



The relationship between substance misuse and complicated grief: A systematic review



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ABSTRACT

Complicated grief is a prolonged, bereavement-specific disorder with significant psychological and physical consequences. Although complicated grief represents a risk to individuals with substance misuse, this relationship is poorly understood. Consequently, this systematic literature review examined empirical findings regarding the relationship between substance misuse and complicated grief. We searched 11 databases to identify pertinent quantitative studies published in English. Our search yielded 12 peer-reviewed journal articles ($N = 1749$) published between 1997 and 2017. Included studies evaluated the prevalence, assessment, etiology, correlates, risk factors, and treatment of complicated grief and substance misuse among individuals with one or both conditions. Our review found evidence of a positive relationship between complicated grief and substance misuse. Individuals with substance misuse were at increased risk for subsequent development of complicated grief, particularly when increases in substance consumption preceded bereavement. Conversely, complicated grief predicted increases in smoking and alcohol dependence. Multiple risk factors for individuals with complicated grief and substance misuse were identified and discussed. An existing complicated grief assessment performed well among individuals with substance misuse, and grief interventions were effective in reducing symptoms of complicated grief and substance misuse simultaneously. Given the severity of consequences associated with both conditions, more research is needed to understand this relationship, identify effective assessment tools, and evaluate intervention strategies to improve outcomes.

1. Introduction

The death of a loved one is a common experience. On average, the annual U.S. death rate is 2.7 million people, most of who leave behind an average of one to five close attachments (Murphy, Xu, Kochanek, Curtin, & Arias, 2017). Following a loss, most bereaved individuals experience distressing symptoms of grief that attenuate over time without the need for professional intervention (Rosner, 2015). However, some bereaved persons develop elevated, prolonged, and debilitating symptoms of grief that result in substantial functional impairment (Lundorff, Holmgren, Zachariae, Farver-Vestergaard, & O'Connor, 2017). Moreover, the effects of grief can lead to substance misuse or be compounded by existing substance misuse.

Research conducted over the past few decades has yielded in-

creasing support for the existence of a distinct clinical disorder affecting a significant minority of bereaved individuals (Shear, Ghesquiere, & Glickman, 2013). This disorder has been described with various terms, but this review uses the term *complicated grief* (CG). CG is currently included as persistent complex bereavement disorder (PCBD) in the most recent edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)* as a condition requiring further study (American Psychiatric Association, 2013). Core symptoms of CG include a clinically significant yearning for the deceased; difficulty accepting the loss; emotional numbness, bitterness, or anger; excessive avoidance of loss reminders; difficulty trusting others; and expressing the feeling that life is meaningless (American Psychiatric Association, 2013; Prigerson et al., 2009; Shear et al., 2011). CG represents a discrete syndrome that can be reliably differentiated from commonly co-occurring conditions

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such as major depressive disorder (MDD), posttraumatic stress disorder (PTSD), and anxiety disorders (Prigerson et al., 2009; Rosner, 2015).²

CG affects an estimated 10% of adults bereaved by nonviolent deaths (Lundorff et al., 2017), and is associated with psychological and physical health risks beyond those observed in normal grief (Prigerson et al., 2009). Psychological consequences of CG include depressed mood, decreased sleep, reduced quality of life, functional impairment, increased high-risk behaviors, and low self-esteem (Lichtenthal, Cruess, & Prigerson, 2004; Prigerson et al., 2009). Further, CG is associated with physical health impairments such as hypertension, immunological dysfunction, increased risk or occurrence of cancer, negative changes in eating and smoking habits, and disrupted sleep patterns (Lichtenthal et al., 2004; Prigerson et al., 2009). Notably, the presence of CG is a strong predictor of suicidal behavior (Latham & Prigerson, 2004).

1.1. Substance misuse and CG

CG might be particularly relevant to individuals with substance misuse, who often provide histories replete with extensive personal losses that antedate and follow the development of addiction (Furr, Johnson, & Goodall, 2015; Rugani, Maremmanni, & Dell, 2011). Mortality rates for substance use disorders (SUDs) in the U.S. population increased > 600% between 1980 and 2014, largely due to the substantial increase of opioid overdoses (Dwyer-Lindgren et al., 2018). In 2016, the United States recorded > 63,600 drug overdose deaths, an increase of 21% from the previous year. Consequently, individuals with substance misuse are highly likely to experience death of others within their networks or die themselves, increasing others' risk for CG (Hedegaard, Warner, & Miniño, 2017; Seth, Scholl, Rudd, & Bacon, 2018).

Emerging evidence supports a relationship between substance misuse and grief (Zuckoff et al., 2006). Bereaved children appear to be at elevated risk for later substance misuse, particularly children who experience the loss of both parents or losses between the ages of 6 and 18 years (Høeg et al., 2017; Kaplow, Saunders, Angold, & Costello, 2010). Even losses prior to birth may increase risk for substance misuse later in life; as compared with children of mothers who were not bereaved during pregnancy, children born to mothers who were bereaved by the death of a spouse during their pregnancies have demonstrated nearly a fourfold increase in later substance consumption (Liang et al., 2013). Among adults, the loss of a loved one is associated with increased alcohol misuse, particularly among men (Pfefferbaum & Doughty, 2001; Pilling, Konkoly Thege, Demetrovics, & Kopp, 2012; Stroebe, Schut, & Stroebe, 2007). Moreover, the likelihood of developing an SUD is nearly doubled among young adults who experience multiple deaths in a short period (Gayman, Cislo, & Hansard, 2016).

Although bereavement can increase misuse of substances, substance misuse can be a risk factor for adaptive resolution of grief (Stroebe, Folkman, Hansson, & Schut, 2006). For example, in the first years following the death of a child, substance misuse by bereaved parents has been associated with negative post-loss outcomes such as bereavement-related depression (Harper, O'Connor, & O'Carroll, 2014). Additionally, explanatory frameworks for CG such as the cognitive behavioral model (Boelen, 2006) and the integrative risk factor framework (Stroebe et al., 2006) implicate substance misuse as a risk factor for CG. However, the

²CG = complicated grief; CGSUT = Complicated grief and substance use treatment; CGT = Complicated grief treatment; FBP = Family bereavement program; GMS: Grief Measurement Scale; ICG = Inventory of Complicated Grief; ICG-RC = Inventory of Complicated Grief-Revised for Children; K-SADS-PL = Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version; M.I.N.I.: Mini-International Neuropsychiatric Interview; MMAT = mixed methods appraisal tool; NOS = Newcastle-Ottawa Scale; PCBD: Persistent complex bereavement disorder; SCID-IV = Structured Clinical Interview for DSM-IV Axis I disorders; TRIG = Texas Revised Inventory of Grief.

dynamics and directionality of the relationship between CG and substance misuse are unclear and remain relatively unexplored. This lack of research attention is likely due in large part to the use of an SUD diagnosis as an exclusion criterion within the majority of studies examining the efficacy of CG treatments (Zuckoff et al., 2006).

Understanding the relationship between CG and substance misuse could have significant implications for current SUD treatment practices. Notably, comorbid diagnoses of mental health disorders and SUDs have been associated with a greater number of adverse effects than either condition alone (Compton III, Cottler, Jacobs, Ben-Abdallah, & Spitznagel, 2003; Cridland, Deane, Hsu, & Kelly, 2012; Drake, Wallach, & McGovern, 2005). Moreover, numerous studies have demonstrated superior outcomes when these comorbid conditions are treated simultaneously (McKee, 2017). By extension, persons with CG and substance misuse may similarly benefit from effective grief interventions (Zuckoff et al., 2006). Although previous research has supported the potential benefit of grief treatment for persons with substance misuse (Denny & Lee, 1984), more research is needed to identify interventions that simultaneously and effectively address both conditions.

Numerous systematic reviews and meta-analyses have synthesized findings regarding the trajectories of typical grief as compared with CG in various populations (Rosner, 2015). However, no available systematic review has yet explored associations between substance misuse and CG. To fill this gap, we conducted a systematic review to provide a critical evaluation and consolidation of the scientific literature examining the association between substance misuse and CG.

2. Methods

2.1. Objectives

This review aimed to provide a comprehensive summary of empirical findings regarding the relationship between substance misuse and CG. Our review was guided by the following four research questions: (a) What are the risk factors, prevalence, and correlates of CG among individuals with SUDs or history of substance misuse? (b) What are the risk factors, prevalence, and correlates of SUDs or substance misuse among individuals with CG? (c) What are the treatment outcomes among people with SUDs or history of substance misuse in treatment for CG? (d) What are the treatment outcomes of individuals with CG who are in treatment for substance misuse or SUDs? Our primary outcome of interest was data regarding the relationship between substance misuse and CG. These data of interest included information regarding the risk factors, prevalence, epidemiology, etiology, screening, assessment, and treatment of substance misuse or CG among individuals with one or both conditions.

2.2. Search strategy and selection criteria

The review protocol was submitted to PROSPERO (Parisi, Sharma, & Howard, 2018; registration number, CRD42018095740), and our literature search and selection followed the standards specified by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Moher, Liberati, Tetzlaff, Altman, & Group, 2009). Relevant literature was identified through searches of 7 electronic databases and repositories: Pubmed, PsycInfo, CINAHL, Cochrane, Campbell, Embase, and Web of Science. In addition, we searched the following four databases for gray literature: Dissertation Abstracts and Masters Theses, Sociological Abstracts, Social Services Abstracts, and Social Work Abstracts. The reference lists of all relevant articles were examined. All searches were conducted in May of 2018. Search terms were developed through consultation with a health sciences research librarian, and were chosen to identify quantitative studies that examined the association between substance misuse (of any severity) and CG. Search terms related to CG were extensive and designed to reflect the substantial diversity in terminology used to describe this disorder. Search

terms are provided in the Appendix.

2.2.1. Selection criteria

Quantitative studies that examined the association between substance misuse and CG were included in this review. Selection criteria for studies evaluating primary data allowed for multiple definitions of CG (i.e., did not restrict studies to DSM-5 criteria or definitions), but required that CG had been assessed with a standardized, validated instrument that used a cut-off score to distinguish persons experiencing uncomplicated grief versus CG. Consistent with broadly accepted standards for the duration of symptoms necessary to meet criteria for CG, we restricted selection to articles reporting outcomes for study participants who had been bereaved for at least 6 months (Prigerson et al., 2009). Our selection criteria limited review inclusion to articles published in English but with no restrictions on publication dates or age of participants.

Articles were excluded from review if the study evaluated uncomplicated general grief responses (i.e., general grief); evaluated losses unrelated to bereavement such as divorce; or evaluated CG and substance misuse as separate issues without exploring the interaction. Additionally, the review excluded articles reporting on studies that were qualitative, mixed-methods, case studies, opinion papers, and general reviews.

2.3. Search results

Search results are illustrated in Fig. 1. Initial database searches

yielded 1206 published articles and two documents from reference harvesting. Removing duplicates reduced the sample to 688 articles. Two reviewers (AP and AS) worked independently to conduct a title and abstract review to assess articles' eligibility for inclusion, using Covidence (n.d.) systematic review software; this step yielded 52 articles for full-text review. The reviewers then independently evaluated the articles using prespecified inclusion/exclusion criteria. Disagreements were resolved through discussion until consensus was reached. This process produced 10 articles, and an additional 2 articles were identified through reference harvesting. A final sample of 12 articles was identified for systematic review.

2.4. Data items

Data were abstracted by two reviewers (AP and AS) working independently, using an abstraction tool developed by the review team. The data abstraction form was pilot tested with two randomly selected articles and refined accordingly. The reviewers compared abstracted data, discussing discrepancies until consensus was reached; consensus data were used in the final analysis. Abstracted data included information regarding study setting, year of publication, study design, study objective, criteria used to define CG, type of substance misuse, assessment tools for CG, assessment tools for substance misuse, sample size, sample characteristics, participant inclusion and exclusion criteria, data collection time points, methods of statistical analyses, study findings, and comments. These data are summarized in Table 1.

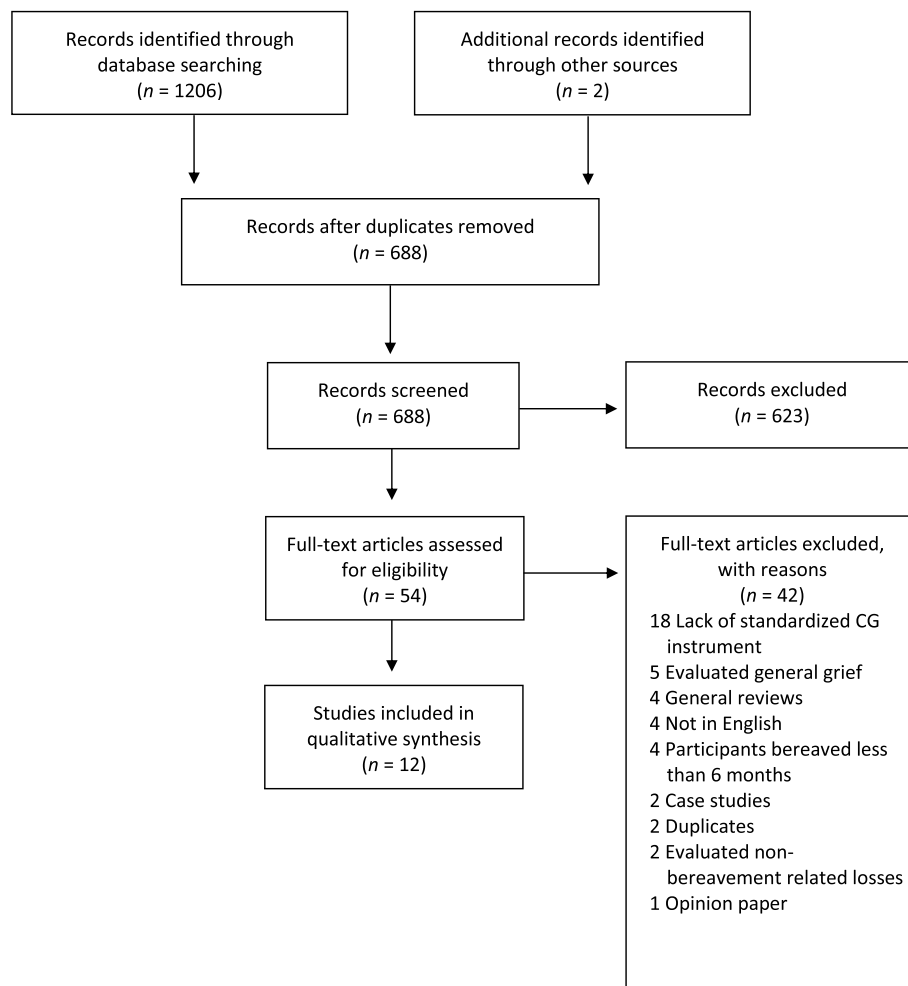


Fig. 1. Flow chart for literature search and screening results.

Table 1
Systematic review of studies examining Complicated Grief (CG) and substance misuse (N = 12).

Study & Country	Study type	Data time points	Objectives	Sample characteristics	Assessment tools for CG and substance misuse	Results	Limitations
Brent, Melhem, Donohoe, & Walker, 2009 USA	Cohort	9 months post-bereavement (see Melhem, Walker, Moritz, & Brent, 2008). 21 months post-bereavement.	Describe trajectory of grief disorders & symptoms in cohort of parentally bereaved children compared with non-bereaved counterparts.	176 children whose parents died through suicide (n = 53), accident (n = 44), natural cause (n = 79). Suicide group: M age = 15 yrs. (SD = 3.8), 50.9% male, 94.3% White. Accident group M age = 14.3 yrs. (SD = 4.1), 45.5% male, 81.8% White. Natural cause group: M age = 14.6 yrs. (SD = 3.5), 59.5% male, 78.5% White. 168 comparison youth: M age 13.9 yrs. (SD = 3.1), 50% male, 86.9% White.	Participants < 18: CG assessed with ICG without specified cut-point. Substance misuse assessed with SCID-IV. Participants ≥ 18: CG assessed with the ICG-RC without specified cut-point. Substance misuse assessed with K-SADS-PL.	Bereaved youth had higher rates of alcohol and substance misuse (4.5%) than non-bereaved youth (0%) p = 0.008. Youth bereaved by suicide had highest rates of alcohol/substance misuse (7.5%, p < 0.007). CG scores for youth bereaved by accidents (53.1) were higher than scores of youth bereaved by sudden natural death (14.5, p < 0.05).	No definition of CG provided. No comparison of sample with those who declined to participate. Psychometric properties and cut-point were not provided for CG scale.
Masferrer, Garre-Olmo, & Caparrós, 2015a Spain	Descriptive	Cross-sectional	To explore differences in bereavement and sociodemographic variables between people who increased substance use before bereavement (A-B) and people who increased substance use after bereavement (B-A).	No significant group differences. 196 bereaved adults from a public addiction treatment center (B-A: n = 50; A-B: n = 146) with alcohol, cocaine, or heroin dependence. B-A group: M age = 43.3 yrs. (SD = 9.86) 68% male. A-B group: M age = 46.4 yrs. (SD = 10.15). 81.5% male. B-A group had a higher proportion of women (32% vs. 18.5%, p < 0.05), increased their substance consumption at an older age (M = 30.8; SD = 11.02 vs. p < 0.001), and was bereaved at a younger age (M = 21.0, SD = 10.7 vs. M = 37.9; SD = 10.53) than the A-B group.	CG assessed with ICG score ≥ 25 Substance misuse assessed via interview with “clinical specialists” according to DSM-IV-TR criteria.	83.2% of all participants increased substance consumption after the death of a significant person. More in A-B group reported increased substance use after bereavement (45.2% vs. 38%) or suffered a relapse (12.3% vs 0%). A-B group reported both higher level of suffering related to the death (M = 7.17, SD = 2.83 vs. M = 5.81, SD = 3.47, p = 0.007) and higher level of CG symptoms ICG (M = 24; SD = 17.12 vs. M = 15.26; SD = 13.54, p = 0.001)	Percentages of individuals who chose not to participate were not provided. No comparison of demographic differences between clinical and control samples and no assessment of sample representativeness. Cut-off score for CG was not validated for Spanish-speaking populations or populations with SUDs. Disciplinary or professional status of clinical specialists used to evaluate SUDs was not provided. Bereavement and substance misuse-related variables assessed by self-report. Sample was limited to individuals with alcohol, cocaine, and heroin dependence. Possible overlap between A-B and B-A group, and differences between these groups were uncontrolled.

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Table 1 (continued)

Study & Country	Study type	Data time points	Objectives	Sample characteristics	Assessment tools for CG and substance misuse	Results	Limitations
Masferrer, Garre-Olmo, & Caparrós, 2015b Spain	Descriptive	Cross-sectional	To determine the prevalence of suicide risk among bereaved, drug-dependent individuals; examine variables that might distinguish those with and without a risk of suicide; and examine which of these variables predict suicide risk.	196 bereaved participants from a Spanish public addiction treatment center. Mean age: 45.6 (SD = 10.14) Average time since loss: 12 years.	Same as Masferrer et al., 2015a.	62.1% of all participant indicated suicide risk. Symptoms of CG were higher among participant with suicide risk compared to participants with no risk of suicide (86.8% vs. 52.5%, $p < 0.001$). CG was found to predict suicide risk when controlling for marital status, social support, previous suicide attempts, and family history of suicide ($\beta = 0.058, p < 0.001$).	Percentages of individuals who chose not to participate were not provided. No comparison of demographic differences between clinical and control samples and no assessment of sample representativeness. Cut-off score for CG was not validated for Spanish-speaking populations or populations with SUDs. Disciplinary or professional status of clinical specialists used to evaluate SUDs was not provided.
Masferrer, Garre-Olmo, & Caparrós, 2016 Spain	Descriptive	Cross-sectional	To assess the association between clinical symptoms of MDD, anxiety, PTSD, and CG symptoms among bereaved individuals with SUDs.	The overall sample was the same as Masferrer et al. (2015b). The sample was divided into normal ($n = 129$) and complicated grievers ($n = 67$).	Same as Masferrer et al. (2015a)	CG was significantly positively associated with being a woman ($\beta = 1.25, \text{Wald } \chi^2(1) = 4.78, p = 0.03$), having lost a sibling ($\beta = 1.68, \text{Wald } \chi^2(1) = 6.86, p = 0.09$), and negatively associated with being separated or divorced ($\beta = -1.75, \text{Wald } \chi^2(1) = 7.92, p = 0.01$) CG was also positively associated with PTSD ($\beta = 0.04, \text{Wald } \chi^2(1) = 4.34, p < 0.04$), and MDD ($\beta = 0.03, \text{Wald } \chi^2(1) = 7.56, p < 0.01$), but not anxiety. The Spanish ICG showed high internal consistency (Cronbach's alpha = 0.9), divergent validity, and each item was substantially correlated with the total. Four factors were found: "discomfort", which accounted for 42.3% of the variance; "non-acceptance", which explained 7.3% of the variance; "loneliness, isolation", which explained 6.3% of the variance; and "presence of the	Sample was limited to individuals with alcohol, cocaine, and heroin dependence. Bereavement and substance misuse-related variables were assessed by self-report. Same as Masferrer et al., 2015b
Masferrer, Garre-Olmo, & Caparrós, 2017a, Spain	Factor analysis	Cross-sectional	To establish the psychometric properties of the Spanish adaptation of the ICG among a sample of drug dependent participants	Same as Masferrer et al. (2015b)	Same as Masferrer et al. (2015a)	CG was significantly positively associated with being a woman ($\beta = 1.25, \text{Wald } \chi^2(1) = 4.78, p = 0.03$), having lost a sibling ($\beta = 1.68, \text{Wald } \chi^2(1) = 6.86, p = 0.09$), and negatively associated with being separated or divorced ($\beta = -1.75, \text{Wald } \chi^2(1) = 7.92, p = 0.01$) CG was also positively associated with PTSD ($\beta = 0.04, \text{Wald } \chi^2(1) = 4.34, p < 0.04$), and MDD ($\beta = 0.03, \text{Wald } \chi^2(1) = 7.56, p < 0.01$), but not anxiety. The Spanish ICG showed high internal consistency (Cronbach's alpha = 0.9), divergent validity, and each item was substantially correlated with the total. Four factors were found: "discomfort", which accounted for 42.3% of the variance; "non-acceptance", which explained 7.3% of the variance; "loneliness, isolation", which explained 6.3% of the variance; and "presence of the	Limitations in recruitment, design, sampling, and assessment are the same as Masferrer et al., 2015b. Additionally, there was significant cross-loading across all four factors that was not discussed. 16 of 19 items loaded over 0.40 on more than one factor. Lack of control group and cross-sectional design prevented inferences regarding the test-retest

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Table 1 (continued)

Study & Country	Study type	Data time points	Objectives	Sample characteristics	Assessment tools for CG and substance misuse	Results	Limitations
Masferrer, Garre-Olmo, & Caparrós, 2017b; Spain	Case control	Cross-sectional	To determine if the presence of CG is more frequent among a sample of bereaved participants with SUDs compared to a non-SUD control group. To compare normal and complicated grievers with and without SUDs with regards to demographic characteristics, substance misuse-related variables, bereavement-related variables, and perceived social support. To identify variables associated with the presence of CG.	296 bereaved participants. Case group: Same as Masferrer et al. (2015b). Control group: $n = 100$, mean age = 45.6 ($SD = 15.24$), 73% male.	Same as Masferrer et al., 2015a.	decreased", which accounted for 5.5% of the variance. 34.2% of participants in the clinical sample (95% CI: 1.19–1.29) and 5% in the control group (95% CI: 1.19–1.29) met CG criteria. Predictors of CG included having alcohol, cocaine, or heroin dependence ($\beta = -5.13$, $p = 0.01$, 95% CI = -9.04 , -1.22), widowhood ($\beta = 10.6$, $p = 0.04$, 95% CI = 0.40–20.8), loss of a sibling ($\beta = 11.5$, $p = 0.0$, 95% CI = 6.4–16.6), and traumatic circumstances of the loss ($\beta = 5.88$, $p = 0.01$, 95% CI = 1.54–10.21). Social support ($\beta = -0.14$, $p = 0.01$, 95% CI = -0.24 – 0.04) and secondary education ($\beta = -7.21$, $p = 0.00$, 95% CI = -10.82 – -3.60) were associated with lower CG levels. No significant differences for offspring or caregivers emerged for CG or DSM-IV alcohol or substance abuse between three bereaved groups or between bereaved and non-bereaved comparison participants.	reliability or inter-examiner reliability. Limitations in recruitment, design, sampling, and assessment are the same as Masferrer et al., 2015b. Additionally, clinical and control participants were recruited from separate populations.
Melhem et al., 2008; USA	Cohort study	9 months post-bereavement. 21 months post-bereavement (see Brent et al., 2009).	9-month follow-up of a cohort of parentally-bereaved offspring and their caregivers to examine the trajectory of disorders and symptoms compared to non-bereaved comparison subjects.	634 total participants. 211 offspring bereaved by suicide ($n = 66$) accident ($n = 51$) or natural causes ($n = 94$). Of offspring bereaved by suicide, mean age = 13.6 ($SD = 3.7$), 52% male, 92% White. Of offspring bereaved by accident, mean age = 13.1 ($SD = 4.1$), 47% male, 82% white; of offspring bereaved by natural causes, mean age = 13.4 ($SD = 3.4$), 56% male, 73% White. 183 non-bereaved, comparison offspring had a mean age of 12.9 ($SD = 3.2$), 50% male, 85% White. 139 caregivers bereaved by suicide ($n = 43$), accident ($n = 36$) or natural causes ($n = 60$). Of caregivers bereaved by suicide, mean age = 41.8 ($SD = 7.6$) 16% male, 40% White. Of caregivers bereaved by accident,	Same as Brent et al., 2009	Same as Brent et al., 2009.	Same as Brent et al., 2009.

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Table 1 (continued)

Study & Country	Study type	Data time points	Objectives	Sample characteristics	Assessment tools for CG and substance misuse	Results	Limitations
Sandler, Tein, Cham, Wolchik, & Ayers, 2016; USA	RCT	Pretest, posttest, 11 month and 6-year follow-up assessments.	To assess the effects of the FBP on outcomes for spousally bereaved parents.	mean age = 45.2 (SD = 10.6), 19% male, 78% White. Of caregivers bereaved by natural causes, mean age = 45.9 (SD = 7.4), 8% male, 85% White. 101 non-bereaved comparison caregivers, 26% male, 87% white, mean age: 42.4 (SD = 6.3) Median time since death: 9 months. 131 spousally bereaved parents (tx condition = 72; control condition = 59). Mean age = 41.33 (SD = 7.00), 23% male, 67.9% White, 10.0% Hispanic, 6.0% African American, 1.5% Native American, 1.5% Asian American or Pacific Islander, 9.0% other or unknown. Average time since death = 9.95 months (SD = 5.73).	CG was assessed with the ICG and the TRIG with no numerical cut-point identified. Alcohol misuse was measured with the SMAST.	The authors used ITT analysis. FBP was found to improve symptom criteria for CG compared to self-study control group (4.8% vs. 23.5%; OR = 0.08, 95% CI = 0.02–0.34) and symptom criteria for CG with impairment (0.0% vs. 11.8%; OR could not be defined as no parents met criteria in the FBP group; $p = 0.007$). FBP group were less likely to meet criteria for possible alcohol misuse (1.2% vs. 15.1%; OR = 0.09, 95% CI = 0.01, 0.77) or alcohol misuse (0.0% vs. 11.3%, $p = 0.007$). Small to moderate effects were found for FBP on CG symptoms ($d = 0.59$), and alcohol misuse ($d = 0.45$). 24.3% of bereaved respondents met criteria for CG ($M = 33.7$, $SD = 6.9$). CG was associated with significantly higher rates of current ($p = 0.032$) but not lifetime DSM-IV alcohol abuse compared to participant without CG.	Random assignment not fully described. Rates or comparisons of those who agreed to participate and those who refused were not provided. No baseline measures for alcohol misuse and CG.
Simon et al., 2005; USA	Descriptive	Cross-sectional	To investigate the frequency and implications of the death of loved ones among individuals with bipolar disorder.	120 participants with bipolar disorder; mean age = 44.1 (SD = 13.3), 41% male, 95% white. 103 (86%) reported experiencing the death of significant person. Average time since death = 12.3 years prior to assessment (SD = 11.3). 62% had a bipolar I diagnosis, and the prevalence of other bipolar subtypes were not presented. More bereaved participants were in a current mood episode (35% vs. 0%, $p = 0.003$) and reported greater functional impairment ($t(115) = 3.2$, $p = 0.002$) than non-bereaved participants. 253 participants. Depressed patients ($n = 111$) and non-depressed controls ($n = 142$).	CG was assessed with ICG scores ≥ 25 . Substance misuse measured with the M.I.N.I. Plus Version 5.0.	Differences between participants who chose to participate and those who refused were not analyzed. Prevalence of bipolar subtypes was not presented. Sample was self-selected. Relied on self-report measures for bereavement-related variables.	
Sung et al., 2011	Case control	Cross-sectional	To examine rates of CG among an outpatient sample of individuals with MDD compared to controls without MDD.	CG was assessed with ICG ≥ 25 . Substance misuse was CG ($\chi^2(1) = 13.70$, $p > 0.001$).	There was a significant association between lifetime DSM-IV alcohol dependence and comorbid MDD and CG ($\chi^2(1) = 13.70$, $p > 0.001$).	Information regarding the number of eligible who refused to participate was not provided.	

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Table 1 (continued)

Study & Country	Study type	Data time points	Objectives	Sample characteristics	Assessment tools for CG and substance misuse	Results	Limitations
Prigerson et al., 1997; USA	Descriptive	Baseline, 6 weeks, 6 months, 13 months, and 25 months.	To examine the effects of CG on subsequent mental and physical health.	Of the depressed group, mean age = 44.7 (SD = 12.0), 43.2% male, 77.9% white, 3.5% Hispanic/Latino, mean time since loss = 16 years (SD = 13.3). Of the control group, mean age = 44.1 (SD = 13.1), 51.9% male, 70.4% white, 9.3% Hispanic/Latino, mean time since loss = 13.6 years (SD = 11.89). Groups were similar with regard to lifetime rates of significant death, age, gender, race, ethnicity, and time elapsed since the death. Control group members were more likely to be married or living with a partner ($\chi^2(1) = 9.60, p = 0.002$), and were more likely to have attended some degree of secondary education ($\chi^2(1) = 8.21, p = 0.004$) than those in the MDD group. 150 widows and widowers. Mean age = 62.4 (SD = 8.3), 38.7% male, 89.3% White.	assessed with the SCID-IV.	Men with CG and MDD had higher rates of lifetime DSM-IV alcohol dependence compared to men with MDD alone (42.9% vs. 12.5%, $\chi^2 = 4.52, p = 0.034$). Women with CG and MDD had higher rates of DSM-IV alcohol dependence compared to women with MDD alone (37.5% vs. 4.8%, $\chi^2 = 8.00, p = 0.005$).	Different inclusion criteria for participants with and without MDD. Information regarding the nature and timing of bereavement was not provided.
Zuckoff et al., 2006; USA	Uncontrolled intervention study	Baseline, weekly during treatment sessions, and posttreatment.	Pilot study to adapt CGT for persons with SUDs.	Sixteen adults who were ineligible for a previous RCT due to co-occurring SUDs. Mean age = 42.3 (SD = 9.8), 50% African American, 43.8% White, 6.3% Native American. Mean time since death = 9.8 years (SD = 9.7 years).	CG assessed with ICG ≥ 30 . Substance misuse assessed with SCID-IV, TLFB, breathalyzer test, and self-report.	Participants with high levels of CG at six months were more likely to report increases in smoking at 13 months (Wald $\chi^2 = 3.43, p < 0.05$, relative risk = 16.70). No changes were found for alcohol use. The studies relied primarily on of self-report measures. The sample was homogenous, and there was no control group of participants without CG. Mann-Whitney U two-sided exact test indicated significant pretreatment to posttreatment reductions in ITT analysis ($M = 15.3, SD = 19.7, p = 0.01$) with an effect size of 0.78. Days of abstinence from all substances increased significantly among the ITT group ($M = 20.4, SD = 43.4, p = 0.04$), $d = 0.47$. Average cravings for all substances decreased over time ($F(1, 13) = 5.30, p = 0.04, d = 1.30$).	Drop-out rate of 50%.

Note. CGT = Complicated Grief Treatment; FBP = Family Bereavement Program; GMS = Grief Measurement Scale (Jacobs et al., 1986); ICG = Inventory of Complicated Grief (Prigerson et al., 1995); ICG-RC = Inventory of Complicated Grief-Revised for Children (Melhem, Moritz, Walker, Shear, & Brent, 2007); ITT = intent-to-treat; K-SADS-PL = Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version (Kaufman et al., 1997); MDD = Major depressive disorder; M.I.N.I. = Mini-International Neuropsychiatric Interview (Sheehan et al., 1998); PCBD = Persistent complex bereavement disorder; RCT = randomized control trial; SCID-IV = Structured Clinical Interview for DSM-IV (First, Spitzer, Gibbon, & Williams, 1996); SMAST: Short Michigan Alcohol Screening Test (Selzer, Vinokur, & van Rooijen, 1975); TLFB: Timeline Follow Back (Sobell, Brown, Leo, & Sobell, 1996); TRIG = Texas Revised Inventory of Grief (Faschingbauer, 1981); Tx = treatment.

Table 2
Methodological quality rating scale of 12 studies examining complicated grief and substance use published between 1997 and 2017.

Author, Year	Screening ^a									RCT ^b				Non-randomized ^c				Descriptive ^d				
	1	2	3	4	5	6	7	8	9	1	2	3	4	1	2	3	4	1	2	3	4	5
Brent et al., 2009	✓	✓	✓	✓										✓	✓	✓	✓					
Masferrer et al., 2015a	✓	✓				✓	✓		✓									✓			✓	✓
Masferrer et al., 2015b	✓	✓				✓	✓		✓									✓			✓	✓
Masferrer et al., 2016	✓	✓				✓	✓		✓									✓			✓	✓
Masferrer et al., 2017a	✓	✓				✓	✓		✓								✓					
Masferrer et al., 2017b	✓	✓				✓	✓		✓								✓					
Melhem et al., 2008	✓	✓	✓											✓	✓	✓	✓					
Prigerson et al., 1997	✓	✓	✓	✓	✓		✓	✓										✓	✓		✓	✓
Sandler et al., 2016	✓	✓	✓			✓	✓	✓	✓		✓	✓	✓									
Simon et al., 2005	✓	✓	✓	✓		✓	✓	✓	✓											✓	✓	
Sung et al., 2011	✓	✓	✓			✓	✓	✓	✓						✓		✓					
Zuckoff et al., 2006	✓	✓				✓	✓		✓						✓							

Note. RCT = randomized controlled trial.

^a General screening questions: 1. Are research questions or objectives clearly stated? 2. Do the collected data address each of the research questions or objectives? 3. Are the sampling methods clearly described and appropriate to the research questions or objectives? 4. Are the number and proportion of participants asked to participate in the study who refused participation presented? 5. Did the investigators compare persons who agreed vs. refused to participate in the study to assess for sample selection bias? 6. Is a clear and appropriate definition of complicated grief provided? 7. Is information regarding the instrument used to assess complicated grief provided? 8. Are the reliability and validity of the instrument assessed in the specific study under consideration? 9. Did the study provide a specific cut-point they used to differentiate between normal and complicated grief and did they present the rationale for the selection of this cut-point?

^b RCT questions: 1. Is there a clear description of the randomization process or appropriate sequence generation? 2. Is there a clear description of the allocation concealment or blinding when applicable? 3. Do the authors report attrition rates for each follow-up point? 4. Were attrition rates acceptable?

^c Non-randomized questions: 1. Are participants or organizations recruited in a way that minimizes selection bias? 2. Are measurements appropriate regarding the exposure/intervention and outcomes? 3. In the groups being compared, are the participants comparable or do researchers consider differences between these groups? 4. Are there complete outcome data and, when applicable, an acceptable response rate, or an acceptable follow-up rate for cohort studies?

^d Descriptive questions: 1. Is the sampling strategy appropriate for the quantitative research question? 2. Is the sample representative of the population under study? 3. Are measures appropriate? 4. Was the response rate presented? 5. Was this response rate acceptable?

2.5. Quality assessment

The review sample was examined to assess the risk of bias within each study. Bias assessments were carried out independently by two reviewers (AP and AS) using a modified version of the mixed methods appraisal tool (MMAT; Pluye et al., 2011). To align with our selection criteria, the modified MMAT appraised only three subcategories of quantitative method studies: randomized controlled trials (RCTs), nonrandomized studies, and quantitative descriptive studies. Previous research with the MMAT have indicated moderate to perfect interrater reliability (Pace et al., 2012). We further modified the MMAT following the recommendation of the Cochrane Collaboration (2011) regarding bias assessment in systematic reviews: we added three screening questions to assess selection and attrition bias. These items corresponded with other validated measures such as the Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies (Wells et al., 2013). To address current recommendations for CG research, we added four items to evaluate the extent to which each study provided a clear definition of CG, information about the reliability and validity of the³ instrument used to assess CG, and the rationale used to justify the cut-point used for the study's CG assessment measure (Rosner, 2015). In addition, we modified the quantitative domain-specific items to evaluate whether the article provided outcome data and study attrition rates. Although the MMAT can provide an overall quality score, such scores are less informative than a descriptive summary of each study's methodological quality (Pace et al., 2012). Therefore, this review provides a narrative summary of the methodological strengths and

³The MMAT (Pluye et al., 2011) includes two screening questions and 19 assessment criteria that allow researchers to concomitantly describe and appraise the methodological quality of studies using three design approaches: mixed; qualitative; and quantitative, with the quantitative category subdivided into three subcategories of randomized controlled, nonrandomized, and descriptive study design.

limitations for each study.

3. Results

3.1. Sample characteristics

The final sample of 12 articles consisted of peer-reviewed journal articles published between 1997 and 2017. Seven studies were conducted in the United States and one study was conducted in Spain (which generated five of the reviewed articles). Study designs included two cohort studies (Brent et al., 2009; Melhem et al., 2008), one factor analytic study (Masferrer et al., 2017a), two case control studies (Masferrer et al., 2017b; Sung et al., 2011), one RCT (Sandler et al., 2016), one nonrandomized intervention study (Zuckoff et al., 2006), and five quantitative descriptive studies (Masferrer et al., 2015a, 2015b, 2016; Prigerson et al., 1997; Simon et al., 2005). Eight studies used a cross-sectional design and four used a longitudinal design, with post-baseline follow-up ranging from 6 months (Zuckoff et al., 2006) to 6 years (Sandler et al., 2016).

The 12 studies evaluated 1749 participants in total, with sample sizes ranging from 16 (Zuckoff et al., 2006) to 634 (Melhem et al., 2008) participants. One study targeted individuals with comorbid CG and SUDs (Zuckoff et al., 2006); two articles were evaluation studies of the same sample of bereaved caregivers and offspring, one conducted at 9 months (Melhem et al., 2008) and one at 21 months post bereavement (Brent et al., 2009); one article examined a sample of bereaved spouses (Prigerson et al., 1997); one investigated individuals with bipolar disorder (Simon et al., 2005); and one evaluated individuals with MDD (Sung et al., 2011).

3.2. Methodological quality

Table 2 summarizes the methodological attributes of the reviewed studies as assessed using the modified MMAT, with affirmative responses noted as check marks. All studies clearly identified the research

questions that guided the investigation, collected data appropriate to the stated research objectives, and the vast majority (91.7%) used sampling methods that were clearly described and appropriate to the study's research questions. However, only three (25%) articles (Brent et al., 2009; Prigerson et al., 1997; Simon et al., 2005) provided the number of potential study participants and percentage of those invited to participate but who declined to participate; and only one article (Prigerson et al., 1997) assessed potential sampling bias by comparing outcomes of individuals who agreed to participate with outcomes of those who declined to participate. As such, these limitations might have led to a high rate of sampling bias among the 12 studies included in this review.

A majority of studies (75%) provided a clear definition of CG; however, substantial heterogeneity existed across the criteria and labels used to define CG. Additionally, 10 of 12 studies reported the reliability/validity of their CG assessment instruments, whereas two articles did not report reliability of study measures (Brent et al., 2009; Melhem et al., 2008). In addition, three articles did not provide a rationale for the cut-point used in the study to distinguish normative grief from CG (Brent et al., 2009; Melhem et al., 2008; Prigerson et al., 1997).

Five studies used quantitative descriptive designs and were evaluated consistent with this MMAT methodological domain (Masferrer et al., 2015a; Masferrer et al., 2015b; Masferrer et al., 2016; Prigerson et al., 1997; Simon et al., 2005). Of these descriptive studies, 4 of 5 (80%) used appropriate sampling strategies and only 1 of 4 (Simon et al., 2005) reported a response rate < 60%. However, only one study (Prigerson et al., 1997) demonstrated that the sample was representative of the general population, and only one study used appropriate measures for both CG and substance misuse (Simon et al., 2005).

Five studies used a quantitative nonrandomized design, which included two case control studies (Masferrer et al., 2017b; Sung et al., 2011), two cohort studies (Brent et al., 2009; Melhem et al., 2008) and one nonrandomized intervention study (Zuckoff et al., 2006). Of these, 4 of 5 (80%) studies used appropriate measures to assess CG and substance use. A notable exception was the Masferrer et al. (2017b) study that relied on self-report measures to assess variables related to substance misuse. Further, all but one study evaluated within this methodological domain (Zuckoff et al., 2006) reported response rates of 60% or greater. Despite these strengths, the methodological quality of the five nonrandomized studies had substantial limitations. Only 2 of 5 studies (40%) recruited participants using methods to minimize selection bias (Brent et al., 2009; Melhem et al., 2008). These same two studies were also the only to use analytic methods (e.g., matching, stratification) to account for between-group differences (Brent et al., 2009; Melhem et al., 2008).

One study (Sandler et al., 2016) was assessed under the MMAT criterion for RCTs. This study was of sound methodological quality and provided a clear description of the method used to prevent selection bias (i.e., allocation concealment), reported attrition rates, and demonstrated a high response rate. However, according to the (name of measure criteria?) the Sandler et al. article did not provide sufficient description of the randomization process used to assign participants (i.e., parents grieving loss of a spouse) to study conditions.

3.3. CG among individuals with substance misuse

Five studies examined risk factors, prevalence, correlates, assessment, and etiology of CG among persons with substance misuse (Masferrer et al., 2015a, 2015b, 2016, 2017a, 2017b). These studies relied on the same sample of 196 adult patients in a Spanish SUD treatment facility. All participants reported the death of a significant person (e.g., family, best friend, or partner) at least one year prior to the study; met *DSM-IV-TR* criteria for alcohol, cocaine, or heroin dependence; and reported abstinence during the month before the study.

3.3.1. Risk factors

Findings from a descriptive study (Masferrer et al., 2016) and a subsequent case-control study also conducted by Masferrer et al. (2017b) indicated individuals with SUDs have a range of potential risk factors for CG symptomatology, including female gender, widowhood, loss of a sibling, and non-natural loss (accident, suicide, homicide, or overdose). Conversely, secondary education and high levels of social support were found to be protective factors against CG (Masferrer et al., 2016, 2017b).

3.3.2. Prevalence

One study (Masferrer et al., 2017b) evaluated the prevalence of CG and SUD comorbidity. CG was assessed among the clinical sample previously described, as well as among a control sample of 100 bereaved adults without SUDs. Within the clinical sample, 34.2% of participants met criteria for CG, whereas only 5% of the control group participants met CG criteria. As compared with other studies that examined CG in populations without SUDs, Masferrer et al. (2017b) found a higher rate of CG, suggesting that persons with SUDs may be vulnerable to CG. Moreover, the authors noted that theirs was the first study to examine CG and SUD comorbidity (Masferrer et al., 2017b).

3.3.3. Correlates

Two descriptive studies by Masferrer et al. (2015b, 2016) examined correlates of CG and substance misuse. The first study (2015b) investigated the occurrence and correlates of suicide risk. Comparison of ICG scores between participants with suicide risk and those with no risk of suicide found higher ICG scores among those with suicide risk, even when analyses controlled for marital status, social support, previous suicide attempts, and family history of suicide.

Subsequently, the authors used the same sample to assess associations between anxiety, MDD, PTSD, and CG symptoms (Masferrer et al., 2016). Comparisons of individuals with normal and CG were made on sociodemographic variables; bereavement-related variables; and prevalence of anxiety, MDD, and PTSD. Participants with SUDs and CG had notably higher rates of anxiety and PTSD than participants with SUDs but without CG. After controlling for gender, working status, marital status, relationship to the deceased, and circumstances of the death, CG was significantly, positively associated with having diagnoses for PTSD and MDD (Masferrer et al., 2016).

3.3.4. Assessment

Only one study investigated measures to assess CG among persons with substance misuse. Masferrer and colleagues used the same clinical sample of 196 participants described in the previous section to evaluate psychometric properties of the 19-item Spanish version of the Inventory of Complicated Grief (ICG; Masferrer et al., 2017a). Study results showed high internal consistency (Cronbach's alpha = 0.92) and divergent validity of the Spanish ICG in this sample. An exploratory factor analysis yielded four factors related to the CG construct: (a) discomfort, which consisted of memories, beliefs, and negative feelings related to the death; (b) nonacceptance, which included feelings such as emptiness, envy, or unfairness, and thoughts about the deceased; (c) loneliness/isolation, which comprised statements related to trust and feeling distant and alone; and (d) presence of the deceased, which was defined as seeing and/or hearing the voice of the deceased.

The four-factor solution found by Masferrer et al. (2017a) diverges from prior studies indicating a unidimensional structure among samples of bereaved persons with varying grief-related symptoms (Boelen & Hoijtink, 2009; Prigerson et al., 2009). However, a previous factor analysis of the ICG (Simon et al., 2011) similarly identified multiple dimensions after limiting their analysis to persons meeting criteria for CG. Additionally, findings from a prior validation study of the Spanish version of the ICG identified three factors: memories of the deceased, empty feelings, and presence-experience of the deceased (Limonero, Lacasta, García, Maté, & Prigerson, 2009).

Although Masferrer et al.'s (2017a) findings supported a multiple-factor solution, several notable differences emerged in our review of the study. Masferrer et al., (2017a) converted the first two factors identified in the Spanish validation study (i.e., memories of the deceased, empty feelings) into three factors (i.e., discomfort, nonacceptance, and loneliness/isolation) and homogenized the third factor (presence-experience of the deceased) to create a fourth factor (presence of the deceased). The need to make such changes underscores the difficulty many bereaved individuals with SUDs have with accepting the reality of the death and may indicate a distinct factor solution for CG among bereaved individuals with substance misuse (Masferrer et al., 2017a).

3.3.5. Etiology

One study investigated the temporal relationship between the loss of a significant person and drug consumption of bereaved individuals with SUDs (Masferrer et al., 2015a). Participants were divided into two groups: bereaved persons who increased their drug consumption after the death of a significant person (B-A), and those who increased their drug consumption before the death and their bereavement (A-B). However, because participants with SUDs might have increased their drug or alcohol use both before and after a significant death, the two study groups were not mutually exclusive. A majority of the sample reported increased drug consumption following the death of a significant person; however, as compared with the B-A group, the A-B group was more likely to recognize a relationship between bereavement and drug consumption, report a negative relationship between bereavement and substance use, report a higher level of suffering related to the death, and score higher on the Spanish ICG. In addition, participants in the A-B group who were abstinent were more likely than abstinent B-A group participants to report a relapse following a significant death.

3.4. Substance misuse among individuals with CG

3.4.1. Etiology

Across the 12 studies in this review, only one specifically addressed factors related to substance misuse among persons with CG. Prigerson et al. (1997) examined the effects of CG on future morbidity and onset of new conditions among a sample of 150 older individuals who had recently experienced the death of their spouse (i.e., *spousally bereaved*). Prigerson et al. (1997) reported mean levels of tobacco consumption were relatively stable in the entire group of bereaved subjects. However, even when the analyses controlled for pre-bereavement levels of grief, depression, anxiety, age, and gender, the authors found those with high CG levels at 6 months were more likely to report increased smoking at 13 months. Conversely, no significant CG-related changes were found for alcohol consumption (Prigerson et al., 1997).

3.5. CG and substance misuse

Four studies investigated risk factors and correlates for co-occurring CG and substance misuse. These results are reported separately from the four primary research questions guiding this review as they assessed for CG and substance misuse simultaneously. Nevertheless, results from these studies were relevant to the present review's primary outcomes of interest and have implications for individuals with CG and substance misuse (Melhem et al., 2008; Brent et al., 2009).

3.5.1. Risk factors

Two studies investigated psychological consequences of bereavement for offspring and their surviving caregivers following the death of a parent (Brent et al., 2009; Melhem et al., 2008). Families of parents who died suddenly from suicide, accidental death, or natural death were evaluated 9 months after the loss (Melhem et al., 2008) and again at 21 months in a separate follow-up study by Brent et al. (2009). At the 9-month assessment conducted by Melhem et al. (2008), bereaved

children and their caregivers had similar rates of ICG scores and new-onset alcohol or SUDs regardless of the manner of parental death (e.g., suicide, sudden natural death, or accidental death). Further, bereaved offspring and caregivers did not differ significantly from their non-bereaved comparison groups with regard to new-onset alcohol or SUDs (Melhem et al., 2008).

The follow-up prospective cohort study by Brent et al. (2009) examined the bereaved offspring from the 9-month assessment. Caregivers were not evaluated in Brent et al.'s study. No significant differences were found between retained and lost participants. At the 21-month assessment after the loss of a parent, offspring had higher rates of alcohol and substance misuse than did the nonbereaved comparison group. Post hoc pairwise contrasts indicated that offspring of suicide victims had a significantly higher rate of alcohol or substance misuse than nonbereaved comparison subjects. Additionally, offspring whose parents died in accidents had higher CG scores than those bereaved by sudden natural death.

Taken together, findings from the 9-month (Melhem et al., 2008) and 21-month (Brent et al., 2009) follow-up analyses reveal the enduring effects of parental bereavement, with higher rates of substance misuse and CG manifesting 2 years following parental loss. Further, these findings suggest that manner of death may be a shared risk factor for the onset of both conditions.

3.5.2. Correlates

Two studies assessed CG and its clinical correlates among persons with comorbid mental health disorders. Simon et al. (2005) examined the prevalence and implications of CG among adults with bipolar disorder. The presence of CG was associated with significantly higher rates of current *DSM-IV* alcohol abuse, but not lifetime alcohol abuse (Simon et al., 2005). The association between CG and alcohol misuse was also supported by Sung et al. (2011), who examined rates of bereavement and CG among individuals in outpatient therapy for MDD relative to non-depressed controls. Sung et al. (2011) observed that participants with CG and MDD had higher rates of *DSM-IV* alcohol dependence compared to those with MDD alone (Sung et al., 2011).

3.6. Treatment outcomes

Two studies supported the use of grief-focused interventions to address CG and substance misuse (Sandler et al., 2016; Zuckoff et al., 2006). However, no available studies were identified that assessed outcomes of persons with CG who were in treatment specifically for substance misuse or SUDs.

Sandler et al. (2016) conducted a 6-year follow-up of an RCT of the Family Bereavement Program (FBP), a 12-session program for caregivers and children following the death of a parent. The authors explored which aspects of parental adjustment were impacted by the FBP, which factors moderated this impact, and how the FBP affected changes in parental adjustment over the course of 6 years. Participants in the original RCT included families bereaved by parental death with one or more children between the ages of 8 and 16 years. Families were randomly assigned to the FBP or to the control condition, which consisted of a self-study group. The Sandler et al. 6-year follow-up study examined only parent outcomes.

At 6 years post-study and as compared with parents assigned to the self-study control condition, parents assigned to the FBP group were less likely to meet symptom criteria for CG. Between group comparisons also indicated that parents in the FBP group were less likely to demonstrate alcohol misuse. The results of the 6-year follow-up supported the effectiveness of the FBP intervention regarding CG and alcohol misuse (Sandler et al., 2016). These benefits were not greater for participants who had elevated levels of distress at program entry, suggesting the FBP intervention prevents or reduces rates of CG. However, because no significant mediators were found for measures of alcohol misuse, the effects of FBP might have been due to the program effects

on other aspects of the parents' lives not assessed in this study (Sandler et al., 2016).

The second study to evaluate CG treatment (Zuckoff et al., 2006) was a noncontrolled intervention study that adapted Complicated Grief Treatment (CGT), an existing CG treatment, for persons with SUDs. CGT is a well-supported intervention for CG whose benefits have been demonstrated in three clinical trials (Shear et al., 2014; Shear et al., 2016; Shear, Frank, Houck, & Reynolds, 2005). CGT is more effective for CG than standard interpersonal psychotherapy in relieving CG symptoms and is generally considered to be one of the best-studied treatments for CG (Shear & Gribbin Bloom, 2017). However, persons with SUDs have traditionally been excluded in these studies (Zuckoff et al., 2006).

The complicated grief and substance use treatment (CGSUT) consisted of 24 manualized, individual sessions delivered over 6 months by the first author. The sample consisted of 16 adults deemed ineligible for a prior RCT of CG treatment due to co-occurring SUDs. Significant pre- to posttreatment reductions were found in ICG scores for completers and intent-to-treat (ITT) groups. Both groups demonstrated significant increases in days of abstinence and decreases in ICG scores. Further, a significant negative slope was found in the mixed-model analysis of the ITT group such that average cravings decreased over time. The large effect sizes for changes in CG-related symptoms and accompanying reductions in substance consumption and cravings suggest that CGSUT benefits individuals with both CG and substance misuse.

4. Discussion

This systematic review analyzed 12 studies examining the relationship between CG and substance misuse published through May 2018. Included studies used different designs, methodologies, and evaluated diverse populations with a variety of substance misuse and bereavement-related characteristics. Our review found preliminary evidence of a positive relationship between CG and substance misuse. However, given the methodological limitations and heterogeneity of included studies, these results should be interpreted with caution.

Findings of several studies in this review indicated that individuals with either CG or substance misuse are vulnerable to the subsequent development of the other condition. As compared with individuals who did not have SUDs, a significantly higher prevalence of CG was found among persons with SUDs (Masferrer et al., 2017b). The presence of an SUD also predicted risk for CG beyond other common risk factors for CG such as gender, age, education level, marital status, relationship to the deceased, working status, and circumstances of the death (Masferrer et al., 2017b). Conversely, high levels of CG predicted subsequent increases in smoking among persons grieving the loss of a spouse (Prigerson et al., 1997). Moreover, the presence of CG was associated with increased risk of alcohol misuse among individuals with bipolar disorder (Simon et al., 2005) and individuals with MDD (Sung et al., 2011).

Two studies identified a range of potential risk factors for individuals with comorbid CG and SUDs, including female sex, unemployment, lower level of education, lower level of social support, widowhood, taking prescription medication, history of incarceration, loss of a sibling, recency of the death, and traumatic circumstances of the death (Masferrer et al., 2016, 2017b). Although previous CG literature supports the majority of these risk factors (Chan, Livingston, Jones, & Sampson, 2013; Leach, Burgess, & Holmwood, 2008; Lobb et al., 2010; Melhem et al., 2004; Tsai et al., 2016), Masferrer et al.'s results conflict with prior research in non-SUD populations that reported the highest risk of CG stemmed from the loss of a spouse or child (Fujisawa et al., 2010; Kersting, Brähler, Glaesmer, & Wagner, 2011; Masferrer et al., 2017b). Although taking prescription medication was identified as a predictor of CG, it may be an indication of the presence of a comorbid psychiatric disorder, which is a known risk factor for CG (Prigerson et al., 2009).

Grief related to the death of a parent, particularly due to accident or

suicide, increased the risk of CG and substance misuse; however, this risk was not observed until approximately 2 years following bereavement (Brent et al., 2009; Melhem et al., 2008). These findings are supported by previous research implicating parental death as a risk factor for developing CG and substance misuse (Enez, 2018; Kaplow et al., 2010).

Only one study specifically examined the directionality of the relationship between CG and substance misuse. Pre-bereavement increases in substance misuse were associated with a larger increase in CG symptoms than post-bereavement increases (Masferrer et al., 2015a). Although Masferrer et al.' (2015a) study was the first to investigate the temporal ordering of CG and substance misuse, the study's cross-sectional design and lack of control group precluded causal inference.

A later study by Masferrer et al. (2017a) found the Spanish ICG performed well among persons with SUDs. The study further suggested a multidimensional factor construct of CG among this population (Masferrer et al., 2017a). A series of studies using the same sample of bereaved individuals indicated CG was associated with increased risk of suicide, anxiety, PTSD, and MDD among individuals with SUDs (Masferrer et al., 2015b, 2016). These findings are consistent with prior studies demonstrating significantly higher levels of CG among persons with comorbid mood or anxiety disorders than the general population and suggest this risk extends to adults with substance misuse (Nakajima, 2018; Simon et al., 2007).

Two intervention studies indicated that both CG and substance misuse can be targeted within the same intervention. Empirically validated CG interventions, such as CGT, reduced grief-related symptoms and cravings for drugs and/or alcohol and increased days of abstinence among individuals with comorbid CG and SUDs (Zuckoff et al., 2006). These findings suggest that interventions for CG can be safely adapted and efficacious for persons with substance misuse.

A 6-year follow-up study to an RCT showed that the FBP, a preventative intervention, demonstrated significant improvements in CG symptoms and lower rates of alcohol misuse for parents grieving the loss of a spouse (Sandler et al., 2016). Given that prior systematic reviews (Currier, Neimeyer, & Berman, 2008; Wittouck, Van Autreve, De Jaegere, Portzky, & van Heeringen, 2011) did not find evidence supporting the use of preventative interventions for CG, replication of Sandler et al.'s study is warranted to determine if FBP is an effective preventative intervention for CG.

4.1. Implications for practice

The findings of our review provide preliminary evidence for the benefit of grief management in substance misuse treatment. These early findings suggest the value of incorporating indicators of grief into screening, intake, and assessment procedures. For clients who identify grief-related issues, further assessment may be indicated to determine the presence of CG (Masferrer et al., 2017a). If clients meet criteria for CG and substance misuse, it may be appropriate to consider referral to interventions that specifically target both conditions (Zuckoff et al., 2006). These early findings are unique in their corresponding implications for treatment practices for bereaved individuals, who may similarly benefit from identification and treatment of these comorbid conditions (Zuckoff et al., 2006).

4.2. Limitations

This review has several limitations that must be considered when interpreting the findings. Although the search terms and databases used were extensive, our search might have missed studies pertinent to this review. We attempted to mitigate risk of bias through a comprehensive selection process conducted independently by two researchers. To ensure the identification of relevant literature, we manually examined the reference lists of included studies and consulted with a university social and health sciences reference librarian regarding our search procedure.

Our exclusion of non-English language studies might have created a language bias reflected in the results of this review (Egger, Juni, Bartlett, Hohenstein, & Sterne, 2003). All studies were conducted in Western countries and therefore do not account for cultural variations in the experience or expression of grief. Although two researchers worked independently to conduct a risk of bias assessment using a validated tool (Pluye et al., 2011), the modifications made to this tool were not validated and might have been open to researcher bias.

Methodological limitations were prevalent among the reviewed studies and may have limited the validity and generalizability of findings. For example, methodological limitations included nonprobability sampling, failure to assess for sample selection bias by comparing participants and nonparticipants, cross-sectional designs, and reliance on self-report measures. In addition, substantial variation existed across studies in bereavement-related variables such as the relation of the bereaved to the deceased, type of loss (e.g., violent), and mean temporal interval since death. Last, we found significant variation in substance misuse-related variables such as the length and severity of substance misuse, types of substances used, and measures used to evaluate substance misuse. These factors limited our ability to make comparisons between and across the included studies.

4.3. Recommendations for future research

This systematic review provides preliminary evidence regarding the directionality, prevalence, etiology, and risk factors for the association of CG and substance misuse. However, the small number of pertinent published studies, their overlap in samples, and their questionable external validity limit inferences regarding this relationship. To establish empirical evidence of the relationship between CG and substance misuse and provide guidelines to inform treatment practices, special efforts must be made to address key areas of research.

First, future research should address the methodological limitations of the extant literature to improve internal and external validity of published investigations. Specifically, researchers should focus on consistent terminology and criteria used to identify and define CG, increased homogeneity in substance and bereavement-related variables, and use of validated diagnostic measures of CG and substance misuse. In addition, research reports should provide detailed information regarding sampling procedures, comparisons between treatment and control groups, and assessment procedures. Further, increased use of RCTs and longitudinal designs is needed to enhance understanding of the mechanisms underlying the relationship of CG and substance misuse, which in turn is critical to evaluating the efficacy of interventions.

Second, studies examining the psychometric properties of CG measures such as the ICG are needed to determine the factor structure, validity, reliability, and cut-points for assessment of CG among individuals with substance misuse. Future studies should include participants with all types of substance misuse (rather than limiting samples to cocaine, heroin, or alcohol use disorders) to increase the generalizability of results and provide a validated tool for additional studies. The existence of a validated tool is also needed to help treatment professionals assess for the presence of CG among bereaved clients in treatment for substance misuse.

Third, additional research is needed regarding the prevalence and correlates of CG among individuals with substance misuse (and vice versa) to attain definitive conclusions regarding directionality and risk factors. Moreover, this research should explore subpopulations of individuals with substance misuse such as persons with chronic pain or opioid misuse.

Fourth, a pressing need exists to optimize treatment for persons with comorbid substance misuse and CG. The findings of this systematic review suggest that bereavement may precipitate increases in substance misuse and that elevated levels of grief are more prevalent among persons with SUDs than among the general population. Consequently, it

is likely that persons seeking treatment for substance misuse may have grief-related treatment needs and vice versa. However, although two studies supported the potential benefit of grief-focused interventions, no available studies were identified that specifically targeted substance misuse. Therefore, further research is needed to understand the mechanisms underlying the positive results observed in the present review and determine appropriate targets for treatment.

Although CGT is the most well-studied intervention for CG, there are a range of other treatments that may be adapted for use in this population that should also be evaluated (Simon, 2013). Future intervention studies for CG and substance misuse would benefit from use of RCT designs, validated measures to assess substance misuse, analytic methods to control for potentially confounding variables such as concomitant psychiatric treatment, and follow-up assessments.

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Declaration of Competing Interest

None

Appendix A. Search terms

(“complicated grief” OR “prolonged grief” OR “traumatic grief” OR “delayed grief” OR “dysfunctional grief” OR “abnormal grief” OR “absent grief” OR “chronic grief” OR “inhibited grief” OR “distorted grief” OR “morbid grief” OR “maladaptive grief” OR “atypical grief” OR “unresolved grief” OR “complex grief” OR “complicated bereavement” OR “prolonged bereavement” OR “traumatic bereavement” OR “delayed bereavement” OR “dysfunctional bereavement” OR “abnormal bereavement” OR “chronic bereavement” OR “inhibited bereavement” OR “distorted bereavement” OR “morbid bereavement” OR “maladaptive bereavement” OR “atypical bereavement” OR “unresolved bereavement” OR “complex bereavement” OR “complicated mourning” OR “prolonged mourning” OR “traumatic mourning” OR “delayed mourning” OR “dysfunctional mourning” OR “abnormal mourning” OR “absent mourning” OR “chronic mourning” OR “inhibited mourning” OR “distorted mourning” OR “morbid mourning” OR “maladaptive mourning” OR “atypical mourning” OR “unresolved mourning” OR “complex mourning” OR “pathological grief” OR “pathological bereavement” OR “pathological mourning” OR “persistent complex bereavement disorder” OR “pathological grief disorder”) AND (“substance abuse” OR “substance use” OR “substance misuse” OR “drug abuse” OR “addiction” OR “addict” OR “SUD” OR “substance use disorder” OR “alcohol” OR “drug” OR “smoking” OR “tobacco”)

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⁴ * indicates article included in the systematic review

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