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Review article

A systematic review of substance use and substance use disorders in patients with cancer

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ABSTRACT

Objective: Few studies examined substance use in cancer patients. The aims of this systematic review were to summarize this evidence, identify methodological limitations, and provide future research directions.
Method: Articles on substance use in cancer (focused on illicit substance, opioid, and alcohol use) were searched in Medline, PsycINFO, and PsycARTICLES.
Results: On the basis of inclusion criteria, 28 studies were reviewed. Twenty-one contained empiric data from 500,123 participants; seven were review or conceptual papers. All studies were published between 1995 and 2018. Quality assessment revealed relatively low risk of bias and high methodological quality. Five studies examined substance use or substance use disorder (SUD) broadly. Mean ages ranged from 17.6 to 74.7 years. Substance use rates ranged from 2% to 35%, with a median opioid rate of 18% and 25.5% for alcohol. Nine of the studies had samples comprised either mostly or exclusively of advanced cancer patients. Disease groups included breast, head & neck, and gastric cancer. None of the studies used a theoretical framework or model.
Conclusions: Given the prevalence of substance use in cancer patients, interventions are needed. Further theory-grounded studies are warranted to foster the translation of research into clinical practice and elucidate substance use management recommendations.

1. Introduction

According to the World Health Organization (2019), substance use disorders (SUDs) involve "harmful use" and are associated with health consequences [1]. Substance use and SUDs are pervasive across the cancer continuum, with increasing concern given the opioid epidemic [2]. While use of some substances, such as alcohol, may predispose individuals to cancer, [3] substance use can also develop after a cancer diagnosis in the setting of cancer pain management. Additionally, individuals with cancer may use substances in attempts to cope with psychological distress or poorly-controlled physical symptoms, sometimes referred to as "chemical coping". As of 2014, substance use disorder rates have been reported to be as high as 35% among cancer populations [4], compared to 8.4% for the general population [5].

Many deleterious consequences are associated with substance use comorbid with cancer. First, substance use can complicate the course of cancer [66], for instance compromising treatment adherence [6]. Relatedly, substance use may lead to comorbidities that negatively impact cancer care, including Hepatitis C and other infections [7]. Relatedly, substance use is associated with decreased immune function; previously demonstrated in non-cancer populations [8–10]. Second, substance use may also obstruct pain and symptom management [11]. Finally, it can negatively impact quality of life [12]. In sum, substance use may introduce potential consequences for cancer treatment efficacy and follow-up or rehabilitation.

Prior work extensively examined associations between substance use and cancer. However, most research investigated relationships between substance use and cancer *risk* or *incidence*. For instance, Scoccianti and colleagues reviewed the association between alcohol use and onset of cancer [3]. Other reviews similarly examined associations between cannabis use and cancer onset [e.g., 13]. Finally, most studies examined relationships between tobacco use and cancer [14], particularly lung cancer, and numerous reviews have supported these associations [15]. Therefore, most literature on this intersection is focused on cancer risk.

Oncology clinicians often encounter substance use or substance use disorder (SUD) in their patients. A study of Hospice & Palliative Medicine fellows across 34 programs revealed that 77.2% of fellows

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treated at least one patient with SUD and 43.9% treated a patient who may have been "misusing" opioids [16]. Of note, pseudo-addiction may complicate estimation of substance use disorder rates and prevalence [17–19]. In another study, a quarter of individuals with cancer (26%) reported borrowing an anxiolytic from a family member [6]. Despite these observations, a recent study of 157 physicians and nurse practitioners from national palliative care organizations revealed that only 27% reported having training or systems in place to address addiction in cancer survivors on long-term opioid therapy [20].

1.1. Purpose of present study

Given the clinical relevance of substance use and SUDs in oncology care, we conducted a systematic review of the literature to address the following three questions:

1. What is the rate of substance use or substance use disorders in individuals with cancer?
2. What are the risk factors for substance use or substance use disorders in individuals with cancer?
3. Are there efficacious or recommended treatments for substance use or substance use disorders in individuals with cancer?

2. Methods

According to the statement of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [21], we conducted a systematic literature review using Medline, PsycINFO, and PsycARTICLES databases to identify peer-reviewed articles that examined substance use or substance use disorders in cancer populations in the last 50 years. For all three databases, the exact search date was January 1, 1968 to December 1, 2018. We excluded nicotine and cannabis, limiting substances evaluated to alcohol and other drugs, including prescription medications. A Boolean search strategy was conducted with the following keywords and logic: ("drug" OR "alcohol" OR "addiction" OR "alcoholism" OR "anabolic steroids" OR "cocaine" OR "dependence" OR "drugs of abuse" OR "drug use" OR "ecstasy" OR "fentanyl" OR "heroin" OR "illicit" OR "intoxication" OR "K2" OR "narcotic" OR "prescription drug use" OR "psychedelic" OR "street drug" OR "withdrawal" OR "opioid" OR "substance") AND ("cancer" OR "oncology" OR "oncologic" OR "leukemia" OR "tumor"). Google searches were performed to identify additional articles that may have been missed in database searches.

A study was included if it: 1) examined substance use or substance use disorder in individuals with cancer; not cancer risk associated with substance use; 2) had an adult sample or, if mixed (children and adults), data for adults were reported separately; and 3) examined patients who were either pre-treatment or on treatment for cancer. A study was excluded if it: 1) examined tobacco/nicotine or cannabis use only; 2) focused only on cancer risk or incidence associated with substance use; 3) had a pediatric sample (i.e., ages < 18 years only); or 4) had an exclusive survivor sample; however, if a sample was mixed (e.g., pre-treatment, on treatment, and in post-treatment survivorship), then it was included to examine the non-survivor samples. Survivor studies were excluded due to existing literature on this topic [20,22–23]. No limitations were set on study setting or country. After screening all abstracts for these criteria, all references of eligible studies were additionally screened to identify eligible studies, resulting in one study. Based on the exclusion and inclusion criteria, 28 studies were included in this systematic review (Fig. 1).

The first author extracted the following baseline characteristics from the original (empiric) articles: lead author, publication year, study design, study site, sample size, mean age of sample, substance of interest, assessment used, rates of substance use or substance use disorders, cancer characteristics, cancer treatment status, and country of study (Table 1). For the remaining seven review or conceptual publications, the following characteristics were extracted: lead author, year of publication, study design, substance of interest, screening recommendation, and treatment/management approach (Table 2). The rationale for extracting these study characteristics was to broadly encompass the literature on substance use in cancer. Methodological quality and risk of bias was assessed using the Joanna Briggs Institute Critical Appraisal Checklist for Studies Reporting Prevalence Data [24; Table 3].

3. Results

3.1. Included studies

3.1.1. Description of studies

Of the 28 included studies, 21 were empiric studies and seven were review or conceptual papers. All were written in English and all published in peer-reviewed journals.

Table 1 provides sample and study characteristics for the 21 empiric studies. Sixteen were conducted in the United States. Studies were published between 1995 and 2018. Eleven were single-site studies. Of the nine multi-site studies, two used Medicare-linked data [25–26] and one used national veteran health administration data [27].

Table 2 provides study characteristics for the studies that were either review or conceptual papers. Publication year ranged from 1998 to 2017.

3.1.2. Risk of bias and quality assessment

According to the Critical Appraisal Checklist for Studies Reporting Prevalence Data [24], all studies met criteria 1–3; the sample was appropriate to address the target population, study participants were appropriately sampled, and sample size was adequate. However, the study subjects and settings were inadequately described in two studies [criteria 4;28–29]. Adequacy of response rate (criteria 9) was irrelevant in 11 studies, as these studies were chart reviews or large-scale investigations of existing data that did not enroll participants [e.g., 29–30]. Overall, quality assessment revealed a generally low risk of bias and high methodological quality. See Table 3.

3.1.3. Description of samples

Sample sizes for the 21 empiric studies ranged from 42 [31] to 482,688 [27] (median = 216), resulting in a total of 501,123 participants across the 21 studies. Mean sample ages ranged from 17.6 [31] to 74.7 [26] (Table 1) across the 21 included studies. Six studies did not have a sample size, as they were either review or conceptual papers (Table 2).

3.1.4. Cancer characteristics

Cancer characteristics ranged substantially across included studies. Most studies had a mixed cancer sample [e.g., 26]; five focused on head and neck patients [e.g., 32–34]; one studied gastric cancer patients [28], one oral cavity cancer patients [35], and one breast cancer patients [30]. Cancer stage also varied across all studies. For example, nine studies were comprised either exclusively [36] or mostly [33–35] of advanced cancer patients. Ten studies reported cancer treatment status; for example, one of the studies had a newly diagnosed sample, though their specific treatment status was not reported [31] and three were pre-treatment [4,30,35]. Another study reported a mixed sample, comprised of patients who had mono-therapy (surgery, radiation), multimodal treatment, and no treatment (categorized as "watchful waiting") [26]. Another study found that 45% of patients presented for an on-treatment visit, while 39% and 15% presented for a follow-up and consult, respectively [29].

3.1.5. Assessment of substance use

Substance use assessment ranged considerably, even across studies that assessed the same substance. Assessments for substance use and

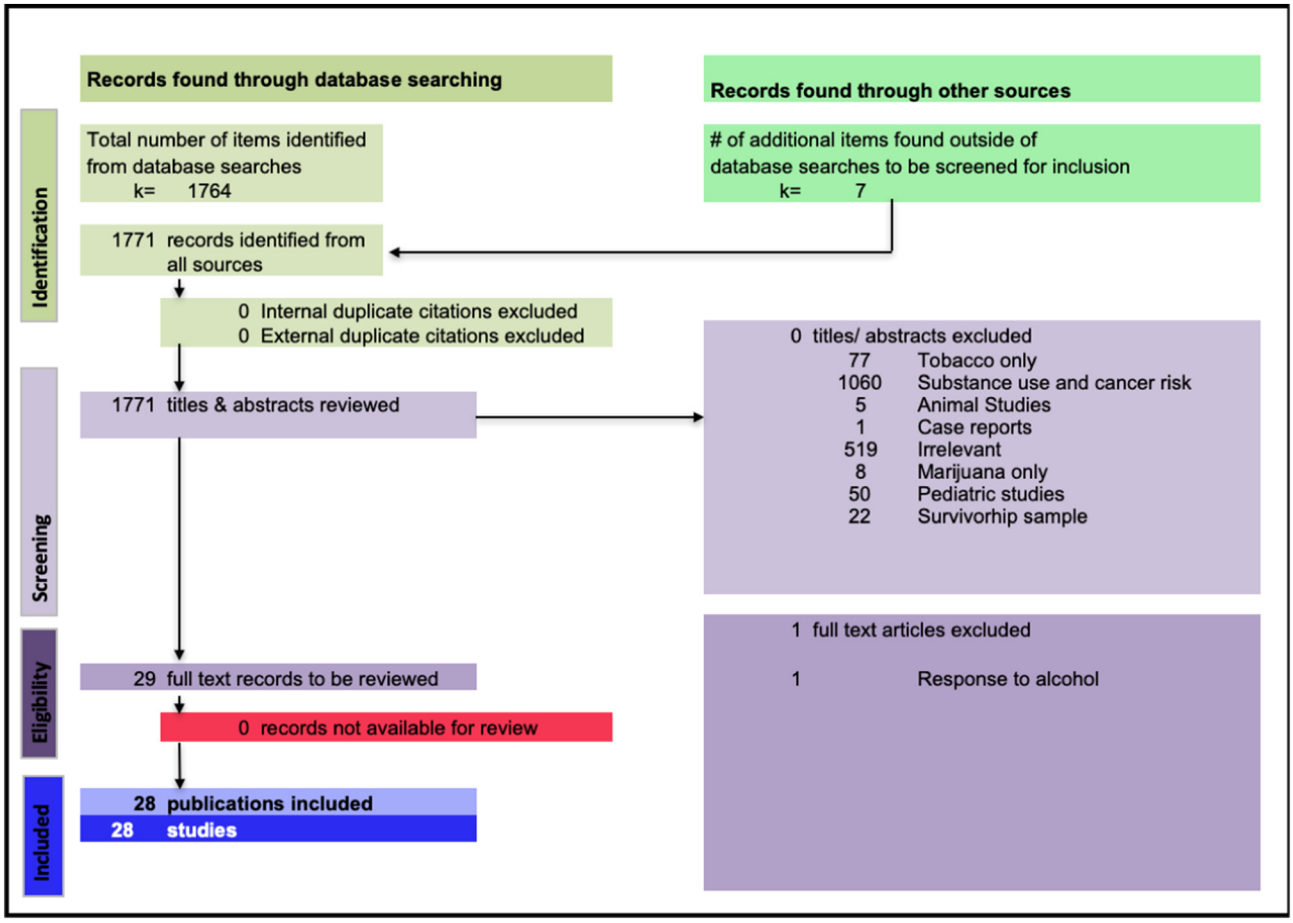

Fig. 1. Flowchart of the screening and eligibility evaluation phases.
Note. This flowchart has been modeled after: [21] Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & PRISMA Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Medicine*. 6(7): e1000097.

SUDs in studies with unspecified substances included ICD-9 diagnoses, using claims data (three studies, [25–27]); Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders (SCID) [four studies, 4,35,37–38]; and one chart review for substance use documentation (one study, [29]).

Alcohol use assessments included the CAGE questionnaire [five studies, e.g.,30;39], the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders (SCID) [four studies, 4,35,37–38], the Alcohol Use Disorders Identification Test (AUDIT) [three studies; 32–34], and the Diagnostic and Statistical Manual of Mental Disorders III-Revised (DSM-IIIR) criteria [one study; 35].

Opioid use assessments included evaluation of "dependence" and "misuse", "chemical coping", and opioid "misuse risk". Instruments included the Opioid Risk Tool [one study; 40], Screener and Opioid Assessment for Patients with Pain (SOAPP-R; [two studies; 41,42], SCID [one study; 37], and Pain Assessment and Documentation Tool (PADT; [one study; 41]).

Of note, terminology varied across studies, likely in part due to changes between the DSM-IV and DSM-5 categories [43]. According to the DSM-IV, "abuse" is defined as "a maladaptive pattern of substance use manifested by recurrent and significant adverse consequences related to the repeated use of substances". "Dependence" is defined as "a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues use of the substance despite significant substance-related problems". In contrast to the DSM-IV, the DSM-5 no longer separates substance "abuse" from substance "dependence". Instead the DSM-5 bases severity of "substance use disorder" on the number of criteria endorsed [43]. However, other terminology, not present in DSM-IV or DSM-5, such as "misuse" and "problem drinking," was also used.

3.2. Empiric data

3.2.1. Substances

Of the 21 empiric studies, 8 examined substance use or SUD across multiple substances without presenting separate data for each substance [e.g., 4]. Seven investigated opioids [e.g., 28]; eight investigated alcohol; three examined alcohol and illicit drugs [29,31,44] and one investigated both opioids and alcohol [e.g., 39]. Notably, most opioid studies focused on prescription medications and only one of the studies [44] presented data on heroin use as well.

3.2.1.1. General substance use or substance use disorder rates. Across all studies, rates ranged from 2% to 35%. A study of individuals pre- and post- diagnosis revealed that 2.0% met criteria for substance "dependence" prior to cancer diagnosis [4]. Further, a Drug-Taking Behaviors Interview revealed that 5% reported a prior drug problem, with no distinction between "misuse" and "abuse" [38]. Another study revealed that 6.64% of veterans with cancer also met criteria for SUD [27]. Rosenberg and colleagues reported that 23% endorsed illicit substance use, with no specification of the extent [31]. Additionally, a study that examined attitudes towards substance "misuse" and "abuse" revealed that 28.8% of participants worried they could lose control over their prescribed pain and/or anxiety medications [44]. Finally, Choflet and colleagues examined substance use, without specifying severity or identifying SUD [29].

Table 1
Characteristics of original studies[d,j].

Study	Design	Site	N	Age	Substance	Assessment	Terminology	Rate	Cancer site; stage	Cancer treatment	Country
Barclay, 2014	Retrospective	Single	114	53	Opioids	ORT	misuse	43%	Mixed	NR	U.S.A.
Bruera, 1995	Retrospective	Single	100	[c]64.67/61.89	Alcohol	CAGE	alcoholism	[c]27/28%	Mixed; terminal	NR	Canada
Chhatre, 2018	Retrospective	Multi	11,335	71.8–74.7	NR	ICD-9 diagnoses	use	NR	Advanced prostate cancer	Mixed	U.S.A.
Chhatre, 2014	Observational cohort	Multi	1509	72.4	NR	ICD-9 diagnoses	use	10.6%	Advanced prostate cancer	Mixed	U.S.A.
Choflet, 2016	Chart review	Single	397	NR	Alcohol, illicit drugs	Chart-identified	use	[h]2–3%	Mixed	Mixed	U.S.A.
Dev, 2011	Retrospective	Single	598	[i]58.6/61.3	Alcohol	CAGE	alcoholism	13%	Advanced	NR	U.S.A.
Duffy, 2002	Pilot	Multi	81	61.9	Tobacco, alcohol	AUDIT	use	18%	Head & neck; 43% I & II	NR	U.S.A.
Duffy, 2006	Randomized controlled trial	Multi	184	57	Tobacco, alcohol	AUDIT	problem drinking	28%	Head & neck; 61% III & IV	NR	U.S.A.
Duffy, 2007	Correlational	Multi	973	61	Tobacco, alcohol	AUDIT	problem drinking	16%	Head & neck; 67% III & IV	Mixed	U.S.A.
Henry, 2018	Longitudinal	Multi	223	62.9	Opioids	SCID	use	23.8%	Head & neck	Mixed	Canada
Kangas, 2005	Prospective	Single	82	[f]57.5; 65.6	NR	SCID	use	35%	Head & neck; lung	Pre-treatment	Australia
Hegel, 2006	Prevalence	Single	236	57.4	Tobacco, alcohol	CAGE	use	4%	Breast; I-III	Pre-treatment	U.S.A.
Ho, 2018	Cross-sectional	Multi	482,688	62.8	NR	ICD-9 diagnoses	use	6.64%	NR	NR	U.S.A.
Kugaya, 2000	Correlational	Single	107	61	Alcohol, nicotine	SCID for DSM-IIIR	dependence/abuse	[e]33.6/6.5%	Oral cavity/larynx/pharynx; 61% III-IV	Pre-treatment	Japan
Kwon, 2015	Prospective	Single	432	57	Opioids	CAGE	chemical coping	18%	60% breast; advanced	NR	U.S.A.
Parsons, 2008	Retrospective	Single	598	[a]58/60	Alcohol, opioids	CAGE	alcoholism	17%	Varied, advanced	NR	U.S.A.
Passik, 2000	Pilot	Single	52	46.3	Alcohol, illicit drugs	Developed survey	abuse	[g]2–10.2%	Mixed	50% chemo	U.S.A.
Passik, 2006	Prospective	Multi	100	[b]51.6	Opioids	SCID	dependence	2%	NR	NR	U.S.A.
Reyes-Gibby, 2016	Cross-sectional	Single	209	54.2	Opioids	SOAPP-R	misuse	34%	Mixed	NR	U.S.A.
Rosenberg, 2017	Prospective	Multi	42	17.6	Alcohol, illicit drugs	RPCA survey; semi-structured interviews	use	23%	Mixed	Newly diagnosed	U.S.A.
Tabei, 2006	Prevalence	Single	177	58.13	Tobacco, opioids	DSM-IV criteria	dependence	5.65%	Gastric	NR	Iran

Note. AUDIT = Alcohol Use Disorders Identification Test; CAGE = cut-annoyed-guilty-eye questionnaire; DSM = Diagnostic and Statistical Manual of Mental Disorders; ICD-9 = international classification of diseases – 9th edition; NR = not reported; ORT = opioid risk tool; PADT = Pain Assessment and Documentation Tool; RPCA = Resilience in Pediatric Cancer Assessment; SCID = Structured Clinical Interview for DSM; SOAPP-R = Screener and Opioid Assessment for Patients with Pain - Revised.

[a] Mean age for total sample of AIDS and cancer patients.

[b] CAGE+ and CAGE-, respectively.

[c] 1989 group and 1992 group, respectively.

[d] 21% and 22% of patients were classified as high and medium-risk, respectively; 12% had a personal history of prescription drug abuse [33].

[e] Alcohol dependence and abuse, respectively.

[f] Head & neck and lung cancer patients, respectively.

[g] A variety of drug-taking behaviors were assessed, ranging from taking opioids from a friend or spouse without informing them (2%) to borrowing opioids from a friend or spouse (10.2%).

[h] 2% of the sample was currently engaging in illicit substance use, 2% had a prior history of illicit substance use; 23% of the sample was consuming 1–5 drinks/week; 7% consumed 6–11 drinks/week; and 3% consumed 12+ drinks/week.

[i] CAGE+ and CAGE-, respectively; median ages reported.

[j] The "terminology" column specifies which term studies used to described their rates and findings.

Table 2
Characteristics of conceptual or review papers.

Study	Design	Substance	Screening	Treatment/management approach
Anghelescu, 2013	Review	Opioids	Valid & reliable screening tools (e.g., SOAPP)	Multidisciplinary approach
Compton, 2017	Narrative review	Opioids	Valid & reliable screening tools (e.g., SOAPP)	Clinician education; referral
Del Fabbro, 2014	Conceptual	Opioids	AUDIT; CAGE; ORT; PADT; SOAPP; SOAPP-SF; STAR	Counseling; psychotherapy
Passik, 1998a	Conceptual	Opioids	N/A	N/A
Passik, 1998b	Conceptual	Opioids	Urine toxicology	Multidisciplinary approach; realistic goal-setting
Passik, 2004	Conceptual	Opioids	Interview suggested	Clear treatment goals (harm reduction); multidisciplinary approach
Starr, 2010	Conceptual	Opioids	SOAPP-R; ORT; PADT	Collegial consultation

AUDIT = Alcohol Use Disorders Identification Test; CAGE = cut-annoyed-guilty-eye questionnaire; ORT = opioid risk tool; PADT = Pain Assessment and Documentation Tool; SOAPP-R = Screener and Opioid Assessment for Patients with Pain - Revised.

Table 3
Methodological quality, risk of bias, and quality assessment for the 21 included empiric studies.

	Sample	Sampling	Sample size	Description	Data analysis	Methods	Measures	Statistical analysis	Response rate
Barclay, 2014	+	+	+	+	+	+	+	+	+
Bruera, 1995	+	+	+	+	+	+	+	+	N/A
Chhatre, 2018	+	+	+	+	+	+	+	+	N/A
Chhatre, 2014	+	+	+	+	+	+	+	+	N/A
Choflet, 2016	+	+	+	–	+	–	+	+	N/A
Dev, 2011	+	+	+	+	+	+	+	+	N/A
Duffy, 2002	+	+	+	+	+	+	+	+	+
Duffy, 2006	N/A: Randomized controlled trial								
Duffy, 2007	+	+	+	+	+	+	+	+	?
Hegel, 2006	+	+	+	+	+	+	+	+	N/A
Henry, 2018	+	+	+	+	+	+	+	+	+
Ho, 2018	+	+	+	+	+	+	+	+	N/A
Kangas, 2005	+	+	+	+	+	+	+	+	?
Kugaya, 2000	+	+	+	+	+	+	+	+	+
Kwon, 2015	+	+	+	+	+	+	+	+	N/A
Parsons, 2008	+	+	+	+	+	+	+	+	N/A
Passik, 2000	+	+	+	+	+	?	+	+	+
Passik, 2006	+	+	+	+	+	+	+	+	N/A
Reyes-Gibby, 2016	+	+	+	+	+	+	+	+	?
Rosenberg, 2017	+	+	+	+	+	?	+	+	+
Tabei, 2006	+	+	+	–	+	+	+	+	N/A

Note. + yes; − no;? unclear; N/A = not applicable.
Contents for this table were guided by the "Critical Appraisal Checklist for Studies Reporting Prevalence Data" from Munn, Z., Moola, S., Lisy, K., Riitano, D., Tufanaru, C. (2015). Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and incidence data. *International Journal of Evidence Based Healthcare*, 13(3)147–153.

3.2.1.2. Risk factors. Several variables were associated with SUDs. One study reported a higher proportion of patients with SUD had one or more psychiatric comorbidities (e.g., depression, anxiety). Further, individuals with SUD were younger than those without it [25–26]. In contrast, another study of veterans revealed that older age was associated with SUD [27]. Finally, Chhatre and colleagues found that those with SUD were less likely to be married and to be from a metropolitan area [25]. Chhatre and Jayadevappa reported that African Americans had a higher proportion (15.7%) of SUD, compared to Whites and Hispanics. In sum, most variables associated with SUD were demographic (e.g., age, race).

3.2.1.3. Treatment. No studies reported on treatment outcomes. However, several provided clinical implications. For example, Choflet and colleagues underscored the importance of substance use risk assessment in oncology care, as well as collaborating with mental health, substance use, and social work colleagues to deliver care [29]. Another study recommended the use of interdisciplinary care, using a multimodal framework, as well as a stepped-care approach for anxiety management [37].

3.2.2. Opioids

3.2.2.1. Rates. All studies on opioids focused on prescription opioids. One that also evaluated heroin use [44] highlighted that none of the cancer patients assessed were using heroin. One study revealed that 55% of patients were prescribed opioids within 12 months post-diagnosis, 37.7% before treatment, 40.8% during treatment, and 31.4% post-treatment [37]. Two studies reported rates of opioid "dependence", one in individuals with gastric cancer (5.65%) [28] and one in a sample which excluded individuals with SUD (2%) [38]. Nine studies reported risk associated with opioid use, which ranged from 21% of patients in a palliative care clinic being at high risk to 34% of emergency room patients with cancer being high risk [42]. A study of 431 palliative care patients revealed that 18% of patients were chemically coping with prescription opioids. With regard to the general population, 0.7% of adults (i.e., 1.8 million) had a past-year substance use disorder associated with non-medical use of prescription pain relievers in 2014 [5]. Additional opioid use rates are presented in Table 1.

3.2.2.2. Risk factors. Five studies investigated characteristics associated with opioid use risk. One study revealed that opioid-"dependent" individuals were older than non-opioid "dependent" individuals [28]. Barclay and colleagues found that the most common risk factors for opioid use were being between age 16 and 45 years, a personal history of alcohol "abuse", or a personal history of illicit drug "abuse" [40]. A study of emergency department cancer patients found that depression, poor coping, severe pain, and current illicit substance use were associated with high risk of opioid "misuse" [40]. Kwon and colleagues revealed that chemical coping risk increased for patients

who were CAGE+ (i.e., at risk for alcohol "misuse"), younger, had better performance status, had worse pain scores, and worse well-being scores at their initial visit [45]. Passik and colleagues revealed that inadequate pain management was associated with aberrant behaviors in 73 patients with HIV-related pain and a history of substance "abuse" and 100 patients with cancer pain and no history of "abuse" [38]. Thus, this data underscores the need to consider the possibility of pseudo-addiction in assessing for and treating substance use disorder [17–19].

3.2.2.3. Treatments. Of the nine studies that examined opioid use in cancer patients, none reported on intervention or treatment.

3.2.3. Alcohol

3.2.3.1. Rates. Alcohol use rates ranged considerably across studies, with inconsistent terminology across studies. For example, alcohol "dependence" was identified in 3% of individuals with cancer which excluded those with known SUDs (i.e., although individuals with known SUDs were excluded from the study, 3% of the sample met criteria for "alcohol dependence" based on the SCID) [38]; 4% in a breast cancer sample using the CAGE questionnaire [30]; and 33.6% in a newly diagnosed head and neck cancer sample [35]. Another study revealed that 12.2% and 20.4% met criteria for alcohol "abuse" and alcohol "dependence", respectively [4]. At-risk alcohol use was categorized in different ways across six studies, ranging from 13% to 49%. At the lower end, 13% of 100 palliative care consults reported a history of alcohol "abuse" [44]; 16% of 973 individuals with head and neck cancer met criteria for "problem drinking" [34]; and 17% of 598 individuals with advanced cancer had alcohol "issues" [39]. At the higher end, 27% and 28% of 100 and 66 individuals with terminal cancer in 1989 and 1992, respectively, were reported to have "alcoholism" [46] and 28% of 184 advanced (stage III and IV) head and neck cancer patients were classified as "problem drinkers" [33].

3.2.3.2. Risk factors. Studies of alcohol use examined numerous associated variables. Dev and colleagues reported that CAGE+ patients were likely to be male, younger, have a history of tobacco/nicotine use, a documented history of illegal recreational drug use, and on "strong opioids" prescribed by their oncologist or primary care provider, but prior to palliative care consultation [36]. Another study found that compared to women, men scored higher on alcohol problems and that smoking and alcohol problems were associated [32]. A multi-site study revealed that "problem drinkers" were more likely to be younger, not married, from a Veterans Administration (VA) hospital, and within one year of their cancer diagnosis [34]. Parsons and colleagues found that CAGE+ patients were likely to be younger, male, and have head and neck malignancies. Notably, CAGE+ patients also had worse pain, sleep, dyspnea, and symptom distress scores and were more likely to be referred to palliative care earlier [39]. Finally, a pilot study revealed that 46% of head & neck cancer patients drank alcohol within the past six months, despite negative consequences associated with continued alcohol use, and 44% screened positive for depressive symptoms [32].

3.2.3.3. Efficacious treatments. One randomized controlled trial (i.e., treatment study) was identified. Individuals randomized to the intervention received a Cognitive Behavioral Therapy workbook, 9–11 sessions of CBT telephone counseling, and pharmacologic management [33]. The intervention resulted in significantly more smoking cessation, depression reduction, and drinking reduction but no significant differences in 6-month alcohol outcomes [33]. None of the other reviewed studies reported on an alcohol use intervention. However, only 9% of those who consumed alcohol in one study were interested in addressing their alcohol use [32].

3.3. Review and conceptual papers

Of the 28 included studies, seven were either review or conceptual papers that did not contain empiric data, but rather recommendations for the management of substance use in cancer (Table 2). Three major recommendations were identified across these publications: screening individuals' opioid use risk; reflective prescribing in the context of standards or a multidisciplinary team; and the utilization of behavioral treatments.

3.3.1. Screening

Although screening was recommended for both opioids and alcohol, the intent differed somewhat for opioids compared to alcohol. Screening for opioid risk and aberrant behaviors represents attempts to prevent or respond early to developing opioid-related substance use disorder in the context of prescribing pain medications, whereas screening for alcohol aims to identify individuals who may need intervention for current alcohol consumption [39,46].

Multiple methods of screening were recommended across included studies. Recommendations included validated measures,[e.g., 64,65] semi-structured diagnostic interviews, and unstructured interviews. For example, two papers suggested the 5-item Opioid Risk Tool (ORT) and Screener and Opioid Assessment for Patients with Pain (SOAPP) [41,47]. Del Fabbro and colleagues [47] recommended using brief validated screening tools to identify patients at risk for chemical coping. Another paper suggested the Pain Assessment and Documentation Tool (PADT) to be used throughout opioid therapy. Notably, Passik and Krish recommended the use of an interview opening with broad questions about substances in the patient's life, including nicotine and caffeine, and subsequently assessing for illicit drug use. The authors highlighted that this interview approach may provide valuable information regarding comorbid psychiatric disorders contributing to substance use [48].

Recommended methods for alcohol screening included the 4-item CAGE questionnaire [46,39], 5-item Screening Instrument for Substance Abuse Potential (SISAP), Alcohol Use Disorders Identification Test (AUDIT), and Screening Tool for Addiction Risk (STAR) [47].

3.3.2. Prescribing in context of standards or a team

Starr and colleagues discussed a decision-making approach with regard to opioid prescribing, noting the value of collegial consultation and establishing a standard of care. Specifically, Starr and colleagues discussed the concepts of "in the box" and "out of the box" prescribing, underscoring that even with a standard of care, substantial variability across clinician approaches and patient responses to opioids exists [41]. Passik and Kirsch highlighted the value of a multidisciplinary approach, noting that mental health professionals are instrumental in the management of substance use [48]. Similarly, Passik and colleagues underscored the importance of multidisciplinary teams as a treatment approach that best reflects the multifactorial nature (biological, chemical, social, and psychiatric) of substance use [49]. Specifically, the authors recommend a team comprised of an oncologist, palliative care physician, nurse, social worker, and mental health professional with expertise in addiction [49]. Such a team, they argue, will be equipped to assess and treat psychiatric disorders comorbid with substance use, while also minimizing withdrawal symptoms [49].

3.3.3. Behavioral management

Del Fabbro and colleagues recommended counseling and psychotherapy to manage comorbid conditions (e.g., depression) associated with substance use [47]. Of note, this paper also suggested use of motivational interviewing, positive reinforcement, and referral to substance use specialists [47]. Further, Passik and Kirsch recommended setting clear treatment goals, underscoring that treatment team members should not expect substance use remission and that a harm reduction approach may be most realistic [48]. Specifically, clinicians'

reinforcement of social support and treatment compliance may minimize and manage potential harm during relapses. Guidelines include establishment of an empathic relationship, use of behavioral interventions, and frequent reassessment of pain and symptom control [48].

4. Discussion

The present review generates multiple findings that may be used to inform future research. Of note, although prior work has examined substance use in cancer, this is the first *systematic review* on this topic. First, across all empiric studies ($k = 21$), substance use rates ranged from 2% [29] to 35% [4], with a median opioid rate of 18% and 25.5% for alcohol. Second, this systematic review revealed several substances of use (e.g., alcohol, opioids), with varying degrees of extent or severity. Third, this investigation identified a range of methods for detection and description of substance use in cancer patients. Finally, this review suggests that knowledge on substance use treatment and management in cancer is limited and that additional research is warranted.

While this review demonstrates that substance use disorder rates in oncology patients vary considerably across studies (i.e., 2% [29] to 35% [4]), several key findings highlight the limitations of the available evidence. First, almost half of the studies examined "substance use disorders" or "substance misuse," categorizing all substances together rather than use of particular substances. Second, half of the studies did not report cancer treatment status, precluding conclusions regarding associations between cancer treatment and substance use. Third, variability in identification of substance use or substance use disorder (i.e., assessments, diagnostic approaches) may be contributing to variability in rates. Fourth, lack of distinction between pre-existing substance use and substance use that began after cancer diagnosis may further the variability in rates. Taken together, these findings underscore the need to examine criteria and methodological approaches used to generate substance use rates.

Findings also suggest substantial variability with regard to substance type and severity of use. Most studies used terminology interchangeably, making it challenging to comprehend severity. For instance, studies used the terms "abuse", "misuse", "use", and "dependence". Although we excluded nicotine and cannabis, it is also notable that we were able to identify studies for only alcohol and prescription opioids and no illicit substances such as cocaine. However, one study reported that no cancer patients had a prior or current history of heroin use [44]. Nonetheless, several studies reported on illicit substance use without specifying substance type [4].

Methodological approaches to identify and describe substance use in cancer are variable and inconsistent. Different categorizations of substance use complicate the aggregation or synthesis of data. Without standards or similar methods, it is difficult to compare studies in different types of cancer and different substances. To illustrate, the ICD underestimates prevalence of conditions and diseases [50–51] and coding is challenging [52]. Further, pseudo-addiction complicates assessment accuracy in oncology populations [17–19]. This makes it challenging to draw inferences about substance use rates and risk factors. Of note, changes from the DSM-IV to DSM-5 further complicate aggregation and summary of data across studies. Specifically, while the DSM-IV distinguished between "abuse" and "dependence", the DSM-5 now provides criteria for "substance use disorder" [43]. Nonetheless, it is crucial to establish and maintain judgment-free terminology to assess and intervene on substance use in cancer patients. Ideally, such terminology would be standardized, stable, constant, and meaningful – with the goal of fostering our understanding and clinically managing substance use in cancer patients.

One reason that specific trends may not be readily discernable is the nature of data collection. First, most studies used convenience samples. Studies of rates of the same substance (alcohol) in convenience samples of individuals with the same cancer (head and neck cancers, $n = 4$) produced a range of 16–34%. These observations clearly warrant future investigations using nationally-representative or population-based samples. Second, measures, even for the same substances, vary from study to study, making it challenging to compare findings. For example, some studies used semi-structured interviews or diagnostic criteria [4,35,37], whereas others used validated instruments (e.g., AUDIT [32–34], CAGE [30,39,45]). Relatedly, categorizing studies by assessment type (CAGE vs. AUDIT vs. diagnostic criteria/interview) revealed a pattern. Use of the AUDIT revealed the smallest range of substance use rates: 16% to 28% (median = 18%), while use of diagnostic interview or interview revealed the greatest variability: 2% to 35% (median = 10.6%). The CAGE generated a range of 4% to 28% (median = 17%).

Despite challenges with aggregating and synthesizing data, we made several observations with regard to the current literature base. First, rates of overall substance use remain relatively stable across years – ranging between a quarter and a third of cancer patients evaluated between 1995 and 2005. To illustrate, a 1995 study reported a rate of 27–28% [46] and 35% in a 2005 study [4]. However, a 2015 study reported a rate of 18%, demonstrating a decline, though this study was comprised primarily of breast cancer patients [45]. Second, while the reported rates were variable in the studies that specified substance type, among the ten that examined alcohol, the median rate was 25.5% and among the seven that examined opioids the median rate was 18%. Of note, studies on opioid use have been increasing over time. No studies examined opioid use in cancer prior to the year 2006, before the second wave of the opioid epidemic [1]. Since then, a 2008 study revealed a rate of 17% for opioid use [39], followed by a rate of 43% in 2014 [40], 18% in 2015 [45], 34% in 2016 [42], and 23.8% in 2018 [37].

This systematic review revealed that knowledge on substance use treatment in cancer is limited. Specifically, providing guidelines and treatment recommendations is challenging, given the limited literature on substance use management in this population. We identified one randomized controlled trial of a substance use treatment in individuals with cancer. However, the review and conceptual papers tended to have recommendations for clinical management in this population. These recommendations may have been based on principles or evidence from the treatment of SUDs in non-cancer populations, but their applicability and translation to individuals with cancer treatment have not been examined. Notably, management recommendations primarily focused on preventing and monitoring use, rather than interventions for existing substance use disorder. Therefore, more research is needed on treatment, with an emphasis on rates and consequences for cancer populations. Nonetheless, future investigations may apply collaborative care models to substance use in cancer that have been developed for other diseases or conditions, including HIV [e.g., 8].

The studies in this review had many limitations. Limitations included assessment of substance use (interview versus validated measure), cancer characteristics (site, prognosis), and study location. The confinement of study participants in specific locations (i.e., countries) introduces socioeconomic status (SES) and associated environmental factors as confounds. For example, of the 21 empiric studies that reported country of study setting, 16 (76%) were in the United States. Use of participants from such geographic confines naturally limits generalizability of findings. Although the scope of this systematic review does not include cancer risk, it is important to note that the three head and neck cancer papers were published in 2006 [35], 2007 [34], and 2000 [33]. Thus, given that the human papilloma virus (HPV) is now considered a greater risk factor for cancer than alcohol [53], it is important to note a shift in cancer risk associated with alcohol and HPV.

At the review level, several limitations need to be considered when assessing findings. First, negative or inconclusive data often remain unpublished, leading to potential publication bias. Second, 76% of the studies were conducted in the United States, raising issues of generalizability. It is important to note that this may have been the result of setting the database search to include only studies published in English; thus, studies published in other languages were not included. Third,

another critical limitation of this review is the heterogeneity and limited quantity of studies on this topic, presenting challenges for conducting a quantitative investigation (e.g., meta-analysis) [54]. For example, of the 20 included empiric studies, four were retrospective, one was an RCT, and one was observational. Additionally, RCTs and longitudinal studies on substance use and cancer are infrequent. Such investigations may foster the establishment of a causal relationship between substance use disorder and cancer. Specifically, these studies could elucidate whether substance use predates cancer diagnosis and treatment, predisposing the patient to continued substance use or whether the diagnosis and treatment *causes* the substance use.

Nevertheless, the present systematic review has numerous advantages with respect to previous investigations. First, it presents, to our knowledge, the most comprehensive and updated assessment on this issue using a systematic approach. Most prior reviews were narrative [55] or conceptual in nature. Of note, most studies focused on tobacco and nicotine use in cancer populations [22,23,55–58]. In contrast, the present review examines other substances, including alcohol and opioids. This work contributes a broad, yet detailed, systematic exploration of this issue to the literature.

In light of findings from this systematic review, several recommendations for future research are provided. First, no longitudinal studies have examined individuals' changes in substance use, contemporaneously with cancer diagnosis and treatment, thwarting the ability to establish any causal links or observe changes over time. Thus, future studies may conduct longitudinal studies of substance use across the cancer continuum (e.g., increase in use from diagnosis to palliative care). Relatedly, the research designs used in the 21 included empiric studies are relational in nature and frequently do not control for confounding variables or for alternative explanations. Second, substance use is related to numerous confounds aside from cancer, including psychopathology [59], age [60], and gender [61]. Therefore, future studies should evaluate and report on psychopathology that may contribute to substance use and the development of substance use disorder. Third, given that substance use often develops early in life [62], it may be beneficial for studies to have lower mean baseline ages.

4.1. Conclusions

Substance use or substance use disorder occurs in a substantial minority (ranging from 2% [29] to 35% [4]) of individuals with cancer, but further characterization of rates and risk factors is needed. Of note, given that most studies do not identify onset of substance use (i.e., prior to versus after cancer diagnosis and treatment), screening assessments should identify personal or family history of substance use as a risk factor. In light of our findings, we recommend reporting of comorbid psychopathology (e.g., major depressive disorder, generalized anxiety disorder) and use of current diagnostic language ("substance use" or "substance use disorder") to minimize judgment and maximize consistency and accuracy. Future investigations should also go beyond alcohol and prescription opiates and include specifics about other substances such as cocaine. It would especially be important to examine heroin use, given that individuals with opioid-related substance use disorder occasionally transition to heroin for cost reasons [63]. Ultimately, methodological rigor across such studies might contribute towards convergence within the field with regard to clinical recommendations in the prevention and management of substance use in cancer populations.

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References*

[1] World Health Organization. https://www.who.int/mental_health/mhgap/evidence/substance_abuse/en/; 2019.
[2] Hedegaard H, Warner M, Miniño AM. Drug overdose deaths in the United States, 1999–2016. NCHS Data Brief, no 294. Hyattsville, MD: National Center for Health Statistics. 2017/CDC. Wide-ranging online data for epidemiologic research (WONDER). Atlanta, GA: CDC, National Center for Health Statistics; 2016. Available at http://wonder.cdc.gov.
[3] Scoccianti C, Lauby-Secretan B, Bello PY, Chajes V, Romieu I. Female breast cancer and alcohol consumption: a review of the literature. Am J Prev Med 2014;46(3):S16–25. https://doi.org/10.1016/j.amepre.2013.10.031.
[4] *Kangas M, Henry JL, Bryant RA. The course of psychological disorders in the 1st year after cancer diagnosis. J Consult Clin Psychol 2005;73(4):763–8. https://doi.org/10.1037/0022-006X.73.4.763.
[5] Lipari, R. N., & Van Horn, S. L. (2017). Trends in substance use disorders among adults aged 18 or older. In *The CBHSQ Report*. Substance Abuse and Mental Health Services Administration (US).
[6] Passik SD, Portenoy RK. Prevalence of substance abuse disorders in cancer patients. Cancer Netw 1998;12(4).
[7] Bhattacharya R, Shuhart MC. Hepatitis C and alcohol: interactions, outcomes, and implications. J Clin Gastroenterol 2003;36(3):242–52.
[8] Carrico AW. Substance use and HIV disease progression in the HAART era: implications for the primary prevention of HIV. Life Sci 2011;88(21 – 22):940–7.
[9] Fox HC, D'sa C, Kimmerling A, Siedlarz KM, Tuit KL, Stowe R, et al. Immune system inflammation in cocaine dependent individuals: implications for medications development. Hum Psychopharmacol Clin Exp 2012;27(2):156–66.
[10] Rehm J, Samokhvalov AV, Neuman MG, Room R, Parry C, Lönnroth K, et al. The association between alcohol use, alcohol use disorders and tuberculosis (TB). A systematic review. BMC Public Health 2009;9(1):450. https://doi.org/10.1186/1471-2458-9-450.
[11] Ling W, Mooney L, Hillhouse M. Prescription opioid abuse, pain and addiction: clinical issues and implications. Drug Alcohol Rev 2011;30(3):300–5. https://doi.org/10.1111/j.1465-3362.2010.00271.x.
[12] Rudolf H, Watts J. Quality of life in substance abuse and dependency. Int Rev Psychiatry 2002;14(3):190–7. https://doi.org/10.1080/09540260220144975.
[13] Hashibe M, Straif K, Tashkin DP, Morgenstern H, Greenland S, Zhang ZF. Epidemiologic review of marijuana use and cancer risk. Alcohol 2005;35(3):265–75. https://doi.org/10.1016/j.alcohol.2005.04.008.
[14] Hecht SS. Cigarette smoking and lung cancer: chemical mechanisms and approaches to prevention. Lancet Oncol 2002;3(8):461–9. https://doi.org/10.1016/S1470-2045(02)00815-X.
[15] Giovannucci E. An updated review of the epidemiological evidence that cigarette smoking increases risk of colorectal cancer. Cancer Epidemiol Prevent Biomark 2001;10(7):725–31.
[16] Childers, J. W., & Arnold, R. M. (2012). "I feel uncomfortable 'calling a patient out'": educational needs of palliative medicine fellows in managing opioid misuse. J Pain Symptom Manage, 43(2), 253–260. doi:https://doi.org/10.1016/j.jpainsymman.2011.03.009
[17] Bell K, Salmon A. Pain, physical dependence and pseudoaddiction: Redefining addiction for 'nice' people? Int J Drug Policy 2009;20(2):170–8.
[18] Kwon JH, Tanco K, Hui D, Reddy A, Bruera E. Chemical coping versus pseudoaddiction in patients with cancer pain. Palliat Support Care 2014;12(5):413–7.
[19] Greene MS, Chambers RA. Pseudoaddiction: fact or fiction? An investigation of the medical literature. Curr Addict Rep 2015;2(4):310–7.
[20] Merlin JS, Patel K, Thompson N, Kapo J, Keefe F, Liebschutz J, et al. Managing chronic pain in cancer survivors prescribed long-term opioid therapy: a national survey of ambulatory palliative care providers. J Pain Symptom Manage 2019;57(1):20–7.
[21] Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6(7):e1000097.
[22] Bryant J, Boyes AW, Hall A, Girgis A, D'Este C, Sitas F. Prevalence and factors related to smoking and smoking cessation 6 months following a cancer diagnosis: a population-based study. J Cancer Surviv 2016;10(4):645–53. https://doi.org/10.1007/s11764-015-0510-7.
[23] Burcu M, Steinberger EK, Sorkin JD. Health care access and smoking cessation among cancer survivors: implications for the Affordable Care Act and survivorship care. J Cancer Surviv 2016;10(1):1–10. https://doi.org/10.1007/s11764-015-0446-y.
[24] Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and incidence data. Int J Evid Based Healthc 2015;13(3):147–53.
[25] *Chhatre S, Metzger DS, Malkowicz SB, Woody G, Jayadevappa R. Substance use

* Included in the systematic review.

disorder and its effects on outcomes in men with advanced-stage prostate cancer. Cancer 2014;120(21):3338–45. https://doi.org/10.1002/cncr.28861.
[26] *Chhatre S, Jayadevappa R. Racial and ethnic disparities in substance use disorders and outcomes in elderly prostate cancer patients. J Ethn Subst Abuse 2018;17(2):135–49.
[27] *Ho P, Rosenheck R. Substance use disorder among current cancer patients: rates and correlates nationally in the department of veterans affairs. Psychosomatics 2018;59(3):267–76. https://doi.org/10.1016/j.psym.2018.01.003.
[28] *Tabei SZ, Heydari ST, Mehrabani D, Shamsina SJ, Ahmadi J, Firouzi SM. Current substance use in patients with gastric cancer in Southern Iran. J Cancer Res Ther 2006;2(4):182. https://doi.org/10.4103/0973-1482.29828.
[29] *Choflet A, Narang AK, Hoofring LH, Bonerigo S, Mian OY, Katulis L, et al. Prevalence of substance use in patients with cancer receiving radiation therapy. Clin J Oncol Nurs 2016;20(4):397–402.
[30] *Hegel MT, Moore CP, Collins ED, Kearing S, Gillock KL, Riggs RL, et al. Distress, psychiatric syndromes, and impairment of function in women with newly diagnosed breast cancer. Cancer 2006;107(12):2924–31. https://doi.org/10.1002/cncr.22335.
[31] *Rosenberg, A. R., Bona, K., Ketterl, T., Wharton, C. M., Wolfe, J., & Baker, K. S. (2017). Intimacy, substance use, and communication needs during cancer therapy: a report from the "resilience in adolescents and young adults" study. J Adolesc Health, 60(1), 93–99. doi:https://doi.org/10.1016/j.jadohealth.2016.08.017
[32] *Duffy SA, Terrell JE, Valenstein M, Ronis DL, Copeland LA, Connors M. Effect of smoking, alcohol, and depression on the quality of life of head and neck cancer patients. Gen Hosp Psychiatry 2002;24(3):140–7. https://doi.org/10.1016/S0163-8343(02)00180-9.
[33] *Duffy SA, Ronis DL, Valenstein M, Lambert MT, Fowler KE, Gregory L, et al. A tailored smoking, alcohol, and depression intervention for head and neck cancer patients. Cancer Epidemiol Prevent Biomark 2006;15(11):2203–8. https://doi.org/10.1158/1055-9965.EPI-05-0880.
[34] *Duffy SA, Ronis DL, Valenstein M, Fowler KE, Lambert MT, Bishop C, et al. Depressive symptoms, smoking, drinking, and quality of life among head and neck cancer patients. Psychosomatics 2007;48(2):142–8. https://doi.org/10.1176/appi.psy.48.2.142.
[35] *Kugaya, A., Akechi, T., Okuyama, T., Nakano, T., Mikami, I., Okamura, H., & Uchitomi, Y. (2000). Prevalence, predictive factors, and screening for psychologic distress in patients with newly diagnosed head and neck cancer. *Cancer*, *88*(12), 2817–2823. doi:https://doi.org/10.1002/1097-0142(20000615)88:12 < 2817::AID-CNCR22 > 3.0.CO;2-N.
[36] *Dev R, Parsons HA, Palla S, Palmer JL, Del Fabbro E, Bruera E. Undocumented alcoholism and its correlation with tobacco and illegal drug use in advanced cancer patients. Cancer 2011;117(19):4551–6. https://doi.org/10.1002/cncr.26082.
[37] *Henry M, Alias A, Frenkiel S, Richardson K, Hier M, Zeitouni A, et al. Contribution of psychiatric diagnoses to extent of opioid prescription in the first year post-head and neck cancer diagnosis: a longitudinal study. Psycho-Oncology 2018. https://doi.org/10.1002/pon.4917.
[38] *Passik SD, Kirsh KL, Donaghy KB, Portenoy RK. Pain and aberrant drug-related behaviors in medically ill patients with and without histories of substance abuse. Clin J Pain 2006;22(2):173–81.
[39] *Parsons HA, Delgado-Guay MO, El Osta B, Chacko R, Poulter V, Palme JL, et al. Alcoholism screening in patients with advanced cancer: impact on symptom burden and opioid use. J Palliat Med 2008;11(7):964–8. https://doi.org/10.1089/jpm.2008.0037.
[40] *Barclay JS, Owens JE, Blackhall LJ. Screening for substance abuse risk in cancer patients using the Opioid Risk Tool and urine drug screen. Support Care Cancer 2014;22(7):1883–8. https://doi.org/10.1007/s00520-014-2167-6.
[41] *Starr TD, Rogak LJ, Passik SD. Substance abuse in cancer pain. Curr Pain Headache Rep 2010;14(4):268–75.
[42] *Reyes-Gibby CC, Anderson KO, Todd KH. Risk for opioid misuse among emergency department cancer patients. Acad Emerg Med 2016;23(2):151–8. https://doi.org/10.1111/acem.12861.
[43] American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). DC: Washington; 2013.
[44] *Passik SD, Kirsh KL, McDonald MV, Ahn S, Russak SM, Martin L, et al. A pilot survey of aberrant drug-taking attitudes and behaviors in samples of cancer and AIDS patients. J Pain Symptom Manage 2000;19(4):274–86. https://doi.org/10.1016/S0885-3924(00)00119-6.
[45] *Kwon JH, Tanco K, Park JC, Wong A, Seo L, Liu D, et al. Frequency, predictors, and medical record documentation of chemical coping among advanced cancer patients. Oncologist 2015;20(6):692–7. https://doi.org/10.1634/theoncologist.2015-0012.
[46] *Bruera E, Moyano J, Seifert L, Fainsinger RL, Hanson J, Suarez-Almazor M. The frequency of alcoholism among patients with pain due to terminal cancer. J Pain Symptom Manage 1995;10(8):599–603. https://doi.org/10.1016/0885-3924(95)00084-4.
[47] *Del Fabbro E. Assessment and management of chemical coping in patients with cancer. J Clin Oncol 2014;32(16):1734–8. https://doi.org/10.1200/JCO.2013.52.5170.
[48] *Passik, S. D., & Kirsh, K. L. (2004). Opioid therapy in patients with a history of substance abuse. *CNS drugs*, *18*(1), 13–25. doi: https://doi.org/10.2165/00023210-200,418,010-00002
[49] *Passik SD, Portenoy RK, Ricketts PL. Substance abuse issues in cancer patients. Part 2: evaluation and treatment. Oncology (Williston Park) 1998;12(5):729–34.
[50] Woo JG, Zeller MH, Wilson K, Inge T. Obesity identified by discharge ICD-9 codes underestimates the true prevalence of obesity in hospitalized children. J Pediatr 2009;154(3):327–31.
[51] Leslie PJ, Patrick AW, Hepburn DA, Scougal IJ, Frier BM. Hospital in-patient statistics underestimate the morbidity associated with diabetes mellitus. Diabet Med 1992;9(4):379–85.
[52] O'malley KJ, Cook KF, Price MD, Wildes KR, Hurdle JF, Ashton CM. Measuring diagnoses: ICD code accuracy. Health Serv Res 2005;40(5p2):1620–39.
[53] Hobbs CGL, Sterne JAC, Bailey M, Heyderman RS, Birchall MA, Thomas SJ. Human papillomavirus and head and neck cancer: a systematic review and meta-analysis. Clin Otolaryngol 2006;31(4):259–66.
[54] Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21(11):1539–58.
[55] Parsons A, Daley A, Begh R, Aveyard P. Influence of smoking cessation after diagnosis of early stage lung cancer on prognosis: systematic review of observational studies with meta-analysis. Bmj 2010;340:b5569. https://doi.org/10.1136/bmj.b5569.
[56] Florou AN, Gkiozos IC, Tsagouli SK, Souliotis KN, Syrigos KN. Clinical significance of smoking cessation in subjects with cancer: a 30-year review. Respir Care 2014;59(12):1924–36. https://doi.org/10.4187/respcare.02559.
[57] Gritz ER, Fingeret MC, Vidrine DJ, Lazev AB, Mehta NV, Reece GP. Successes and failures of the teachable moment: smoking cessation in cancer patients. Cancer 2006;106(1):17–27. https://doi.org/10.1002/cncr.21598.
[58] McCarter K, Martínez Ú, Britton B, Baker A, Bonevski B, Carter G, et al. Smoking cessation care among patients with head and neck cancer: a systematic review. BMJ Open 2016;6(9):e012296https://doi.org/10.1136/bmjopen-2016-012296.
[59] Bukstein OG, Brent DA, Kaminer Y. Comorbidity of substance abuse and other psychiatric disorders in adolescents. Am J Psychiatry 1989;146(9):1131.
[60] Grant BF, Dawson DA. Age at onset of alcohol use and its association with DSM-IV alcohol abuse and dependence: results from the National Longitudinal Alcohol Epidemiologic Survey. J Subst Abuse 1997;9:103–10. https://doi.org/10.1016/S0899-3289(97)90009-2.
[61] Tuchman E. Women and addiction: the importance of gender issues in substance abuse research. J Addict Dis 2010;29(2):127–38. https://doi.org/10.1080/10550881003684582.
[62] Mayes LC, Suchman NE. Developmental pathways to substance abuse. Developmental psychopathology: volume three: risk, disorder, and adaptation 2015. p. 599–619. https://doi.org/10.1002/9780470939406.ch16.
[63] Mars, S. G., Bourgois, P., Karandinos, G., Montero, F., & Ciccarone, D. (2014). "Every 'never' I ever said came true": Transitions from opioid pills to heroin injecting. Int J Drug Policy, 25(2), 257–266. doi:https://doi.org/10.1016/j.drugpo.2013.10.004
[64] *Anghelescu DL, Ehrentraut JH, Faughnan LG. Opioid misuse and abuse: risk assessment and management in patients with cancer pain. J Natl Compr Canc Netw 2013;11(8):1023–31. https://doi.org/10.6004/jnccn.2013.0120.
[65] *Compton P, Chang YP. Substance abuse and addiction. Clin J Oncol Nurs 2017;21(2).
[66] *Passik SD, Portenoy RK, Ricketts PL. Substance abuse issues in cancer patients. Part 1: prevalence and diagnosis. Oncology (Williston Park) 1998;12(4):517–21.