive care center between 2015 and 2016	Current smokers vs former smokers vs never smokers	To examine the association between tobacco use in patients with advanced cancer with symptom expression as measured by the Edmonton Symptom Assessment System (ESAS) and the use of strong opioids	SOAPP-SF
Donovan et al., 2017[56] Abstract	US, Moffitt Cancer Centre, Supportive Care Clinic	Cross-sectional	22	1108 Cancer (54% stage III–IV)	Age ⩾18 years, cancer diagnosis, new referral to clinic; underwent urine drug test	NA	To investigate utility of urine drug test at first clinic visit by determining prevalence of abnormal results; to examine relationship of demographic and clinical characteristic to presence of illegal drugs	Urine drug test
Edwards et al., 2018[62] Abstract	US, MD Anderson Cancer Centre, Supportive care[a] inpatient consultation, supportive care outpatient	Longitudinal	NR	283 Cancer	Initially seen during inpatient supportive care consultation and had an outpatient follow up within 3 months	NA	To ascertain CAGE-AID scores and clinical and demographic characteristics of consecutive adult patients who were initially seen during inpatient consultation and had an outpatient follow up within 3 months	CAGE-AID

(Continued)

Table 2. (Continued)

Author, year, reference type	Location, setting	Study design	Study duration (months)	Sample size population	Eligibility criteria	Comparator or control	Primary study objective	Assessment tools
Gabbard et al., 2019[17] Full text	US, Wake Forest School of Medicine[g] Inpatient palliative care unit, home hospice, inpatient hospice home	Case report	NR	1 Advanced cancer	NA	NA	To offer strategies on how to manage pain in patients who have active substance use disorders or at risk for developing substance use disorders in those dying in hospice	Urine drug test
Garcia, 2017[73] Full text	US, University of Virginia Medical Centre, Gynecology Oncology or Palliative Care Clinics	Cross-sectional	54	118 Gynecologic cancer (staging NR)	Gynecologic cancer seen in gynecologic oncology or palliative care clinics; have existing active or receiving new opioid prescription	NA	To characterize risk for opioid misuse among gynecologic oncology patients	ORT
Go et al., 2018[84] Full text	South Korea, Gyeongsang National University Changwon Hospital[g]	Case report	NR	1 Advanced cancer	NA	NA	To report a case of an opioid-addicted terminal cancer patient who had suffered from strong craving behavior that was controlled by olanzapine	Opioid craving 5-point Likert scale
Greiner et al., 2020[63] Full text	US Oncology palliative medicine clinic in community-based cancer institute	Cross-sectional	6	223 (215 SOAPP-SF, 83 toxicology testing) Cancer (patients who completed SOAPP-SF and toxicology test: 61% metastatic; Patients who only completed SOAPP-SF: 62% metastatic)	New patients	NA	To identify characteristics associated with a high-risk SOAPP-SF score and noncompliant toxicology tests; to determine SOAPP-SF utility to predict noncompliant toxicology tests	SOAPP-SF, urine drug test
Jablonski et al., 2018[54] Abstract	US, University of Pittsburgh Medical Centre, Palliative Care Clinic	Cross-sectional	5[e]	30 Cancer (staging NR)	Patients prescribed chronic opioid therapy	NA	To discuss feasibility of opioid risk screening in an outpatient palliative care oncology clinic; to quantify capacity of opioid risk screening tools to provide results that influence prescribing decisions	ORT, SOAPP-SF
Koyyalagunta et al., 2011[75] Full text	US, MD Anderson Cancer Centre, Pain Centre	Case series	NA	2 Advanced cancer	NA	NA	To present an algorithm of multidisciplinary care for treatment of cancer patients at risk for abusing opioids	CAGE, SOAPP-SF
Kwon et al., 2014[76] Full text	US, MD Anderson Cancer Centre, Supportive Care Clinic[a]	Case series	NA	2 Advanced cancer	NA	NA	To describe patients with aberrant drug-related behaviors and similar patterns of dose escalation	CAGE

(Continued)

Table 2. (Continued)

Author, year, reference type	Location, setting	Study design	Study duration (months)	Sample size population	Eligibility criteria	Comparator or control	Primary study objective	Assessment tools
Kwon et al., 2015[77] Full text	US, MD Anderson Cancer Centre, Supportive Care Centre[a]	Cross-sectional	3	432 Cancer (92.4% advanced stage)	NA	NA	To determine proportion of patients diagnosed with chemical coping by palliative medicine specialists and concordance of chemical coping diagnosis between physician assessment and medical record documentation; to determine association between chemical coping and CAGE positivity, history of substance abuse and psychiatric disorder, opioid daily requirements, cancer type, performance status, and other demographic factors	CAGE
Langford et al., 2017[53] Abstract	US, University of Texas Health Sciences Centre, Palliative Care Clinic	Cross-sectional	5.25	91 Palliative care (79% cancer, staging NR)	Patients being considered for chronic opioid therapy	NA	To report on experience with instituting a safety assessment for patients receiving chronic opioid therapy	ORT, urine drug test
Ma et al., 2014[72] Full text	US, University of California San Diego,[g] Moores Cancer Centre, Palliative Care Clinic	Cross-sectional	1	114 Cancer (94% with 53% metastatic) Sickle cell (6%)	Age ⩾18 years, new consults	NA	To risk stratify possible opioid misuse and determine the most common patient risk factors associated with misuse utilizing the ORT	ORT
Nguyen et al., 2013[78] Full text	US, MD Anderson Cancer Centre, Supportive Care Clinic[a]	Cross-sectional	4	198 Advanced cancer	Age ⩾18 years, advanced cancer diagnosis, prescription for regular and/or as needed oral opioids for cancer pain prescribed the visit before. Patients who did not speak English or impaired cognition were excluded	NA	To evaluate frequency and severity of self-reported opioid deviation and barriers to opioid pain management	CAGE
Nunez Olarte et al., 2018[68] Abstract	Spain, Hospital General Universitario Gregorio Marañón, Early Palliative Care Clinic	Cross-sectional	7	100 Cancer (100%, staging not reported)	NA	NA	To audit quality of the prevention, detection and management of aberrant opioid induced behaviors	NS, urine drug test
Oberoi-Jassal et al., 2017[64] Abstract	US, Outpatient palliative clinic	Cross-sectional	48	963 Cancer (16% of patients were between 18 and 39 years)	Newly referred patients to clinic	NA	To determine the prevalence of illicit substance use and potential opioid misuse in adolescent and young adult cancer patients relative to adult patients and to examine correlates of use and misuse	Urine drug test

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Table 2. (Continued)

Author, year, reference type	Location, setting	Study design	Study duration (months)	Sample size population	Eligibility criteria	Comparator or control	Primary study objective	Assessment tools
Olczak et al., 2019[88] Full text	Poland Palliative Medicine Clinic, Palliative Medicine Department	Case report	NR	1 Metastatic cancer	NA	NA	To evaluate the decision to continue therapy with a short-acting fentanyl	Self-Designed Opioid Dependence Assessment
O'Mahony et al., 2018[71] Full text	US, Rush University Medical Centre, Senior Care Palliative Care Clinic	Cross-sectional	12	74 Palliative care (18% cancer, staging NR)[f]	Clinic patients seen by a single physician	NA	To investigate the use of opioid treatment plans that included validating a screening tool and urine drug tests	ORT, urine drug test
Pagan-Ferrer et al., 2017[57] Abstract	US, University of Texas Health Sciences Centre, Palliative Care Clinic	Cross-sectional	3	77: 61.0% considered for chronic opioid therapy Palliative care (77% cancer, staging NR)	All patients considered for chronic opioid therapy	NA	To report experience with instituting a safety assessment for patients being considered for chronic opioid therapy	ORT, urine drug test
Peck et al., 2019[87] Full text	US, University of Mississippi[g] Inpatient pain service, outpatient	Case report	NR	1 Metastatic cancer (diagnosed at 17 years old)	NA	NA	To illustrate how undertreated pain and treatment-related anxiety affected the opioid use of a young adult with cancer	SOAPP-R
Pelkofski et al., 2015[58] Abstract	US, University of Virginia Medical Centre, Gynecology Oncology or Palliative Care Clinics	Cross-sectional	5	53 Gynecologic cancers (staging NR)	Gynecologic cancer seen in gynecologic oncology or palliative care clinics, have existing active or receiving new opioid prescription	NA	To determine propensity for opioid abuse and evaluate risk factors	ORT
Rauenzhan et al., 2017[91] Full text	US, Virginia Commonwealth University,[g] National Cancer Institute Centre, Supportive care clinic	Cross-sectional	18	232 (82 patients had at least one urine drug test) Cancer ("active disease:" 59% appropriate urine drug test, 57% inappropriate urine drug test)	At least one urine drug test. Excluded if urine drug test ordered by another service, only seen by ancillary staff without a palliative physician or nurse practitioner visit, no diagnosis of cancer	NA	To characterize patients with abnormal urine drug tests; to describe non-prescribed opioids and illicit drugs identified by urine drug tests; to identify potential role for urine drug tests in therapeutic decision making	Urine drug test
Reddy et al., 2014[79] Full text	US, MD Anderson Cancer Centre, Supportive Care Clinic[a]	Cross-sectional	6	383 Cancer (89% advanced)	Age ⩾18 years, received opioids for ⩾1 month, able to read, write and converse in English, no cognitive impairment	NA	To determine patterns of storing, using, and disposing of opioids among cancer outpatients	CAGE
Reisfield et al., 2009[93] Full text	US, University of Florida Health Science Centre[g] Inpatient Hospice Facility	Case report	NR	1 Advanced cancer	NA	NA	Case discussion of abnormal urine drug test results	Urine drug test
Sager et al., 2019[92] Full text	US, VA Boston Healthcare System[g] Palliative Care Clinic	Case report	NR	1 Advanced cancer	NA	NA	To explores the case of a patient with opioid use disorder and pancreatic cancer	Urine drug test

(Continued)

Table 2. (Continued)

Author, year, reference type	Location, setting	Study design	Study duration (months)	Sample size population	Eligibility criteria	Comparator or control	Primary study objective	Assessment tools
Silvestre et al., 2017[80] Full text	US, MD Anderson Cancer Centre, Emergency Department	Cross-sectional	NR	203 Cancer (86% advanced)	Age ⩾18 years, received opioids for ⩾2 months, able to read, write and converse in English, no cognitive impairment	NA	To determine the patterns of storage, use, and disposal of opioids in patients presenting to emergency department	CAGE
Tsukanov, 2017[59] Abstract	US, Virginia Commonwealth University,[g] Supportive Care Clinic	Cross-sectional	NR	173 (49 urine drug test) Cancer (staging NR)	NR	NA	To describe urine drug test findings and subsequent changes in opioid management	Urine drug test
Tsukanov et al., 2018[67] Abstract	US, Virginia Commonwealth University,[g] Outpatient Palliative Care Clinic	Case report	NR	1 Advanced cancer	NA	NA	To identify the challenges of managing cancer pain in a patient with substance misuse	Urine drug test
Yennurajalingam et al., 2018[69] Full text	US, MD Anderson Cancer Centre, Supportive Care Clinic[a]	Cross-sectional	8	751 Current or past history of cancer	Age ⩾18 years, current or past diagnosis of cancer, received opioids for ⩾1 week, new consults	NA	To determine frequency and factors associated with aberrant behavior using SOAPP; to examine screening performance of CAGE compared to SOAPP as a gold standard	CAGE-AID, SOAPP
Yennu et al., 2018[65] Abstract	US, MD Anderson Cancer Centre, Supportive Care Clinic	Cross-sectional	27	1501 Cancer	Cancer, on opioids for pain for at least 1 week	Aberrant opioid behavior negative	To determine the association between current tobacco smoking, daily opioid use, pain response, and risk for aberrant opioid use behaviors among patients receiving outpatient supportive care consultation at a comprehensive cancer center	SOAPP
Yennu et al., 2019[66] Abstract	US, MD Anderson Cancer Centre, Supportive Care Clinic[a]	Cross-sectional	28	3588 Cancer	Cancer, on opioids for pain for at least 1 week	NA	To develop a nomogram to predict the probability of occurrence of inappropriate opioid use among patients receiving outpatient supportive care consultation at a comprehensive cancer center	SOAPP

CAGE: cut down, annoyed, guilty, and eye-opener (alcoholism screen); CAGE-AID: CAGE-adapted to include drugs (alcoholism and drug screen); DSM-5: diagnostic and statistical manual of mental disorders, Fifth Edition; MEDD: morphine equivalent daily dose; NA: not applicable; NR: not reported; ORT: opioid risk tool; SOAPP: screener and opioid assessment for patients with pain; SOAPP-SF: screener and opioid assessment for patients with pain—short form.

[a]This cancer center refers its palliative care service as "supportive care."[97]

[b]These studies defined "chronic opioid therapy" as treatment of pain with opioids for ⩾7 days.

[c]First weeks of October 2016, January 2017, and April 2017.

[d]Published article reports both 76 and 77 new patients. First author contacted and data could not be clarified.

[e]Data obtained by contacting first author.

[f]First author contacted and shared that common diagnoses seen in their clinic besides cancer are congestive heart failure, chronic obstructive pulmonary disease, chronic kidney disease, chronic liver disease, connective tissue disorders, and inflammatory bowel disease.

[g]First author's institutional affiliation. Exact location was not provided in the study.

impact of questionnaire results on opioid prescribing (*n* = 1, 3%).[54] Of these studies, only two evaluated the psychometric properties of the questionnaires that were used.[63,69] One study (3%) developed a nomogram based on SOAPP to determine probability of inappropriate opioid use.[66]

A majority of the studies routinely administered paper questionnaires to patients (*n* = 21, 66%),[53,54,57,58,61–63,65,66,69–72,73,74,75,78,81,82,85,89] particularly during initial clinic visits (*n* = 12, 38%),[62,63,66,69–72,74,75,78,81,89] or to specific patients being considered for (*n* = 2, 6%)[53,57] or receiving opioids (*n* = 7, 22%).[54,58,61,65,73,81,85] One study delivered the ORT through verbal, face-face interviews;[72] and, in one study, clinical assistants helped patients complete the ORT.[61] Twelve studies (38%) did not provide information about how they administered questionnaires to pati ents.[55,68,76,77,79,80,83,84,86,87–89] Furthermore, the studies used the questionnaires to measure multiple constructs related to problematic opioid use including ones that the questionnaires have not been validated to assess. Detailed findings about use of these questionnaires in palliative care are presented in the following sections and Table 3.

*Cut down, annoyed, guilty, and eye-opener (CAGE) (*n = *8).* We identified eight studies that adopted the CAGE as a proxy screening tool for problematic opioid use.[70,74–80] This questionnaire was previously validated for constructs related to problematic alcohol use, but not opioid use, in populations such as psychiatric inpatients and primary care outpatients (Supplemental Appendix D). Our included studies reported using the CAGE to assess for the following problematic opioid-related constructs in palliative care: misuse,[70,75] abuse,[75,79] addiction,[75] higher use,[78] and rapid dose escalation.[79] The CAGE was also reported as a measure of general substance abuse,[75,79] chemical coping,[76–78] and problematic alcohol use (Table 3).[74,75,78,79] We identified only one study conducted in a setting (emergency department) other than outpatient palliative care clinics (Table 2).[80] Excluding the two case series,[75,76] the sample sizes ranged from 76 to 432 participants with cancer; and, the reported prevalence of positive CAGE scores ranged from 10% to 19% in cross-sectional studies (*n* = 6).[70,74,77–80] One study had reporting errors that made data interpretation and synthesis challenging.[70]

CAGE scores were correlated with patient characteristics (age,[70] cancer diagnosis,[70] pain type,[70] treatment status[70]) and specific problematic opioid use (chemical coping,[77] opioid dose deviation[78]). Chemical coping was defined as "using prescribed opioids to control non-nociceptive symptoms."[77,96] While opioid dose deviation was defined as when "patient-reported [morphine equivalent daily dose (MEDD)]. . . falls 30% above or below the prescribed MEDD range."[78] One study compared the characteristics of CAGE-positive and CAGE-negative patients, including history of illegal drug use, use of strong opioids and MEDD.[74] Two studies assessed compared CAGE scores between patients with safe and unsafe opioid use and storage practices.[79,80] We identified no studies that evaluated the psychometric properties of the CAGE in the context of palliative care.

*Cut down, annoyed, guilty, and eye-opener-adapted to include drugs (CAGE-AID) (*n = *6).* We identified six studies that assessed the use of CAGE-AID in a palliative care context.[62,69,81–83,89] This questionnaire has been validated for problematic alcohol and general substance use but not opioid use in settings outside of palliative care (Supplemental Appendix D). Our included studies reported using the CAGE-AID to assess for the following constructs in palliative care: alcoholism,[69,82,83] general drug use,[69,81,83] rapid opioid dose escalation,[83] opioid abuse,[81,83] opioid misuse,[69,82] chemical coping,[69,82] high expression of symptom distress,[69] and maladaptive[81,82] or aberrant drug behaviors[62,69] (Table 3). All studies were conducted in outpatient palliative care clinics in a single US cancer center (Table 2).[62,69,81–83,89] Excluding the case series,[81] the studies had samples sizes ranging 100 to 751 patients with cancer; and the reported frequency of positive CAGE-AID scores ranged from 9.9% to 19.3% in all study participants in the case control (*n* = 2),[82,89] cross-sectional studies (*n* = 1),[69] longitudinal (*n* = 1),[68] and prospective cohort (*n* = 1)[83] studies.

In addition to reporting the CAGE-AID scores, one study correlated CAGE-AID scores with frequency of physicians ordering urine drug tests.[82] Two studies compared the prevalence of positive CAGE-AID scores before and after an intervention for problematic opioid use: one study assessed an education program about safe opioid use, storage and disposal;[83] the other assessed an interdisciplinary approach for patients with cancer with "aberrant opioid-related behaviors."[89] Only one study evaluated the psychometric properties of the CAGE-AID for identification of patients at risk of "aberrant drug behaviors" in the context of palliative care: specifically, the questionnaire's validity (sensitivity, specificity, positive, and negative predictive values) but not its reliability, responsiveness, and interpretability.[69] Although the SOAPP has not been validated in palliative care (refer to SOAPP section below), this study used the SOAPP questionnaire as the "gold standard" to determine whether patients had a high risk of "aberrant opioid use."[69]

*Opioid risk tool (ORT) (*n = *9).* We identified nine studies that assessed the use of the ORT in a palliative care context.[53,54,57,58,61,71,72,73,85] Previous attempts had been made to validate this tool as a measure of problematic opioid use in chronic non-cancer pain (Supplemental Appendix D). Our included studies reportedly used the ORT to assess for the following constructs in palliative care: opioid

Table 3. Reported characteristics and findings of problematic opioid use questionnaires used in palliative care.

Author, year	Reported use of questionnaire	Reported construct measured	Administration	Cut-off score	Frequency of positive scores
Cut down, annoyed, guilty, eye-opener (CAGE)					
Childers et al., 2015[70]	Report use and results; association with patient characteristics (age, cancer, pain type, treatment status—active or palliative)	Risk of opioid misuse	Patient completed questionnaire; all patients; initial clinic visit	⩾2	15% in all new patients[a]
Dev et al., 2011[74]	Report use and results; compare the following between CAGE positive and negative patients: sex, race, cancer type, history, and active tobacco use, history of illegal drug use, strong opioids before consult, median MEDD, use of ⩾ sedative, hypnotic, anxiolytic	Alcoholism	Patient completed questionnaire; all patients; initial clinic visit	⩾2	17% in all study participants; 64% tobacco use and 21% no tobacco use
Koyyalagunta et al., 2011[75]	Report use, results	Risk of opioid misuse, abuse, addiction; history of alcohol and substance abuse	Patient completed questionnaire; initial visit	NR	NA
Kwon, 2014[76]	Report use, results	Risk of chemical coping	Patient completed questionnaire	NR	NA
Kwon et al., 2015[77]	Report use, results; correlate with chemical coping	Risk of chemical coping	Patient completed questionnaire	NR	19.4% in all study participants ($n = 84$); 32% chemical coping ($n = 27$)[b]
Nguyen et al., 2013[78]	Correlate misuse of opioid analgesics (deviation from prescribed dose—30% above or below prescribed MEDD) with alcohol abuse/chemical coping (CAGE)	Recent history of alcoholism; diagnosis of alcohol abuse and/or dependence; chemical coping; higher mean opioid use	Patient completed questionnaire; all patients; initial clinic visit	⩾2	10% in all study participants; 16% of opioid deviators
Reddy et al., 2014[79]	Report and compare results of CAGE between patients with unsafe opioid storage and use, with those with safe storage and use	History of alcoholism; increase likelihood to engage in recreation drug use and thus risk of rapid opioid dose escalation and abuse; chemical coping	Patient completed questionnaire	NR	19% in all study participants; 10% unsafe storage; 40% unsafe use
Silvestre et al., 2017[80]	Report results; compare patients unsafe with safe use and storage (age, cancer type, race, sex, CAGE, history of illicit drug use, MEDD, level of education, marital status)	Not reported	Patient completed questionnaire	NR	14% in all study participants
CAGE-adapted to include drugs (CAGE-AID)					
Arthur et al., 2016[82]	Correlate results with urine drug test ordering	Risk of alcoholism; chemical coping; maladaptive drug behaviors; opioid misuse	Patient completed questionnaire; all patients; initial visit	⩾2	19% in all participants; 33% of patients who had urine drug tests done; 12% no urine drug tests done
Arthur et al., 2016[81]	Report use, results	Risk of illegal recreational drug use; maladaptive behaviors; opioid abuse	Patient completed questionnaire; patients on opioid therapy; initial visit	NR	NA
Arthur et al., 2018[89]	Compare results before and after intervention (interdisciplinary approach for patients with cancer with “aberrant opioid-related behaviors”)	NR	NR; initial, intervention and last visits	NR	14% in all participants; 30% aberrant behaviors; 7% control

(Continued)

Table 3. (Continued)

Author, year	Reported use of questionnaire	Reported construct measured	Administration	Cut-off score	Frequency of positive scores
De La Cruz et al., 2017[83]	Report results before and after intervention (educational program about safe opioid use, storage and disposal)	History of alcoholism or drug use; increase likelihood of recreational drug use, rapid opioid dose escalation and abuse	Patient completed questionnaire	NR	17.7% in all participants; 19.3% before intervention and 15.5% after intervention to manage aberrant behaviors
Edwards et al., 2018[62]	Evaluated frequency of CAGE-AID positivity and change in score between first inpatient supportive care consultation and first outpatient follow up visit within 3 months	Risk of aberrant drug related behaviors in cancer patients receiving opioids	NR; Inpatient supportive care consultation and first outpatient follow up within 3 months	⩾2 for males ⩾1 for females	9.9% inpatients; 13.1% outpatients
Yennurajalingam et al., 2018[69]	Report use, results; correlate results with SOAPP	Alcoholism; illicit drug use; maladaptive behavior; chemical coping; opioid misuse; high expression of symptom distress	Patient completed questionnaire; all patients; initial consult	⩾2	10.5%
Not specified					
Nunez-Olarte et al., 2018[68]	Report use	Opioid misuse, abuse	NR	NR	NR
Opioid craving 5-point Likert scale					
Go et al., 2018[84]	Report use	Opioid craving	NR	"It was difficult for me to forget about taking BTFC:" 1: not at all; 5: very much	NR
Opioid risk tool					
Barclay et al., 2014[85]	Report use and results including risk categorization and specific risk factors; correlate overall risk and risk factors with abnormal urine drug tests	Risk of opioid and substance misuse	Patient completed questionnaire; all patients receiving controlled substances	NR; cited low, moderate, high risk classifications	High risk 21%, moderate risk 22%, low risk 57%
Chua et al., 2019[61]	Report use and results	Risk stratifies for opioid abuse	Patient completed questionnaire with help from clinical assistants; new patients in palliative care clinic prescribed opioids by oncologists or palliative care providers	NR	High risk 6.67%, medium risk 15.56%, low 77.78%
Garcia et al., 2017[73]	Report use and results—categorize based on risk; correlate moderate and high-risk scores with patient demographics and clinical characteristics (race, smoking, insurance type, cancer, clinic performing screening)	Risk of opioid misuse; aberrant behaviors related to opioid use; opioid abuse	Patient completed questionnaire; patients enrolled in study and receiving opioid prescriptions	Low risk: ⩽3; moderate risk: 4–7; high risk: ⩾7	High risk 6%, moderate risk 7%, low risk 87%
Jablonski et al., 2018[54]	Report use, results, and impact on opioid prescribing	Risk of opioid abuse, misuse and diversion	Patient completed questionnaire; all patients prescribed chronic opioid therapy	Low risk: ⩽3; moderate risk: 4-7; high risk: ⩾7[c]	High risk 20%; low to moderate risk: 77%[c]

(Continued)

Table 3. (Continued)

Author, year	Reported use of questionnaire	Reported construct measured	Administration	Cut-off score	Frequency of positive scores
Langford et al., 2017[53]	Report use and results	Opioid safety, misuse	Patient completed questionnaire; all patients considered for chronic opioid therapy	NR	Min 0, 1st quartile 1, mean 4, 3rd quartile 8, max 14
Ma et al., 2014[72]	Report use and results of individual ORT items and overall risk categorization; compare risk groups (age, sex, presence of metastatic disease, pain score, cancer type)	Risk of opioid misuse and aberrant behavior; identify known risk factors for opioid misuse	Clinician administered questionnaire; all patients; initial clinic visit	Low risk: ⩽3; moderate risk: 4–7; high risk: ⩾8	High risk 24.6%, moderate risk 18.4%, low risk 57%
O'Mahony et al., 2018[71]	Report use and results	Risk of opioid dependence; substance abuse; observed aberrant behaviors	Patient completed questionnaire; initial consult	Low risk: ⩽3; moderate risk: 4–7; high risk: ⩾8	High risk 50%, moderate risk NR, low risk NR
Pagan-Ferrer et al., 2017[57]	Report use and results	Risk of abuse of narcotics; opioid safety, misuse	Patient completed questionnaire; all patients considered for chronic opioid therapy	NR	Min 0, 1st quartile 1, mean 3, quartile 7, max 14.
Pelkofski et al., 2015[58]	Report on use and results; correlate with patient characteristics (race, cancer status, insurance type, age)	Propensity for opioid misuse, abuse	Patient completed questionnaire; all patients on or receiving new prescription for opioids	Low risk: ⩽3; moderate risk: 4–7; high risk: ⩾7	High risk 7.5%; moderate risk 13%; low risk 79%
Screener and opioid assessment for patients with pain (SOAPP)					
Yennu et al., 2018[65]	Report use and results; correlate with ESAS pain scores, MEDD, smoking history, sex, anxiety, prior alcoholism/illicit drug use	Risk for aberrant opioid use behaviors	Patients with diagnosis of cancer, on opioids for pain for at least 1 week, referred to supportive care clinic	⩾7	16.8%
Yennurajalingam et al., 2018[69]	Report use and results; correlate with CAGE, gender, ESAS pain, ESAS depression, ESAS anxiety, ESAS financial distress	Alcoholism; illicit drug use; maladaptive behavior; chemical coping; opioid misuse; high expression of symptom distress	Patient completed questionnaire; all patients; initial consult	⩾7	19.6%
Yennu et al., 2019[66]	Report use and results; correlated with gender, race, marital status, smoking status, depression, anxiety, financial distress, MEDD and CAGE; develop nomogram to determine probability of inappropriate opioid use	Inappropriate opioid use	New patients referred to supportive care clinic	⩾7 Nomogram scores 58: probability of inappropriate opioid use is 0.1 88: probability of inappropriate opioid use is 0.2	20.4%
Screener and opioid assessment for patients with pain—short form (SOAPP-SF)					
Childers, 2015[70]	Report use and results; correlate with patient characteristics (age, cancer, pain type, treatment status)	Risk of opioid misuse	Patient completed questionnaire; all patients; initial clinic visit	⩾4	46%[a]

(Continued)

Table 3. (Continued)

Author, year	Reported use of questionnaire	Reported construct measured	Administration	Cut-off score	Frequency of positive scores
Dev, 2019[86]	Report use and results; correlate with smoking status (active, former, or non-smoker)	Risk of using medications in a non-prescribed manner, aberrant drug use, substance/opioid use disorder	NR	Positive: ⩾4	Positive: 73.9% of active smokers, 12.7% of former smokers, 9.3% of non-smokers
Greiner et al., 2020[63]	Report use and results; correlated high-risk SOAPP-SF scores with patient characteristics (age, gender, race, cancer stage, ESAS pain score, anxiety score, depression, score distress score) and "non-compliant" toxicology tests	Assess for opioid misuse, risk, predict noncompliant toxicology tests	Patent completed paper questionnaire; consult appointment; patients who spoke or read English	High risk: ⩾4	High risk: 28% of patients who completed SOAPP-SF; 35% of patients who completed SOAPP-SF and toxicology testing
Jablonski et al., 2018[54]	Report use and results; correlate with patient characteristics (age, cancer, pain type, treatment status like active or palliative); impact on opioid prescribing	Risk of opioid abuse, diversion, misuse	Patient completed questionnaire; all patients prescribed chronic opioid therapy	Low risk: <4; high risk: ⩾4[c]	Low risk: 70%[c] High risk: 30%
Koyyalagunta et al., 2011[75]	Report use, results	Identify high risk of opioid misuse, opioid abuse, addiction; likelihood of aberrant drug-related behavior	Patient completed questionnaire; initial visit	Low risk: <3; high risk: ⩾4	NA
Screener and opioid assessment for patients with pain—revised (SOAPP-R)					
Broglio, 2018[55]	Report use, results[d]	Opioid risk	NR; all patients	NR	NR
Peck et al., 2019[87]	Report use, results	Aberrant opioid-associated behavior	NR; pain consult	⩾18	Patient in case scored 15 but authors noted he endorsed several items associated with aberrant opioid-associated behavior
Self-designed opioid dependence assessment					
Olczak et al., 2019[88]	Report use	Addiction, opioid drug dependence	NR	3	NA

Cut down, annoyed, guilty, and eye-opener (CAGE, alcoholism screen); CAGE-AID: CAGE-adapted to include drugs (alcoholism and drug screen); ESAS: Edmonton symptom assessment system; MEDD: morphine equivalent daily dose; NA: not applicable; NR: not reported; ORT: opioid risk tool; SOAPP-14: screener and opioid assessment for patients with pain—14 questions; SOAPP-SF: screener and opioid assessment for patients with pain—short form.

[a]Study reports 76 or 77 new patients were seen. Of these patients, 57 patients completed the SOAPP-SF and 32 completed the CAGE.

[b]27 patients were diagnosed with chemical coping and had positive CAGE scores. There was a total of 84 patient with positive CAGE scores and total of 76 patients with chemical coping based on the protocol definition.

[c]Information obtained through direct communication with first author. ORT was obtained for 26 patients, not 30. SOAPP-SF was obtained for 30 patients.

[d]The first author shared that they used the SOAPP-R through direct communication.

abuse,[54,58,61,73] dependence,[69] misuse,[53,54,57,58,72,73,85] diversion,[54] aberrant behaviors,[71–73] and safety.[53,57] Three studies used the ORT to measure general substance abuse[71] and misuse (Table 3).[85] All studies were cross-sectional studies that were conducted in outpatient palliative care clinics in the US (Table 2).[53,54,57,58,61,71–73,85] The sample sizes ranged from 30 to 231, with the primary study population in eight studies being patients with cancer.[53,54,57,58,61,72,73,85] One study was conducted in a geriatric palliative care clinic and only 18% of participants had current or prior cancer diagnoses. Details about the remaining participants' medical diagnoses were not provided.[71]

ORT administration in palliative care varied between the studies. Though the ORT was mainly self-administered by patients (n = 7);[53,54,57,58,71,73,85] one study had clinicians administer the questionnaire[72] and another had clinical assistants help patients complete the ORT.[61] Three studies administered the ORT for participants who were being considered for[53,57] or already receiving chronic opioid therapy;[54] whereas, three studies administered the ORT to participants who had existing active or were receiving new opioid prescriptions.[58,61,73] One retrospective study collected data on ORT administered to all participants who received a controlled substance. If ORT scores were missing, medical records were reviewed to calculate it.[85] Information about study participants' opioid histories were not provided in two studies.[71,72]

Based on their ORT scores, patients were categorized into low, medium, or high risk of developing aberrant behavior if prescribed chronic opioid therapy (Table 3 provides cut-off values used in the studies). The reported frequency of high-risk individuals in seven studies ranged from 6% to 50%.[54,58,61,71,72,73,85] The ORT scores in two studies were not interpretable as they were reported as interquartile ranges.[53,57] Additionally, the ORT scores were correlated with urine drug test results,[85] participant demographics (e.g. age,[58,72] sex,[72] race,[58,73] insurance type,[58,73] smoking[73]) and clinical characteristics (e.g. cancer diagnosis,[72,73] presence of metastatic disease,[72] pain score[72]). We identified one study that performed the ORT to determine if the results influenced opioid prescribing decisions for outpatient palliative care patients who were already on chronic opioid therapy.[54] Of the 30 patients, 20% were deemed high-risk on the ORT and opioid prescribing decisions were changed for 33% of these patients. However, the most common prescribing decision for the high-risk participants was to maintain the same opioid dose.[54] We did not identify any studies that examined the psychometric properties of the ORT in the context of palliative care.

*Screener and opioid assessment for patients with pain (SOAPP) (*n *= 10).* We identified ten studies that assessed the use of SOAPP in palliative care: three on the SOAPP,[65,66,69] five on the SOAPP-Short Form (SOAPP-SF),[54,63,70,75,86] and two on the SOAPP-Revised (SOAPP-R).[55,87] The SOAPP was originally developed to assess risk or predict problematic opioid use; it was subsequently shortened (SOAPP-SF) and revised (SOAPP-R) (Supplemental Appendix D). Our included studies reportedly used the SOAPP and its variants to assess for the following constructs in palliative care: opioid misuse,[54,63,69,70,75] abuse,[54,75] diversion,[54] risk[63]; inappropriate opioid use[66]; risk of aberrant opioid-related behaviors[65,87] and opioid use disorder[86]; and, general drug-related aberrant behaviors (Table 3).[65,69,75,86] One study used a total SOAPP score of $\geqslant$7 as their "gold standard" to identify participants with a high risk of "aberrant opioid use."[69] All studies were conducted in outpatient palliative care clinics in the US (Table 2). Excluding the case series,[75] the sample sizes ranged from 30 to 1051 patients with cancer; and, the reported frequency of positive or "high-risk" scores on the SOAPP and its variants ranged from 9.3% to 46% in the cross-sectional studies.[54,55,65,69,70,75]

In addition, the scores from SOAPP and its variants were correlated with patient demographics (e.g. age,[63,70] gender[63]), clinical characteristics (e.g. cancer diagnosis,[63,70] cancer treatment status,[70] pain type[70]), Edmonton Symptom Assessment System scores,[63,69] and concurrent substance use (alcohol,[65] tobacco,[86] illicit drug use[65]). One study assessed the impact of SOAPP-SF scores on opioid prescribing.[54] We identified one study that found SOAPP-SF score of $\geqslant$4 was not significantly associated with "noncompliant" toxicology tests (p = 0.83); however, a threshold of $\geqslant$3 was most associated with "aberrant toxicology tests" in an outpatient palliative care clinic in a cancer institute (OR 5.14, 95% CI [1.86 to 14.26], p = 0.002; sensitivity 0.75, specificity 0.64).[63] "Aberrant toxicology tests" were defined as the absence of prescribed opioid, presence of non-prescribed opioid, presence of cannabis, and other substances (presence of cocaine, non-prescribed benzodiazepine, ethanol).[63] When the presence of cannabis was not considered aberrant, SOAPP-SF $\geqslant$3 was still found to be significantly associated with abnormal urine drug tests.[63]

*Urine drug tests (*n *= 21)*

Urine drug tests are clinical tools that are used to monitor compliance with prescription opioid therapy, development of problematic opioid use and use of non-prescription drugs.[97] Two common types of urine drug tests are: immunoassays, which are used at the point of care, and gas-chromatography/mass-spectroscopy (GC-MS), which are processed at a laboratory.[97] We identified 21 studies that examined urine drug test use in a palliative care setting.[17,53,55–57,59,60,63,64,67,68,70,71,81,82,85,89–93] The majority of studies were conducted in the US (n = 19, 91%),[17,53,55–57,59,60,63,64,67,70,71,81,82,85,89,91–93] and in outpatient clinics (n = 20, 95%) (Table 2),[53,55–57,59,60,63,64,67,68,70,71,81,82,85,89–93]

and published between 2016 and 2020 (*n* = 18, 86%).[17,53,55–57,59,60,63,64,67,68,71,81,82,89–92] The main population was patients with cancer, but two studies (14%) did not specify their participants' medical diagnoses.[55,71] One case report was about the ethical challenges of opioid prescribing for a young patient with muscular dystrophy where clinicians were concerned about drug diversion by his mother.[90] The most common study design was cross-sectional (*n* = 13, 62%) (Table 2).[53,55–57,59,60,63,64,68,70,71,85,91]

The reported primary study objectives were: to identify factors associated with ordering urine drug tests;[82] to report on the use of urine drug tests;[17,53,55,57,59,64,67,68,71,85,90,92,93] and to correlate abnormal urine drug tests with patient characteristics, including age,[64,70,89] gender,[64,60] marital status,[64] cancer diagnosis,[70] type of pain,[70] symptoms (e.g. anxiety, appetite),[60] treatment status (active or palliative),[70] and problematic opioids risk tools (ORT,[85] SOAPP-SF[63]) (Table 2). One study compared the characteristics of patients with "appropriate" and "inappropriate" urine drug tests.[91] "Inappropriate" urine drug tests were defined as the presence of non-prescribed drugs (e.g. opioid, benzodiazepine, cannabis, cocaine) and absence of prescribed opioids.[91] Another study examined the impact of an interdisciplinary approach for patients with cancer on their aberrant opioid-related behavior, which included abnormal urine drug tests.[89]

The type of urine drug tests used to detect prescription and illegal drugs was reported in six (29%) studies (Table 4).[59,63,70,82,91,93] Two studies (10%) conducted in the same supportive care clinic first performed immunoassays and then confirmed the results with GC-MS.[82,91] The other four studies (19%) reported use of only GC-MS.[59,70,93] The urine drug test type used in the remaining 15 studies (71%) was not reported.[17,53,55–57,60,64,67,68,71,81,85,89,90,92]

The 21 studies varied in terms of how they incorporated urine drug tests into clinical care (Table 4). Six studies (29%) routinely used urine drug tests in clinical care: four studies ordered urine drug tests for all clinic patients;[55,56,63,64], and, the two other studies ordered urine drug tests for all patients being considered for chronic opioid therapy.[53,57] In contrast, 11 studies (52%) ordered urine drug tests based on clinician discretion and the presence of specific patient factors.[17,59,60,70,81,82,85,89–92] These factors included: problematic behavior (e.g. early refill requests),[59,82,90,91] history of substance use disorder,[17,59,85,91,92] high-risk classification based on ORT[85] results, CAGE positivity,[59,91] and abnormal findings on prescription drug monitoring programs.[85] One study did not specify how clinicians estimated patients' risk for non-medical use to order targeted urine drug tests.[60] Urine drug test ordering was also associated with the following patient characteristics: non-cancer diagnoses,[70] early-stage cancer or no evidence of disease,[82] non-cancer pain,[70] active treatment status,[70] younger age,[82] African American race,[82] less education,[82] high pain intensity,[82] and less fatigue.[82] Three case reports reported on the use of urine drug tests to help manage patients with a history of OUD.[17,67,92]

The overall frequency of abnormal urine drug test results ranged from 8.6% to 70% (Table 4). These abnormal results can be classified into four categories: (1) prescribed opioid absent from the urine (reported frequency 6.1% to 39%);[56,59,60,63,70,82,91] (2) opioid not prescribed for the patient present in the urine (reported frequency 0% to 44%);[56,59,60,70,71,82,91] (3) benzodiazepine not prescribed for the patient present in the urine (reported frequency: 0% to 12.2%);[56,63,70,71,91] (4) illegal drug present in the urine (reported frequency: 18% to 61%).[56,59,60,63,70,71,82,85,91] The most common drug considered illegal in the studies was cannabis, with a reported frequency of 9.5% to 68%.[56,60,63,70,82,91] Other drugs detected were alcohol (1.4% to 4%),[63,71] cocaine (1.4% to 24.4%),[56,63,70,82,91] amphetamines (0% to 8%),[56,82] heroin (0.20% to 22%),[56,70,91] and phenobarbital.[70] One study found that adolescents and young adult patients with cancer compared to adult patients with cancer have higher prevalence of positive urine drug tests for cannabis (OR = 1.79; 95% CI = 1.19–2.69) and amphetamines (OR = 2.94, 95% CI = 1.15–7.49).[64] Besides young age,[64,91] other factors associated with abnormal urine drug test results were non-white race,[56,91] cancer treatment status,[70] ORT risk stratification,[85] SOAPP-SF question about smoking[63] and family history of "alcohol abuse."[85] One study found that if the presence of cannabis was not considered aberrant, then abnormal urine drug test results were also associated with distress, smoking, and SOAPP-SF question about not taking medications as prescribed.[63]

Discussion

Using established methodology, our scoping review of literature published up until January 31, 2020 identified 42 studies that reported on the use of tools that assessed for the presence or risk of problematic opioid use in palliative care. The main types of tools used were questionnaires and urine drug tests. The primary objectives of only half (*n* = 22; 52%) of the studies were to evaluate the use of these tools in palliative care. The remaining studies only reported on the use of these tools in the context of patients with problematic opioid use. Most of the studies (*n* = 34, 81%) were published within the last 5 years and were conducted in US outpatient palliative care clinics for patients with cancer. A minority of participants across ten studies had early-stage cancers, and only two studies focused on patients without cancer. These findings underscore the need for high-quality studies about assessment tools for problematic opioid use in palliative care, particularly in countries outside of the US and for patients with early stage, advanced cancers, and non-malignant conditions.

Table 4. Reported characteristics and findings of urine drug tests used in palliative care.

Author, year	Urine drug test type	Assessment of urine drug test	Factors associated with urine drug test ordering	Frequency of abnormal findings					Factors associated with abnormal findings
				Overall	Prescribed opioid absent	Non-prescribed opioid present	Non-prescribed benzodiazepine present	Illegal drug present	
Arthur et al., 2016[82]	Immunoassay; GC-MS	Determine factors associated with urine drug test ordering	Clinical suspicion for aberrant opioid use	54%	27%	25%	NR	48% (of these 68% marijuana, 20% cocaine, 8% amphetamine, 4% phencyclidine)	None identified
Arthur et al., 2016[81]	NR	Report use, results	Observed problematic opioid-related behaviors	NA	NA	NA	NA	NA	NA
Arthur et al., 2018[60]	NR	Report use of targeted and random urine drug tests and their results; correlate with patient characteristics (e.g. gender, symptoms)	Targeted urine drug tests ordered based on MD's estimation of patient's risk for nonmedical opioid use; all patients eligible for random urine drug tests	28%	Targeted: 27% Random: 20%	Targeted: 31% Random: 31%	NR	Targeted: 43% (71% marijuana) Random: 50% (91% marijuana)	Urine drug test abnormality associated with age (OR = 0.97 per year, $p = 0.012$), female gender (OR = 0.47, $p = 0.006$), anxiety (OR=1.11 per point, $p = 0.039$), and appetite (OR = 1.14 per point, $p = 0.006$). No significant differences in characteristics between random and targeted patients with abnormal urine drug test findings.
Arthur et al., 2018[89]	NR	Correlate abnormal results with patient characteristics (e.g. age, gender); impact of intervention on abnormal urine drug test	Used to identify aberrant behaviors	Pre-intervention: 46.7% Post-intervention: 8.7%	NR	NR	NR	NR	NR
Barclay et al., 2014[85]	NR	Report use, results; correlate abnormal results with ORT	ORT risk stratification, past history of substance abuse or abnormal drug screening, abnormal findings on prescription monitoring	45.7%	NR	NR	NR	37%[a]	ORT risk stratification (7% low risk vs 62.5% med-high risk, $p = 0.0005$); family history of alcohol abuse ($p = 0.031$); personal history of illegal drug use ($p < 0.0001$); indigent status did not correlate with abnormal urine drug tests ($p = 0.152$)

(Continued)

Table 4. (Continued)

Author, year	Urine drug test type	Assessment of urine drug test	Factors associated with urine drug test ordering	Frequency of abnormal findings					Factors associated with abnormal findings
				Overall	Prescribed opioid absent	Non-prescribed opioid present	Non-prescribed benzodiazepine present	Illegal drug present	
Boerstler et al., 2020[90]	NR	Report use	MD suspicion of drug diversion by 19 years old patient's mother/ surrogate; random ordering	NA	NA	NA	NA	NA	NA
Broglio et al., 2018[55]	NR	Report use	Routine ordering for all patients	NA	NR	NR	NR	NR	NR
Childers et al., 2015[70]	GC-MS	Report use, results; correlate with patient characteristics (e.g. age, cancer diagnosis, treatment status, type of pain)	Physician discretion; ordering more likely for patients without cancer and non-cancer pain	56%	22%	15%	4%	45% (4% cocaine, 15% marijuana, 22% heroin or metabolite, 4% other substance including phenobarbital)	Treatment status
Donovan et al., 2017[56]	NR	Report use, results	Routine for all patients	NR	6.1%	19.9%[b]	19.9%[b]	23.6% (19.9% marijuana, 1.4% cocaine, 2.1% amphetamines, 0.20% heroin)	Age ($p < 0.0001$); ESAS total score ($p = 0.00$); ESAS pain score ($p = 0.04$)
Gabbard et al., 2019[17]	NR	Report use	Weekly test for patient with history of heroin addiction and problematic opioid use	NA	NA	NA	NA	NA	NA
Greiner et al., 2020[63]	MS (urine, blood or saliva)	Report use; correlate SOAPP-SF scores with "non-compliant" or "aberrant" toxicology screens "Aberrant" defined as "presence of non-prescribed opioid, absence of prescribed opioid, presence of marijuana and other (presence of cocaine, non-prescribed benzodiazepine, ethanol)"	All new patients at 1 of 3 subsequent visits or within 6 months of initial consult	32.5%	19%	NR	11%	59% marijuana 7% cocaine 4% ethanol	"Non-compliant" screens associated with SOAPP-SF question about smoking habit ($p = 0.020$)

(Continued)

Table 4. (Continued)

Author, year	Urine drug test type	Assessment of urine drug test	Factors associated with urine drug test ordering	Frequency of abnormal findings					Factors associated with abnormal findings
				Overall	Prescribed opioid absent	Non-prescribed opioid present	Non-prescribed benzodiazepine present	Illegal drug present	
Langford et al., 2017[53]	NR	Report use, results	All patients considered for chronic opioid therapy	NA	NR	NR	NR	NR	NR
Nunez-Olarte et al., 2018[68]	NR	Report use	NR	NA	NR	NR	NR	NR	NR
Oberoi-Jassal et al., 2017[64]	NR	Report use; correlate abnormal results with patient characteristics (e.g. age, marital status); compare abnormal results between adolescent and young adult (AYA) patients and adult patients	Consecutive newly referred patients to outpatient palliative care clinic	31% AYA 19% adults	NR	AYAs not more likely than adults (OR = 1.07; 95% CI = 0.70–1.65)	NR	AYAs more likely to have positive results for marijuana (OR = 1.79; 95% CI = 1.19–2.69) and amphetamines (OR = 2.94; 95% CI = 1.15–7.49). AYAs were no more likely than adults to test positive for cocaine, barbiturates, or heroin	Male sex and being single associated with illicit substance use ($p < 0.05$). No symptoms scores, demographic and clinical characteristics were significantly associated with misuse
O'Mahony et al., 2018[71]	NR	Report use, results	NR	17.6% had "unexpected findings"	NR	0% pre-intake 0% post-intake	0% pre-intake 0% post-intake	10.8% pre-intake 17.6% post-intake[c] Alcohol: 1.4% pre-intake, 0% post-intake Barbituates: 0% pre-intake, 1.4% post-intake Cannabis: 9.5% pre-intake, 9.5% post-intake Amphetamines: 0% pre-intake, 0% post-intake Cocaine: 5.4% pre-intake, 8.1% post-intake	NR
Pagan-Ferrer et al., 2017[57]	NR	Report use, results	All patients considered for chronic opioid therapy	8.6%	NR	NR	NR	NR	NR

(Continued)

Table 4. (Continued)

Author, year	Urine drug test type	Assessment of urine drug test	Factors associated with urine drug test ordering	Frequency of abnormal findings					Factors associated with abnormal findings
				Overall	Prescribed opioid absent	Non-prescribed opioid present	Non-prescribed benzodiazepine present	Illegal drug present	
Rauenzahn et al., 2017[91]	Immunoassay; GC-MS	Compare patients with "appropriate" and "inappropriate" urine drug test results	Clinical judgement based on patient behavior or history of chemical coping (illicit drug use, CAGE score)	70%	39%	13%	7.3%	40.8% cannabis; 12% benzodiazepine; 30% cocaine; 10.2% heroin; 6.1% alcohol; 42.9% polysubstance	Younger age ($p = 0.004$); non-white race ($p = 0.007$)
Reisfield et al., 2009[93]	GC-MS	Report use, results	NR	NA	NA	NA	NA	NA	NA
Sager, 2019[92]	NR	Report use	Regular urine drug test for patient with OUD including IV heroin use	NA	NA	NA	NA	NA	NA
Tsukanov et al., 2017[59]	MS	Report use, results	Patients at risk of substance misuse: those with aberrant behavior, past history of substance abuse and CAGE-AID positivity	69%	38%	44%	NR	61% (cocaine most common)	NR
Tsukanov et al., 2018[67]	NR	Report use	Urine drug tests done at initial consult and then "frequent[ly]" for follow up of a patient with history of polysubstance misuse	NA	NA	NA	NA	NA	NA

CAGE: Cut down, annoyed, guilty, and eye-opener (alcoholism screen); CAGE-AID: CAGE-adapted to include drugs (alcoholism and drug screen); GC-MS: gas chromatography-mass spectroscopy; NR: not reported; NA: not applicable as case report/series.

[a]37% of all urine drug tests had marijuana. About 62% of abnormal urine drug tests had marijuana as the only abnormality.

[b]Non-prescribed opioids and benzodiazepines are reported together.

[c]Article reports the following prevalence of substances detected in urine drug test pre- and post-intake: illicit drug use (10.8% and 17.6%), cocaine (5.4% and 8.1%), marijuana (9.5% and 9.5%), amphetamines (0% and 0%), barbituates (0% and 1.4%) and alcohol (1.4% and 0%). "Illicit drug use" is not defined in the article.

Synthesis of knowledge about questionnaires used to assess for problematic opioid use

Of the 42 included studies, we identified 32 studies that used questionnaires to assess for problematic opioid use in palliative care. The main questionnaires used were CAGE and its variant (CAGE-AID), ORT, SOAPP and its variants (SOAPP-SF, SOAPP-R). The following is an appraisal of these questionnaires in the context of previously published literature.

CAGE and CAGE-AID. The CAGE and CAGE-AID questionnaires were originally developed to identify patients with problematic alcohol and general substance use[98–100] and have not been validated to specifically assess for problematic opioid use.[101] Yet we identified 14 palliative care studies that used the CAGE[70,74–80] and CAGE-AID[62,69,81,82,83,89] to measure problematic opioid-related constructs including opioid abuse,[75,79,82,83] misuse,[69,70,75,81] aberrant drug related behaviors,[62] and chemical coping.[69,76–78,82] All the studies about CAGE-AID were conducted in one tertiary cancer center's palliative care clinic.[60,62,69,81–83] Additionally, one study evaluated the validity of the CAGE-AID to identify patients at risk for "aberrant opioid and drug use behaviors" by comparing it to the SOAPP.[69] However, the measurement properties of SOAPP have not yet been formally evaluated in palliative care and therefore should not be used as a "gold standard"[69] to determine whether patients are at high risk for problematic opioid use. Based on these findings, there is limited evidence to support the use of CAGE and CAGE-AID to measure problematic opioid use in palliative care.

ORT. The ORT is a patient-completed questionnaire developed to identify patients prescribed opioids for chronic pain who are at risk of "aberrant behaviors."[20] Though the original study reported that the ORT has a high degree of sensitivity and specificity ($c = 0.82$ males, $c = 0.85$ females), follow-up studies did not demonstrate that the clinician- nor the patient-completed ORT were predictive of the presence of problematic opioid-related behaviors in patients receiving chronic opioid therapy for non-cancer pain.[20,102,103] Despite this weak evidence to support its use, nine studies in our review used the ORT in outpatient palliative care clinics[53,54,57,58,61,71,72,73,85] to assess for problematic opioid-related constructs, such as abuse,[54,58,61,73] dependence,[71] and diversion.[54] One study found that patients stratified as moderate-high risk on the ORT were more likely to have abnormal urine drug test results.[85] However, none of the studies evaluated the questionnaire psychometric properties.

SOAPP. The SOAPP questionnaires were designed to predict which patients with chronic pain would develop "aberrant behaviors and substance misuse" while on long-term opioid therapy.[104,105] We identified use of multiple versions of the SOAPP to evaluate risk of problematic opioid use in palliative care: the original, conceptually-derived SOAPP, and its shortened version, SOAPP-SF, and the empirically-derived, revised version, SOAPP-R. We identified one study that evaluated the psychometric properties of the SOAPP-SF: SOAPP-SF threshold of $\geqslant 3$ was significantly associated with abnormal urine drug test results in a US cancer institute's outpatient palliative care clinic.[63] However, the correlation between SOAPP-SF scores, abnormal urine drug test results and problematic opioid use by the patients receiving palliative care was not evaluated.

Synthesis of knowledge about urine drug tests used to assess for problematic opioid use

Urine drug tests were another tool used to identify patients who have or are at risk of problematic opioid use in palliative care. Our review found 21 studies that examined the use of urine drug tests in palliative care. The reported overall prevalence of abnormal urine drug tests in palliative care ranged from 8.6% to 70%. Possible explanations for this high reported prevalence in palliative care include patient selection bias and inclusion of cannabis as an abnormal urine drug result. Regarding patient selection bias, most of the included studies ($n = 11$, 52%) reported that urine drug tests were ordered at the discretion of the clinician and specific factors were present, such as observed aberrant behavior,[59,82,90,91] history of substance use disorder,[17,59,85,91,92] and patient characteristics, particularly younger age,[82] African American race,[82] and less education.[82] These results raise concern of the role of stigma, racism, and stereotyping in patient selection for targeted testing. They highlight the need for evaluation of this practice, which can contribute to inequitable access and delivery of palliative care and further stigmatization of marginalized populations. Adoption of an universal precautions approach where all patients are tested, similar to what has been advocated for in chronic non-cancer pain, can potentially reduce stigma, improve patient care and manage opioid-related risk.[106]

Another potential contributing factor to the high prevalence of abnormal urine drug test results in palliative care is the inclusion of cannabis as an "illicit drug."[56,60,63,70,82,91] Cannabis use is common among patients with cancer: 66% have used cannabis at some point in their lives and 24% consider themselves to be active cannabis users.[107] It is legal for medicinal purposes in many high-income countries, including several states in the US, where most of these studies were conducted.[108] Therefore, use of urine drug tests to identify patients who have or are at risk of problematic opioid use need to be validated. Future

studies about urine drug testing in palliative care should clearly define "abnormal" results and consider categorizing these results as how we presented them in our review: prescribed opioids absent, non-prescribed opioid present, non-prescribed benzodiazepine present and illegal drugs present.

Strengths and limitations

Strengths of our study included use of an established methodology for scoping reviews to identify and map existing knowledge.[36,37,39] In addition to conducting comprehensive searches of bibliographic databases from inception to January 31, 2020 and of grey literature, we performed hand searches of references. Study eligibility criteria were broad to capture the extent, range, and nature of the available evidence. We did not restrict study inclusion based on language, location, or study design. The reporting guideline PRISMA-Scr was used to standardize reporting of this review.

Our study also has limitations. Our review focused on patients receiving palliative care who are at risk of or have problematic opioid use, including those with active opioid use disorder. We excluded studies that focused on patients with clinically stable opioid use disorder (e.g. long-term remission) and non-patient populations, such as caregivers and health care providers. Therefore, our study does not capture the entire scope of problematic opioid use in palliative care. Further, our search would not have identified studies that were not indexed as "palliative care," which may have included studies about patients receiving primary (non-specialist) palliative care. This may have contributed to the lack of studies including patients with non-malignant life-threatening conditions.[109] Additionally, we did not conduct a critical appraisal of the included studies as this was beyond the remit of our scoping review. We did not find studies in non-English languages, which may reflect the databases that we searched.

What this study adds

To our knowledge, this study is the first scoping review that identifies tools that have been used to assess for the presence or risk of problematic opioid use in palliative care. We retrieved mainly observational studies that adopted use of questionnaires that were originally developed in the chronic non-cancer pain population. No identified studies adequately assessed the psychometric properties of these questionnaires in palliative care, and none were identified that reported on tools developed specifically for palliative care populations. Despite the paucity of evidence, palliative care experts, and organizations are recommending the use of tools developed for chronic pain populations[17,21,22] in response to increasing concerns about harms associated with opioids;[8–11] our findings suggest that these recommendations are premature. Similarly, palliative care services are increasingly adopting the use of urine drug tests. However, the purpose, administration and impact of urine drug tests on patients receiving palliative care are not clear from the current evidence.

This review highlights significant gaps in knowledge. The duration of palliative care involvement can now range from hours to years, given the increasing and earlier integration of palliative care in life-threatening non-malignant and malignant conditions. Therefore, patients receiving palliative care may be at risk of opioid-related harms that differ from those of chronic pain populations, and that may vary according to country, palliative care setting and stage of illness. The development and validation of tools to assess for problematic opioid use in palliative care are the first critical steps to measure the extent of this problem, and to inform prevention and management strategies in this diverse population.

Acknowledgements

The authors would like to thank Canadian Virtual Hospice, Canadian Hospice Palliative Care Association (Ms. Sharon Baxter) and Canadian Society of Palliative Care Physicians (Dr. David J. Henderson) for their roles as key stakeholders in this review. The authors would also like to thank Dr. Christopher Blake for his assistance with record screening.

Authorship

The conception and design of the study was conducted by JL, PM, ADF, CZ, and RF. Searches of the bibliographic databases and grey literature were performed by RF. Records were screened by JL, PM, SR, ADF, and AT. Data analysis was completed by JL, PM, RF, and AS. ADF and CZ provided methodological support throughout the study. JL drafted the manuscript, which was then revised critically for intellectual content by PM, SR, AS, AJS, AT, RF, ADF, and CZ. All authors approved the final version and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Canadian Institute of Health Research [grant number OCK_156774] for Dr. J Lau.

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Supplemental material

Supplemental material for this article is available online.

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