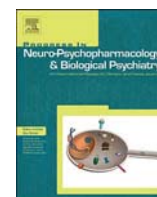




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Chronic pain and suicide risk: A comprehensive review

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ABSTRACT

Death by suicide is one of the leading causes of mortality worldwide. Because individuals with chronic pain are at least twice as likely to report suicidal behaviors or to complete suicide, it is of utmost importance to target which risk factors contribute the most to increasing suicidality. This comprehensive review aims to provide an update on research advancements relating to the identification of potential risk factors for suicidality in individuals with chronic pain. Supporting the results of prior reviews, we found robust evidence that chronic pain itself, regardless of type, was an important independent risk factor for suicidality. The only sociodemographic factor found to be associated with suicidality in individuals with chronic pain was being unemployed/disabled. Depressive symptoms, anger problems, harmful habits (e.g. smoking, alcohol misuse, illicit drugs), childhood or adulthood adversities, and family history of depression/suicide were all also identified as general risk factors. Regarding pain-related factors, sleep problems, poorer perceived mental health, concurrent chronic pain conditions, and more frequent episodes of intermittent pain, were all found to be predictors of suicidality. Unexpectedly, pain characteristics (e.g. type, duration, and intensity/severity) and physical status (e.g. pain interference or disability) were not related to suicide risk. We also identified promising new psychosocial factors (e.g. mental defeat, pain catastrophizing, hopelessness, perceived burdensomeness and thwarted belongingness) associated with suicidality outcomes. A large number of these factors are amenable to change through targeted intervention, highlighting the importance of comprehensively assessing chronic pain patients at risk for suicide, while also incorporating a suicide prevention component into chronic pain management programs.

1. Introduction

Death by suicide is the 17th leading cause of mortality worldwide, accounting for at least 1.4% of all deaths in 2015 (World Health Organization, 2017). Relatively, nationwide lifetime prevalence for suicidal ideation, plans, and attempts has been estimated to be 9.2%, 3.1% and 2.7% respectively (Nock et al., 2008). Suicidal behaviors are often viewed as a continuum, suggesting that there is a progression in suicidality severity over time. In fact, more than 60% of suicidal attempts occur within the first year after the onset of suicidal thoughts, and there is often a progression from reporting suicidal ideation to having plan, and then from having plan to attempting suicide (Nock et al., 2008; Kessler et al., 1999). In this context, early identification of predicting factors associated with increased risk of suicide is of paramount importance.

In 1999, a first literature review (Fishbain, 1999) suggested that chronic pain may be a risk factor for suicidal behaviors (i.e. thoughts, plans, attempts) and suicide completion. Thereafter, another review (Tang and Crane, 2006) demonstrated that individuals with chronic pain were approximately 2 to 3 times more at risk of reporting suicidal

behaviors or to die by suicide. Tang and Crane (2006) also identified potential general risk factors (i.e. being a woman, family history of suicide, previous suicidal attempt(s) and co-occurring depression) and pain-related risk factors (i.e. location and type of pain, higher pain intensity, longer pain duration, sleep-onset insomnia) of suicidality. Furthermore, these authors (Tang and Crane, 2006) hypothesized that other psychological factors, such as feeling helplessness and hopelessness towards pain, desire to escape from pain, pain-related catastrophizing and avoidance, and problem-solving deficits might be important determinants for suicide outcomes. Recently, a narrative review (Fishbain et al., 2014) and a meta-analysis (Calati et al., 2015) found robust evidence confirming the link between chronic pain and suicidal ideation, attempts and completed suicide.

Based on these findings, several clinical practice guidelines highlight the importance of considering chronic pain as a potential risk factor for suicidality (American Psychiatric Association, 2003; National Collaborating Centre for Mental Health, 2011; Magellan Health Services, 2014; Wasserman et al., 2012). Likewise, the World Health Organization (WHO) has acknowledged chronic pain as an individual key risk factor for suicide (World Health Organization, 2010, 2014). As

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part of their global initiative, the WHO recommends that a comprehensive clinical assessment of suicidal behaviors be routinely performed on all individuals of 10 years of age or older who reported having chronic pain (World Health Organization, 2010, 2014). Based on prior groundwork and available clinical recommendations, an emergent and now growing body of research (Hassett et al., 2014; Hooley et al., 2014; Newton-John, 2014) has become interested in better understanding what the specific factors associated with greater risk of suicidality are in persons with chronic pain.

Considering that suicidality has always been a very sensitive topic to touch upon — even more so for health-care professionals who routinely assess, manage and intervene with patients that may present a suicidal at-risk profile — this comprehensive review aims to provide an insightful update on current research advancement with regards to the identification of potential general and pain-related risk factors for suicidality in individuals with chronic pain. More specifically, our objective is twofold: (1) to examine what progress has been made in the last decade, since influential reviews (Fishbain, 1999; Tang and Crane, 2006) on chronic pain and suicidality were published and (2) to identify new promising suicidality risk factors (e.g. harmful health habits, anger problems, health-related quality of life, mental defeat, pain catastrophizing, hopelessness, perceived burdensomeness and thwarted belongingness) in persons with chronic pain. In addition, clinical implications and recommendations will be discussed.

2. Prevalence of suicidality in chronic pain

Chronic pain is a serious, long-standing and debilitating condition affecting approximately 1 person out of 5 worldwide (Boulanger et al., 2007; Gureje et al., 1998; Moulin et al., 2002; World Health Organization, 2004). It is also known to be associated with higher economic burden, poorer quality of life, worse mental well-being and lower physical functioning (Choiniere et al., 2010; Eriksen et al., 2003; Guerriere et al., 2010; Mantyselka et al., 2003; Ohayon, 2004; Phillips, 2009). Additionally, individuals with painful illnesses are at greater risk of suicide compared to those with non-painful illnesses (Juurlink et al., 2004; Stenager and Stenager, 2009; Stenager et al., 1994). Tang and Crane (2006) estimated that around 20% of individuals with chronic pain showed suicidal ideation, that lifetime suicidal attempts varied between 5% and 14%, and that the risk of death by suicide more than doubled in this population. In a more recent narrative review, Fishbain et al. (2014) found that when individuals with chronic pain were compared to a control group, the prevalence of suicidal ideation was between 8% to 41%, and the prevalence of suicide attempts varied between 14% and 38%. Lately, a meta-analysis (Calati et al., 2015) (adjusted for publication biases (Calati et al., 2016; Stubbs, 2016)), showed that death wishes (24.9%), suicidal ideation (current: 14%, lifetime: 23%), plans (current: 2%, lifetime: 9%), attempts (current: 5%, lifetime: 15%) and death by suicide (2%) were more prevalent in people with pain than in those without. The aforementioned work is based on nearly all the available literature, and highlights the importance of chronic pain as a risk factor for suicidality. The following section aims to further describe some of the most recent findings in this regard, while drawing the reader's attention upon the unique and independent contribution that chronic pain has on suicide risk, beyond one's socio-demographic, physical or mental characteristics.

2.1. Epidemiologic studies

In the last decade, several epidemiologic studies have examined chronic pain as an independent risk factor for suicide outcomes. Using a Canadian national survey, Ratcliffe et al. (2008) found that, irrespective of their sociodemographic characteristics or the presence of mental health disorders, individuals reporting at least one chronic pain condition were more likely to endorse having serious suicidal thoughts or having attempted to take their own life within the last 12-month.

Likewise, a national U.S. study (Braden and Sullivan, 2008) reported that beyond sociodemographic, medical and psychiatric factors, the lifetime (but not 12-month) prevalence for suicidal thoughts, plans, and attempt was twice as high in individuals with chronic pain in comparison to the general population. In accordance with earlier findings, a large cross-national study (Scott et al., 2010) found evidence that, along with other physical conditions, almost all chronic pain conditions were associated with lifetime suicidal thoughts and attempts, independent of the effect of relevant clinical factors. Also supporting prior findings, an Australian population study (Campbell et al., 2015) showed that, even after controlling for other covariates, having chronic pain was a significant predictor of suicidal behavior endorsement, while the estimated lifetime and 12-month prevalence of serious suicidal thoughts, plans, and attempts were 2 to 3 times greater than in the general population. In addition, van Tilburg et al. (2011) examined suicidal behaviors in U.S. adolescents and obtained results comparable to those of in adults — i.e. most chronic pain conditions were associated with a greater risk of suicidal ideation and attempts in the last 12-month, and also with an increased likelihood of suicidal behaviors 1 year later. Similar results also emerged in another study (Koenig et al., 2015) in German adolescents. These authors found that teens with chronic pain were more at risk of suicidal attempts compared to those without chronic pain.

With respect to completed suicide, a recent prospective cohort study (Kikuchi, 2009) found that self-reported pain in the last month before death was a strong predictor of committing suicide in Japanese men, irrespective of having (or not) a good health status. Relatedly, a matched case-control study (Manoranjitham et al., 2010) conducted in South India found that chronic pain was a significant determinant of death by suicide, even in the presence of other relevant clinical factors. Similar results were also obtained in a larger matched case-control study (Juurlink et al., 2004) in a population of elderly Canadians, indicating that even after controlling for various illnesses, having moderate or severe pain predicted suicide completion.

2.2. Community, primary care and tertiary care studies

The prevalence estimated in clinical studies seems to abound in the same direction. Chronic tertiary care studies evidenced that current passive suicidal ideation in patients with chronic pain was between 16% and 30% (Dutta et al., 2013; Edwards et al., 2006; Kowal et al., 2014; Okifuji and Benham, 2011; Racine et al., 2014, 2017), current active suicidal thoughts varied between 3% and 17%, and previous suicide attempts ranged between 6% and 23% (Okifuji and Benham, 2011; Racine et al., 2014; Tang et al., 2016). It is worth noting that Tang et al. (2016) have further examined the history of lifetime suicide attempts in patients with chronic pain, and found that 13% of them reported a single attempt, while another 10% reported two or more attempts. One study (Racine et al., 2014) inquired more specifically about patients' suicidal behaviors, since chronic pain onset and their results showed that 27% of them had seriously considered suicide, 21% had reported having a plan at some point, and 6% had made an attempt (Racine et al., 2014). Similar results were obtained in two studies (Fishbain et al., 2009a, 2012) examining different suicidality items. They found that, compared to a community pain-free control group, patient in rehabilitation with chronic pain were more at risk of suicide on most suicidality items. In addition, Meeks et al. (2008) reported that among depressed geriatric patients with or without chronic pain, the former group was at higher risk of endorsing suicidal thoughts.

Several studies have also been interested in suicidal risk in persons with more specific chronic pain conditions. Some studies estimate the prevalence of suicidal behaviors in patients with fibromyalgia to range between 27% and 41% for passive and 6% and 14% for active suicidal ideation (Calandre et al., 2015; Jimenez-Rodriguez et al., 2014; Trinanes et al., 2014), while the prevalence of attempted suicide is reported at 17% (Calandre et al., 2011). Furthermore, compared to the

general population, fibromyalgia was also found to be associated with an increased frequency (3 to 10 times higher) of completed suicide (Dreyer et al., 2010; Wolfe et al., 2011). In patients with migraines, a study (Liu et al., 2015) indicated that the prevalence of suicidal ideation and attempts was 27% and 7% respectively, while those with comorbid fibromyalgia were even likelier to endorse suicidal behaviors than their counterparts. These results are also consistent with other community studies, showing that individuals with migraines (Breslau et al., 2012; Fuller-Thomson et al., 2013a; Wang et al., 2009) or with severe headaches (Breslau et al., 2012; Woolley et al., 2008) had an approximately 2 to 5 times higher risk of suicidal behaviors, even in the presence of other covariates. A tertiary care study (Shim et al., 2017) examining patients with rheumatic diseases found that suicidal ideation, plans, and lifetime attempts were 36%, 3% and 9%, respectively. Similarly, a community study (Fuller-Thomson et al., 2016) examining individuals with and without arthritis reported that the former group was significantly more at risk of attempting suicide than its counterparts. With respect to the complex regional pain syndrome, one small sample study (Lee et al., 2014) showed that 29 patients out of 39 (74%) reported suicidal behaviors.

In short, most if not all of the recent studies seem to agree that chronic pain is an important risk factor for suicidal outcomes, worldwide, while also being at the very least more than a 2-fold risk increase in comparison to the general population. More importantly, this relationship seems to exist independently of a person's socio-demographics, physical health, and mental health status. These aforementioned results highlight the clinical relevance of assessing suicidal behaviors in patients with chronic pain, regardless of their physical (e.g. mildly or not disabled) and mental (e.g. absence of depression) functioning.

3. General risk factors for suicidality in chronic pain

There are several risk factors that are known to be linked with suicide outcomes in the general population (World Health Organization, 2014). The early identification of such risk factors is crucial considering that some of them (e.g. depression, alcohol misuse) can be modified through targeted pharmacological and non-pharmacological treatments. In addition, the awareness of non-modifiable factors that are more inherent to the person itself (e.g. sex, age, family history of suicide) is essential for health care professionals when assessing and intervening with suicidal at-risk patients. However, one question that remains is: are the suicidality risk factors that are commonly found in the general populations the same, or do they differ in individuals with chronic pain? The following section presents recent findings that may, at least to some extent, further elucidate this question. Table 1 provides a summary of potential general risk factors for suicidality that might correspond more closely to persons with chronic pain.

Table 1
Potential general and pain-related risk factors for suicidality in chronic pain.

General risk factors	Description
<ul style="list-style-type: none"> ● Sociodemographic characteristics: ● Personal and family history: ● Psychological disorders: ● Consumption habits and medication use: 	<ul style="list-style-type: none"> Being unemployed or on disability compensation History of childhood adversities (physical/sexual abuse), domestic violence and family dysfunction, family history of depression/suicidality Depressive symptoms, anger problems Smoking, alcohol abuse, illicit drugs, safety assessment before prescribing antidepressant, antiepileptic and opioid drugs
Pain-related risk factors	Description
<ul style="list-style-type: none"> ● Type of chronic pain conditions: ● Chronic pain characteristics: ● Physical factors: ● Health-related quality of life: ● Psychosocial factors: 	<ul style="list-style-type: none"> All types of chronic pain conditions Multiple pain condition, frequency of intermittent pain (e.g. migraine/headache) Sleep problems Poor perceived mental health Pain catastrophizing (magnification and helplessness), coping strategies related to hoping, mental defeat, perceived burdensomeness and thwarted belongingness

3.1. Sociodemographic characteristics

Despite the fact that, in the general population, being a woman, younger aged, less educated, unemployed, unmarried, and earning lower incomes are all important factors that are often found to be related with suicidal ideation, plans, and/or attempts (Nock et al., 2008; Kessler et al., 1999; Borges et al., 2010; Government of Canada, 2006), these associations do not appear to be as obvious in individuals with chronic pain. Some earlier research has suggested that being a woman (Timonen et al., 2003; Treharne et al., 2000) (although not found in Smith et al. (2004a,b) studies) and older aged (Stenager et al., 1994) might be risk factors for suicidality in chronic pain. However, almost all the recent studies examining the association between sociodemographic characteristics in various types of chronic pain conditions did not find support for such relationships with regards to sex (van Tilburg et al., 2011; Edwards et al., 2006; Kowal et al., 2014; Okifuji and Benham, 2011; Racine et al., 2014; Fishbain et al., 2012; Calandre et al., 2011, 2015; Cheatle et al., 2014; Kanzler et al., 2012; McCracken and Morley, 2014; Wilson et al., 2013), age (van Tilburg et al., 2011; Kowal et al., 2014; Okifuji and Benham, 2011; Racine et al., 2014; Fishbain et al., 2012; Lee et al., 2014; Cheatle et al., 2014; Kanzler et al., 2012; Wilson et al., 2013), marital status (Edwards et al., 2006; Kowal et al., 2014; Okifuji and Benham, 2011; Racine et al., 2014; Fishbain et al., 2012; Calandre et al., 2011, 2015; Trinanes et al., 2014; Cheatle et al., 2014; Kanzler et al., 2012), and education levels (Edwards et al., 2006; Kowal et al., 2014; Okifuji and Benham, 2011; Racine et al., 2014; Fishbain et al., 2012; Trinanes et al., 2014; Calandre et al., 2011; Lee et al., 2014; Cheatle et al., 2014). A few studies reported that being a female (Dutta et al., 2013) or male (Racine et al., 2017; Luntamo et al., 2014), older (Edwards et al., 2006) and not being in a relationship (Racine et al., 2017) was related to a more elevated risk of suicide in those with chronic pain. Only one epidemiologic study (Fuller-Thomson et al., 2013a) more specifically examined sex-related difference between migraines and lifetime suicidal ideation. The authors (Fuller-Thomson et al., 2013a) found that suicidal ideation was associated with younger age, being unmarried and being more limited in daily living activities for both sexes, but being poor was a predictor of suicidal ideation only in women, and white racial identity was a risk factor of suicidal ideation only in men.

In addition, some studies (Racine et al., 2014; Fishbain et al., 2009a; Calandre et al., 2011) found on one hand some evidence that employment status might be a potential risk factor for suicide behaviors in individuals with chronic pain, while other studies, on the other hand, have not found such results (Edwards et al., 2006; Kowal et al., 2014; Racine et al., 2017; Trinanes et al., 2014; Cheatle et al., 2014). In their first study, Fishbain et al. (2009a) reported that patients in rehabilitation with chronic pain that received worker compensation, compared to those who did not, had a greater likelihood of endorsing suicidal behaviors while the relative suicidality risk varied from 3 to 7-fold compared to a healthy community non-patient group. However, the authors

failed to find such a relationship in a subsequent study (Fishbain et al., 2012), but found that being unemployed was associated with a higher risk of having a suicide plan. Similarly, in a sample of tertiary care chronic pain patients, Racine et al. (2014) obtained results showing that those who were unemployed or on disability leave were 6 times more likely to present suicidal thoughts compared to those who were working, studying, or retired. Likewise, Calandre et al. (2011) recruited patients through fibromyalgia associations and found that 50% of those who attempted suicide were either unemployed or on sick leave compared with 38% of non-attempters.

In sum, although studies carried out in the general population demonstrated that sociodemographic characteristics were related to suicide risk, this seems not to be the case in people with chronic pain. However, it is worth considering that most chronic pain research was not specifically interested in examining the potential role that socio-demographic variables played in suicidality, instead opting to view them as potential covariates that need to be adjusted for. It is therefore possible that a more in-depth investigation of sociodemographic factors (e.g. sex-related differences) and suicidal outcomes might yield different results. Some evidence suggests that employment status may be a potential risk factor associated with suicidal behaviors; however, study results are somewhat inconsistent in this regard. These mixed findings raise the possibility that other modifiable factors such as the loss of social role (e.g. family provider) and social support (e.g. feeling isolated or not belonging), pain-related negative cognitions (e.g. perceived of self as a burden or useless, feeling guilt or helplessness) or the lack of proactive pain-related coping strategies (e.g. activity pacing) may contribute to patients' inability to work, which in turn leads to increasing suicide risk. Research examining the extent to which work status and other potential underlying mechanisms may be associated with suicide outcomes in people with chronic pain is warranted.

3.2. Personal and family history

The general literature found that family (or close relatives) history of suicidal behaviors/suicide, family history of psychiatric disorders (e.g. depression) and childhood and adulthood adversities were potential risk factors for suicidality (World Health Organization, 2014; Cheng et al., 2000; Johnson et al., 2002; Phillips et al., 2002; Qin et al., 2002). An earlier study by Smith et al. (2004a) showed that, in patients with chronic pain, those reporting a family history of suicide attempts or suicide completion were 7 to 8 times more likely to present passive or active suicidal thoughts. More recently, Cheatle et al. (2014) reported that family history of depression and history of sexual/physical abuse were both associated with current suicidal ideation in patients with chronic pain, while family history of suicide behaviors was not. Likewise, another study (Fishbain et al., 2012), reported that both history of physical or emotional traumatic experiences and family dysfunction was associated, at least to some degree, to suicide risk in rehabilitation patients with chronic pain. In chronic pain patients sample, Okifuji and Benham (2011) found that attempted suicide was best indicated by a history of physical abuse and domestic violence, while history of physical and sexual abuse were discriminant of current suicidal thoughts. Supporting the above-mentioned findings, Fuller-Thomson et al. (2016) conducted an epidemiologic study in persons with arthritis, and their results revealed that childhood sexual or physical abuse and chronic parental domestic violence were significant predictors of elevated risk of suicidal attempts.

There is a paucity of research that examined personal and family history as potential risk factors of suicidality in individuals with chronic pain. However, the emerging literature appears to support that a history of childhood adversities and domestic violence, and perhaps a family history of depression/suicide may be linked with suicidal outcomes. Additional research is needed to confirm these findings, but meanwhile, since family history of suicide and previous trauma and abuse are considered to be important key elements that are part of suicide risk

prevention practice guidelines (World Health Organization, 2014), they should be assessed in individuals with chronic pain.

3.3. Psychological disorders

As one would expect, it is well acknowledged in the general population that mental disorders such as a depressed mood and anxiety are closely related to suicidality (Nock et al., 2008; Kessler et al., 1999; World Health Organization, 2014; Moller, 2003). Several studies have examined the link between psychological factors and suicidality in chronic pain patients. Namely, Edwards et al. (2006) showed that both higher anxiety and depression levels were predictors of the presence of suicidal ideation, but that only depression was significantly associated to its severity (i.e. active versus passive thoughts). Likewise, Fishbain et al. (2012) examined different forms of suicidal behaviors and found that higher depression symptoms, greater somatic complaints, and greater borderline features seemed to be associated with some suicidal behaviors items. Supporting these findings, several tertiary care chronic pain studies found a relationship between anxiety (Okifuji and Benham, 2011; Racine et al., 2017; Tang et al., 2009) or mood disorders (Kowal et al., 2014; Okifuji and Benham, 2011) and suicidal behaviors. Similar results have also been obtained in patients with fibromyalgia — i.e. those who were more depressed or anxious were also more likely to report suicidal thoughts (Calandre et al., 2015; Trinanes et al., 2014; Raphael et al., 2006) or to attempt suicide (Calandre et al., 2011). Interestingly, another fibromyalgia study (Trinanes et al., 2014) used the Beck Depression Inventory (BDI) (Beck and Steer, 1987) and found that self-blame (i.e. sense of failure and disappointment, feeling of guilt and punishment, self-criticism) was the only scale that predicted the endorsement of suicidal thoughts. In a sample of patients with migraines, Liu et al. (2015) found that depression was independently associated with both suicidal ideation and attempts, while anxiety disorders were only associated with suicidal ideation. Two studies examined previous suicidal attempts in patients with bipolar disorders, with and without comorbid migraines, but the link between depression and suicide attempts was found in one study (Ortiz et al., 2010), but not in the other (Brietzke et al., 2012). In addition, Fuller-Thomson et al. (2016) results indicated that, in individuals with arthritis, those with a lifetime history of depression or anxiety disorders were more likely to have attempted to take their own life, while another study (Lee et al., 2014), in a sample of patients with complex regional pain symptoms, reported that depressive symptoms, but not anxiety, were related to suicidal behaviors.

In contrast to the aforementioned findings, there are also several chronic pain studies that found that even though depression was associated with suicidality, this relationship disappeared when other relevant psychological and cognitive factors were taken into account. For example, Cheatle et al. (2014) did not find depression to be a significant risk factor of suicidal ideation in patients with chronic pain when other relevant clinical risk factors (such as feeling socially withdrawn and family history of either depression or sexual/physical abuse) were accounted for. Similar results were obtained in another chronic pain study (Racine et al., 2014), indicating that depression was not associated with suicidal thoughts when perceived mental well-being was included in the regression model. Supporting this view, Tang et al. (2016) reported that both depression and anxiety were not related with worst-ever suicidal thoughts when pain intensity and mental defeat were taken into account. Relatedly, Kanzler et al. (2012) examined perceived burdensomeness in patients with chronic pain and found these factors to be solely associated with suicidal thoughts, while depression was not. Wilson et al. (2013) corroborated these results concerning perceived burdensomeness, but also obtained results showing that depressive symptoms, longer pain duration, and thwarted belongingness were all significant predictors of endorsing suicidal thoughts as well. One study (Shim et al., 2017), however, may have shed some light on these inconsistencies: Shim et al. (2017) did not find a significant association between depression and suicide risk when other factors (e.g.

catastrophizing, perceived social support, and burdensomeness) were accounted for, but depression was mediating the relationship between pain magnification and suicide risk.

Nonetheless, in the general population, anger appears to be a risk factor for suicidality (Hawkins and Coughle, 2013). Besides, anger, hostility, impulsivity, and aggression constructs are known to be associated with negative pain-related outcomes in persons with chronic pain (Fishbain et al., 2011a; Greenwood et al., 2003). There is one tertiary care study (Racine et al., 2017) that recently found that patients with chronic pain that reported higher anger levels were also significantly more at risk of presenting suicidal ideation, irrespective of their depressive symptoms. Two other studies also found some evidence that hostility (Fishbain et al., 2012), aggression, and impulsivity (Margari et al., 2014) may increase suicidality risk in chronic pain patients.

To summarize, prior studies seem to appreciate the crucial role that depression has on suicide risk in patients with chronic pain, while the findings are mixed when it comes to anxiety disorders. Considering that depression is highly comorbid with chronic pain (Arnou et al., 2006; Fishbain et al., 1997) and that depression and suicidality are very much (but not always (Calandre et al., 2015)) intertwined, clinicians should systematically evaluate suicidal behaviors in depressed patients. Clearly, more research examining various mood and anxiety disorders, as well as anger problems, is warranted. A new insight concerns the fact that depression may disappear as a predictor factor when other psychological and cognitive variables (discussed in more details in Sections 4.4 and 4.5) such as health-related quality of life, mental defeat, perceived burdensomeness, or social withdrawal are taken into account. This suggests the possibility that depression may act more as an indirect mediator of suicide risk. This hypothesis necessitates further exploration.

3.4. Consumption habits

Although smoking cigarettes, alcohol misuse and illicit drugs have been shown to increase the risk of suicidality in the general population (Breslau et al., 2005; Makikyro et al., 2004; Pompili et al., 2010; Tanskanen et al., 2000; Wong et al., 2013), these findings are not as clear in individuals with chronic pain. For example, in a chronic pain tertiary care study (Edwards et al., 2006), no difference was found between patients with or without suicidal ideation with respect to smoking, caffeine or alcohol use. Likewise, Racine et al. (2014) found no evidence linking suicidal ideation to the use of alcohol to relieve chronic pain, but reported that those who did use illicit drugs as a form of pain relief were 5 times more likely to present suicidal thoughts compared to those who did not. Partly supporting previous findings, another study (Fishbain et al., 2012) did not find a relationship between smoking and suicide risk, but their results showed that substance abuse was related only to the specific thoughts of wanting to die because of pain. Using a discriminant analysis, Okifuji and Benham (2011) reported that history of substance abuse had a relative contribution on previous suicide attempt, but not on current suicidal intent. Regarding specific chronic pain conditions, Fishbain et al. (2009b) obtained results showing that smoking was related to suicidal thoughts (note: only found when using an expanded definition of suicidal ideation) while the combination of heavy smoking and alcohol problems appeared to increase the likelihood of having suicide thoughts, in a sample with chronic lower-back pain. Another study (Fuller-Thomson et al., 2016) in individuals with arthritis showed that those who were misusing alcohol or were taking illicit drugs were more likely to have attempted suicide than those who were not. These results are, however, contradictory with the ones found in a fibromyalgia sample, where no significant difference emerged with respect to suicidal behaviors in patients that were users or nonusers of cannabis (prescribed and nonprescribed) (Ste-Marie et al., 2012). Even though there are some inconsistencies on the little research that has examined the association

between consumption habits and suicidality in patients with chronic pain, targeted treatment should be considered in light of the detrimental effect they have on patients' health.

3.5. Medication use

Because of their lethal toxicity, medication commonly used to treat chronic pain, such as antidepressants (e.g. serotonin reuptake inhibitors (SSRIs), tricyclics (TCAs)), antiepileptics (e.g. gabapentin, pregabalin) and opioids (e.g. oxycodone, fentanyl) are easily accessible means to commit suicide. A population-based study (Madadi et al., 2013) reported that death by suicide in opioid users was significantly associated with having chronic pain. Racine et al. (2014) found that patients with chronic pain who were taking antidepressant medication were 4 times more at risk of endorsing suicidal thoughts. However, Okifuji and Benham (2011) found no relationship between suicidal behaviors and antidepressants, opioids, antiepileptics or any other kinds of medications (e.g. benzodiazepine, NSAID) used in patients with chronic pain. There are also two topical reviews (Pereira et al., 2014, 2013) that aimed to better understand the link between suicidality and antidepressant or antiepileptic uses in relationship with chronic pain. These authors ((Pereira et al., 2014; Pereira et al., 2013) were not able to draw any firm conclusion based on the inconsistencies of available research, but they raised several important clinical and research issues (see also Cheatle's commentary (Cheatle, 2014a)) including (1) methodological concerns (e.g. small sample, variety of research designs) resulting in inconsistent or contradictory findings, (2) the need to use a standardized suicidality measure when conducting research studies (e.g. Columbia-Suicide Severity Rating Scale (Posner et al., 2011)), (3) carefully considering whether to initiate or continue pharmacotherapy treatment based on a benefit-risk assessment if a patient with chronic pain presents a suicide risk profile, and (4) the need to further investigate the effect of antidepressant treatments for chronic pain on suicidality risk, and whether it differs by pain condition, other demographic characteristics, or psychiatric variables.

Considering that there is robust evidence showing that antidepressant medication decreases suicide risk (Zalsman et al., 2016), it is reasonable to assume that such treatments were prescribed to patients with depressive symptoms and pre-existing suicidal ideation. Furthermore, researchers and clinicians have recently started taking the lethality of opioid drugs even more into consideration, leading to a re-evaluation of the risks and benefits of using opioids while stressing the importance of comprehensively assessing suicide risk, and having a suicide prevention plan ready as part of chronic pain management programs (Cheatle, 2011; Madadi and Persaud, 2014; Webster, 2014). Bearing in mind that pharmacotherapy has an important role in chronic pain management, additional research is needed to address the matter of medication use and suicide risk.

4. Pain-related specific risk factors for suicidality

Earlier research has shown that certain types of chronic pain (back pain (Penttinen, 1995), widespread pain and fibromyalgia (Amir et al., 2000; Macfarlane et al., 2001), abdominal pain (Smith et al., 2004a; Magni et al., 1998; Miller et al., 2004; Spiegel et al., 2007), and migraine (Breslau, 1992)) might be more significant risk factors for suicidality than others (e.g. neuropathic pain (Smith et al., 2004a)). Moreover, longer pain duration (Treharne et al., 2000; Smith et al., 2004a; Fishbain et al., 1997; Hinkley and Jaremko, 1994), higher pain intensity (Smith et al., 2004b; Hinkley and Jaremko, 1994) (not found in Smith et al. (2004a)), and sleep problems (Smith et al., 2004b) were also identified as potential risk factors based on their association with suicidal thoughts. However, most recent chronic pain studies seem to only partially support previous findings, while new potential determinants for suicidality have been identified, including the number of pain conditions, pain-related interference or disability, health-related

quality of life and various psychosocial factors. [Table 1](#) summarizes the potential pain-related specific risk factors for suicidality.

4.1. Types of chronic pain conditions

Several recent epidemiologic studies have been interested in identifying whether or not suicide risks differed across various types of chronic pain conditions. For example, [Ratcliffe et al. \(2008\)](#) examined four types of chronic pain and found that migraines and back problems (to a lesser extent) were both associated with suicidal behaviors in the past 12 months, while arthritis and fibromyalgia were not. One the other hand, another study ([Ilgen et al., 2008](#)) obtained the following results: (1) headaches were significantly related to 12-month suicidal ideation and attempts (2) non-arthritic chronic pain was only associated with suicidal attempt and (3) no relationship between suicidal behaviors and back/neck problems were found. [Campbell et al. \(2015\)](#) found another pattern: they reported that all pain conditions (arthritis, migraines and back/neck problems) were predictors of the presence of suicidal thoughts, and that arthritis was also related to suicidal plans, whereas back/neck problems were also associated with suicidal attempts. Regarding lifetime suicidality, [Braden and Sullivan \(2008\)](#) results showed that headaches and ‘other’ types of chronic pain were strongly related with suicidal behavior endorsement, while arthritis/rheumatism and back/neck problems were not. In a cross-national study ([Scott et al., 2010](#)) investigating the association between physical conditions and suicidal behaviors, all chronic pain conditions (i.e. headache, back/neck problems, arthritis and ‘other’ types of chronic pain) were associated with the presence of lifetime suicidal ideation, and almost all chronic pain conditions (except back/neck problems) predicted suicidal attempts.

One study ([Ilgen et al., 2013](#)) examined various types of chronic pain conditions in relationship to death by suicide, and obtained results showing that migraines, psychogenic pain, and back pain were significantly associated with increased likelihood of suicide completion, while neuropathic pain, headaches, and fibromyalgia conditions were not. In addition, two studies interested in specific pain syndromes found that the rate of death by suicide was more than 10 times higher in hospital-treated patients with fibromyalgia ([Dreyer et al., 2010](#)) and musculoskeletal diseases compared to the general population ([Lofman et al., 2011](#)).

With respect to the adolescent population, one study ([van Tilburg et al., 2011](#)) found that chronic headaches and muscle/joint aches were associated with 12-month suicidal thoughts (but not attempts), while no such results were obtained for stomach aches. Another study ([Koenig et al., 2015](#)) showed that both headaches and abdominal pain (but not ‘general’ pain) increased the likelihood of suicide attempted in teens. Partly supporting these findings, [Fuller-Thomson et al. \(2013b\)](#) obtained results indicating that migraines and back pain were independent risk factors of suicidal ideation in Canadian adolescents. In contrast, one Finnish population-based study ([Luntamo et al., 2014](#)) examined the association between pain symptoms in childhood and severe suicidality in early adulthood, and found that abdominal pain, but not headaches, were related with severe suicidal attempts and completed suicide, in boys only.

Briefly, even though some chronic pain conditions (e.g. headache and migraine, back pain) might possibly be more related to suicide risk than others (e.g. neuropathic pain, fibromyalgia), results from studies are mixed and seem rather inconclusive. One explanation may reside in the often vague and unclear classification used, where some types of chronic pain conditions (e.g. fibromyalgia) may fall under the ‘other’, ‘general’ or ‘nonarthritic’ pain category. Furthermore, most research generally examines only 3 or 4 types of chronic pain, which encompass only a limited number of chronic pain conditions. Based on the abundant evidence linking chronic pain to suicide risk, it is reasonable to suppose that chronic pain itself, irrespective of which type, is a determinant of suicidality. Additional research including a wide array of

chronic pain conditions is warranted to further examine this possibility.

4.2. Chronic pain characteristics

Contrary to previous studies ([Tang and Crane, 2006](#); [Treharne et al., 2000](#); [Smith et al., 2004a](#); [Fishbain et al., 1997](#); [Hinkley and Jaremko, 1994](#)), most recent findings (except [Racine et al. \(2017\)](#) and [Wilson et al. \(2013\)](#)) seems not to support longer chronic pain duration as a risk factor of suicidal behaviors ([Edwards et al., 2006](#); [Kowal et al., 2014](#); [Okifuji and Benham, 2011](#); [Racine et al., 2014](#); [Tang et al., 2016](#); [Calandre et al., 2015, 2011](#); [Lee et al., 2014](#); [Cheatle et al., 2014](#)). Besides, results appear to be mixed and inconsistent with respect to pain intensity or severity: some studies showed evidence that higher pain levels are a risk factor of suicidal behaviors ([Edwards et al., 2006](#); [Tang et al., 2016](#); [Breslau et al., 2012](#); [Lee et al., 2014](#)) while most of them failed to find such a relationship, or this association disappeared when other relevant factors such as demographic, physical, or psychosocial variables were taken into account ([Edwards et al., 2006](#); [Kowal et al., 2014](#); [Racine et al., 2014, 2017](#); [Fishbain et al., 2012](#); [Trinanes et al., 2014](#); [Calandre et al., 2011](#); [Cheatle et al., 2014](#); [Kanzler et al., 2012](#); [Wilson et al., 2013](#); [Magruder et al., 2012](#)). Nonetheless, it is worth highlighting that most epidemiologic studies agreed that severe chronic pain is strongly associated with an increased risk of death by suicide ([Juurlink et al., 2004](#); [Kikuchi, 2009](#); [Ilgen et al., 2010](#)). With respect to the number of pain conditions, [Ilgen et al. \(2008\)](#) obtained results showing that individuals with multiple chronic pain conditions (two or more) were nearly three times more at risk of having attempted suicide in the last 12-month, compared to those without chronic pain. However, in another study, [Ilgen et al. \(2013\)](#) did not replicate these findings in persons with chronic pain having completed suicide. Furthermore, there are some studies in patients with migraines that showed that the frequency of headaches ([Liu et al., 2015](#); [Wang et al., 2009](#); [Zampieri et al., 2014](#)) and fibromyalgia comorbidity ([Liu et al., 2015](#)) (i.e. multiple pain conditions) were risk factors of the presence of suicidal behaviors.

In brief, it seems that there is no strong link between pain duration, intensity or severity and suicidality, while there are some emerging findings supporting that multiple chronic pain condition and frequency of intermittent pain (e.g. migraine/headaches) may contribute to an increased risk of suicide. Perhaps it is possible that, as more time is spent living with chronic pain, suicidal behaviors may be less related with physical symptoms of the disease itself, but rather more with the broader multidimensional and distressing experience of dealing with a debilitating condition. It is also plausible that long-standing severe pain results in a “ceiling effect”, which might have an effect on the discriminatory power of these variables. Another possibility than can also be raised is that, similar to depressive symptoms (see [Section 3.3](#)), pain symptoms may have a mediational indirect effect on other potential mechanisms associated with suicide outcomes. Further research is clearly needed to examine the extent to which pain intensity/severity play a role in suicide outcomes.

4.3. Physical factors

There is a small number of studies that have examined pain-related interference or pain disability as a risk factor for suicidality. With a few exceptions ([Kowal et al., 2014](#); [Racine et al., 2017](#)), most studies found an association between either pain interference or disability, but this relationship vanished when other relevant factor such as pain characteristics, sociodemographics, health-related quality of life, and psychological disorders were accounted for ([Racine et al., 2014](#); [Liu et al., 2015](#); [Wang et al., 2009](#); [Magruder et al., 2012](#)). Likewise, [Edwards et al. \(2006\)](#) found that pain interference was associated with a greater likelihood of endorsing suicidal thoughts, but not its severity (passive versus active thoughts). In contrast, one study ([Shim et al., 2017](#)) found that physical disability was an independent factor associated with

suicide risk while another study (Fishbain et al., 2012) reported that functional disability was a predictor of wanting to die because of pain (i.e. not found to be significant on other suicidal behaviors items). Additionally, in a sample of adolescents, Fuller-Thomson et al. (2013b) reported that being prevented from doing activities because of pain was significantly associated with having suicidal thoughts.

Finally, it seems that studies examining pain-related physical factors are inconsistent with regards to the relationship between this variable and suicidal risk. These results are similar to those obtained for different types of chronic pain conditions and pain characteristics (see Sections 4.1 and 4.2), again suggesting that the physical status of patients might be less, at least directly, associated with suicidality. Relatedly, it might be plausible that pain interference or feeling disabled in daily living activities may elevate the risk of suicide through certain psychosocial pathways as well. Such psychosocial factors, and perhaps many others, may explain the weak relationship between pain-related factors and suicidality to a certain degree. Clearly, more research is needed to elucidate this issue.

4.4. Sleep problems

Sleep disturbance is a well-recognized, unique, and independent risk factor of suicidality (Bernert and Joiner, 2007; Bernert et al., 2015; Goodwin and Marusic, 2008; Pigeon et al., 2012; Wojnar et al., 2009). Furthermore, there is strong evidence supporting that chronic pain experience is intimately tied with insomnia, at least as much as depressed mood and anxiety are (Ohayon, 2005). Smith et al. (2004b) were the first to demonstrate a connection between sleep-onset insomnia severity and presence of suicidal thoughts in patients with chronic pain. Although, some subsequent studies did not find such a relationship (Racine et al., 2017; Trinanés et al., 2014; Lee et al., 2014; Cheatle et al., 2014), some other studies (Racine et al., 2014; Calandre et al., 2015, 2011; Liu et al., 2015) obtained results supporting poor sleep quality as a risk factor of suicidal behaviors. For example, Racine et al. (2014) found that patients with chronic pain reporting poorer sleep were significantly more likely to have suicidal ideation, independent of the effect of other pain characteristics (e.g. pain intensity, pain disability). Similar results were also obtained in fibromyalgia (Calandre et al., 2015, 2011) or migraine (Liu et al., 2015) studies, showing that poor sleep quality was a significantly associated with suicidal behaviors endorsement. With respect to sleep quality, Winsper and Tang (2014) hypothesized that in individuals with chronic pain, sleep problems may increase suicide risk throughout other psychosocial pathways involving catastrophizing thinking and perceived sense of defeat/entrapment. Additional research is warranted to further examine this possibility.

4.5. Health-related quality of life

A small number of studies examined the relationship between suicidal ideation and health-related quality of life (e.g. SF12 (Health Status in Utah: The Medical Outcomes Study SF-12, 2004) and SF36v2 (Ware et al., 1993)) and found that patients with chronic pain who perceived their mental (but not physical) health as being poorer were more likely to endorse having suicidal thoughts (Racine et al., 2014, 2017; Calandre et al., 2015). Trinanés et al. (2014) used the SF36 scale and reported that lower scores on the Emotional role and Physical role dimensions — i.e. reflecting difficulties with work or other activities as a result of physical or mental role limitations — were associated with the presence of suicidal thoughts. In addition, one study (Racine et al., 2014) obtained results showing that depressive symptoms were not found to be predictors of suicidal ideation in the presence of mental health variables, suggesting that the self-perception of being mentally healthy may reduce suicidality risk.

Even though more research is required, the available findings seem consistent throughout all studies: compared to mental well-being, the

physical well-being might be less importantly related to suicide outcomes in patients with chronic pain.

4.6. Psychosocial factors

Psychosocial factors are known to be significant predictors of pain and functioning in individuals with physical disabilities (Jensen et al., 2011). Pain catastrophizing is especially recognized as a key psychosocial factor and it has consistently been associated with pain-related negative outcomes in persons with chronic pain (Keefe et al., 2004; Quartana et al., 2009; Racine et al., 2016; Sullivan et al., 2001). New emerging studies have been interested in the association between pain-related psychosocial factors and suicidality. Using an outpatient clinic sample, Sansone et al. (2014) found a significant association between higher catastrophic thinking and attempted suicide. Likewise, four recent chronic pain tertiary care studies (Edwards et al., 2006; Racine et al., 2014, 2017; Tang et al., 2016) have further examined the relationship between catastrophizing and suicide risk while also considering other pain-related psychosocial factors. Edwards et al. (2006) found that greater pain catastrophizing was uniquely and independently associated with the presence and the severity of suicidal thoughts, while the interaction between catastrophizing and depression, over and above their individual effect, also predicted suicidality outcomes. In addition, another coping strategy emerged: patients who reported praying or hoping to cope with their pain were less likely to report suicidal thoughts (Edwards et al., 2006). In a first study, Racine et al. (2014) examined the three pain catastrophizing components (i.e. helplessness, amplification, and rumination) separately, as well as patients' beliefs towards pain. They found that pain-related helplessness was the only significant psychosocial risk factor related to suicidal thoughts endorsement (Racine et al., 2014). In another larger pan-Canadian study, Racine et al. (2017) found that patients that felt more helpless about their pain and had greater pain magnification were also more likely to present suicidal ideation. In addition, they (Racine et al., 2017) found that patients who believed more in a medical cure for their pain had less suicidal thoughts, suggesting the possibility that having hopes towards a pain treatment may act as a protective factor. Supporting some of Racine's findings, Shim et al. (2017) reported that, in patients with rheumatic diseases, pain magnification was the only catastrophizing scale that predicted suicidal behaviors. Contrasting with previous findings, Tang et al. (2016) results showed that helplessness and self-efficacy were not correlated with neither present nor worst-ever suicidal thoughts. In addition, catastrophizing was associated only with worst-ever suicidal thoughts, but it was not found to be a significant predictor when pain intensity and mental defeat (i.e. state of mind manifested by the loss of autonomy and relinquishing efforts to preserve identity and agency (Tang et al., 2007)) were accounted for (Tang et al., 2016). Relatedly, Fishbain et al. (2012) found that low perseverance (i.e. low levels of self-control, resilience, and optimism) appear to be related to the presence of suicidal ideation.

Several recent studies have also examined suicide risk within the Interpersonal Theory of Suicide (Joiner, 2005; Van Orden et al., 2010), which conceptualized that thwarted belongingness and perceived burdensomeness could lead an individual to develop suicidal thoughts while acquiring suicidal capability. The general literature has consistently linked these two factors to suicidal behaviors (Cukrowicz et al., 2011; Joiner et al., 2009; Van Orden et al., 2008). A retrospective chart review study (Kanzler et al., 2012) obtained preliminary findings indicating that perceived burdensomeness was the only significant predictor of suicidal intent, independent of the effect of demographics, pain severity and depressive symptoms. In a sample of tertiary care chronic pain patients, Kowal et al. (2012) found self-perceived burden to be correlated with suicidal thoughts and Cheatle et al. (2014) reported that patients who felt that they were socially withdrawn or isolated as a result of their pain were twice as likely to present suicidal ideation. Supporting prior findings, Wilson et al. (2013) obtained

results indicating that both perceived burdensomeness and thwarted belongingness were independent predictors of suicidal ideation among other significant factors (e.g. pain duration, depression), but catastrophizing was not one of them. Interestingly, another study (Kowal et al., 2014) showed that, compared to patients with no suicidal ideation, those having low or high suicidal ideation reported more catastrophic thinking, while burdensomeness was only found in the high suicidal ideation group. More recently, one study (Shim et al., 2017) examined the mediating effect of depression, perceived social support and perceived burdensomeness in the relationship between pain magnification (note: rumination or helplessness scales were not found to be significant risk factor) and suicide risk. These authors (Shim et al., 2017) found that greater pain magnification was related to increased suicide risk 1) through burdensomeness and depression, 2) through depression and social support, and 3) through depression, social support and burdensomeness. These findings seem also in line with the hypothesis that catastrophizing and depression interact through complex and shared behavioral, cognitive and neurophysiological pathways, leading to detrimental effects on pain-related outcomes (Edwards et al., 2011).

In summary, new emergent research seems to agree that some pain-related psychosocial factors may be protective of, or contributing to negative suicide outcomes. Since these factors can be modified through targeted chronic pain treatments, they might be key elements with respect to suicide prevention. While there is some evidence that catastrophizing (e.g. helplessness and magnification components) may increase suicide risk, the results are rather inconclusive with respect to other types of coping strategies, except those involving a hoping elements (e.g. praying, hoping for a medical cure). Unfortunately, the actual literature is too limited in this regard, so more research will be required to draw any firm conclusion. Other factors, part of the Interpersonal Theory of Suicide — i.e. perceived burdensomeness and thwarted belongingness — show promising results and merit to be further investigated. Taking into consideration that suicidality is a multifaceted problem to the point that the risk factors would differ upon each unique population characteristic, this suggests that the development of other suicidality theoretical frameworks (or the refinement of existing models) that are more specific to patients with chronic pain is warranted.

5. Clinical implications and recommendations

As a whole, the present comprehensive literature review supports prior reviews and meta-analyses (Fishbain, 1999; Tang and Crane, 2006; Fishbain et al., 2014; Calati et al., 2015) evidencing that chronic pain is a key individual risk factor for suicidality and death by suicide. It seems that all chronic pain conditions — regardless of type — are similarly related with suicidality outcomes, and that individuals with concurrent chronic pain conditions or with more frequent episodes of intermittent pain (e.g. migraines/headaches) may be at greater risk for suicide. The present review also suggests that chronic pain possesses its own unique profile, based on distinctive potential general and pain-related risk factors for suicidality.

With respect to general factors, we found that contrary to the general population, sociodemographic characteristics did not seem to be related to suicide risk in individuals with chronic pain. The only exception was for work status, in that people who were unemployed or on disability compensation (probably due at least in part to their chronic pain condition) were at higher risk of presenting suicidal behaviors. Also, even though there are still very few studies on this subject available in the current literature, it seems that a history of childhood or adulthood adversities, a family history of depression/suicide, and having harmful health habits (e.g. smoking, alcohol misuse, illicit drugs) may increase suicide risk in those with chronic pain. Likewise, depression disorders or anger problems seem to increase the risk of suicidality in persons with chronic pain. With regards to pain-related factors, this review found that the risk of suicidality is more related

with perceived mental well-being and various psychosocial variables (e.g. pain catastrophizing, hopelessness, mental defeat, burdensomeness and belongingness) than to pain characteristics or physical factors (except sleep problems). However, some evidence indicates that severe chronic pain is associated with an increased risk of suicide completion. Keeping in mind that it is easy to prematurely dismiss the role that pain characteristics and physical factors might play on the risk of suicidality, research examining whether or not these factors have a mediational indirect effect on other potential mechanisms involved in suicidality is warranted.

Chronic pain and suicidality are complex biopsychosocial problems. The findings from this review seem to reflect the multidimensionality of experiencing both these distressing conditions, showing that even though there is no ‘one-size fits all’ solution, a large number of the aforementioned suicidality risk factors could be modified through targeted chronic pain management treatments. To our knowledge, there is only one study (Kowal et al., 2014) that has examined patients with either high, low, or no suicidal thoughts before and after receiving a 4-week chronic pain management program: Kowal et al. (2014) found that patients had improved in all clinical outcomes (i.e. pain intensity, functional limitations, depressive symptoms, overall distress, and pain catastrophizing) while at the same time, 52% of the patients who had reported suicidal ideation were no longer endorsing these thoughts post-treatment. However, a few patients (4%) had developed low suicidal ideation while others (48%) still had sustained suicidal ideation post-treatment. The authors found that sustained suicidal ideation was significantly associated with a higher pretreatment level of suicidal thinking and self-perceived burden, as well as a lower overall response to treatment.

Considering that approximately 1 patient out of 4 reports at least some form of suicidal thoughts, the development of a suicide prevention intervention to be included in chronic pain management programs is clearly justified. Recently, a systematic review (Chan et al., 2016) and a meta-analysis (Large et al., 2016) examining suicidality risk factors in psychiatric patients having harmed themselves, irrespective of the motive, (i.e. suicide attempt or an act of deliberate self-harm) found a lack of support for suicide risk assessment, showing that suicide risk factors were only of poor predictive value. Chan et al. (2016) recommended instead to conduct a comprehensive psychosocial assessment tailored to each individual's personal factors, in order to better understand the reason behind the self-harm. Performing a comprehensive assessment of depression symptoms and suicidal behaviors (Cheatle, 2014b) as well as other potential psychosocial factors associated with suicidality early in the treatment process would greatly help clinicians to ‘red flag’ patients with elevated risk of suicide, allowing these to be closely monitored over time. There exists several validated self-administered measures and screening tools that can be used by clinicians to assess depression symptoms (e.g. Patient Health Questionnaire (PHQ-9) (Kroenke et al., 2001)), suicidal behaviors (e.g. Suicidal Behaviors Questionnaire-Revised (SBQ-R) (Osman et al., 2001)) and psychosocial factors (e.g. Pain Catastrophizing Questionnaire (Sullivan et al., 1995), Self-Perceived Burden Scale (Cousineau et al., 2003)). Asking patients to complete such questionnaires would help clinicians to monitor their patients' progress over time, and provide them with useful information that could be of assistance when assessing the patient, with little to no additional burden on their part. With respect to treatment, it is worth noting that a recent systematic review and meta-analysis (Cuijpers et al., 2013) found no evidence that psychological interventions targeting depression were effective at reducing suicidality. Similarly, another review found that targeting mental disorders such as depression or anxiety did not diminish the incidence of suicidality (Linehan, 2008). It seems that psychological interventions such as cognitive-behavioral therapy or dialectical behavior therapy addressing suicidal behaviors and its causes directly show the best empirical results (Brown et al., 2005; Comtois and Linehan, 2006). Therefore, this suggests that an effective chronic

pain management program should take into account potential risk factors for suicidality (not only depression) while adding a suicide prevention component (ex. psychoeducation on the Interpersonal Theory of Suicide, cognitive restructuring on related suicidal factors such as perceived burdensomeness, feeling hopeless etc.) as part of its treatment. As for other chronic pain management components, suicide prevention can be taught in a group-based format, but patients with greater risk for suicidality or with sustained suicidal behaviors may benefit from additional individualized sessions that target their own specific needs. Development of suicide prevention treatments in patients with chronic pain is required, and further research will be needed to evaluate the efficacy of such intervention in reducing suicide risk.

The present literature review has some shortcomings, mainly in that it is comprehensive rather than systematic, so it may not include some previously published papers. However, one of the strengths of this review is that it aims to cover a broader number of topics while being an informative resource for readers interested in suicidality in individuals with chronic pain. We also decided to focus mainly on studies published in the last decade, considering that prior reviews such as the ones by Fishbain (1999) and Tang and Crane (2006) have already thoroughly covered most earlier literature. Additionally, it is worth noting that the present review's scope is limited to chronic pain and suicidality. Other related constructs like homicide-suicide (Fishbain et al., 2011b), self-harm behaviors (Okifuji and Benham, 2011), pain suffering (Fishbain et al., 2015), medical aid in dying, and other pain populations such as acute pain or cancer pain patients (Fishbain et al., 2014, 2009a) were not included here. However, we retained studies from different age groups (e.g. adolescents, geriatrics, and adults), nationalities (e.g. Indian, Japanese) and care settings (e.g. community, primary care, tertiary care). Finally, it is worth noting that the available studies examining suicidality and chronic pain have a number of methodological limitations: their sample size is often smaller (e.g. Lee et al. (2014)), they limit themselves to specific chronic pain syndrome (e.g. Breslau et al. (2012)), they use differing recruitment methods (e.g. Fishbain et al. (2012)) or they use only a single item to measure suicidality (e.g. Racine et al. (2017)). Despite these limitations, this review has important theoretical and clinical implications that may increase clinicians', researchers' and policy decision makers' awareness of suicide prevention in individuals with chronic pain.

6. Conclusions

To summarize, the present comprehensive review supports that there is strong evidence that chronic pain, regardless of type, is a risk factor for suicidality. Several general (e.g. depression, anger problems, being unemployed/disabled, harmful health habits, challenging personal and family history) and pain-related factors (e.g. sleep problems, poor perceived mental health, multiple chronic pain conditions) have been identified as potential predictors of increasing suicide risk. On top of these, new emergent psychosocial factors, such as mental defeat, pain catastrophizing, hopelessness, perceived burdensomeness and thwarted belongingness, were found to be associated with suicidality. This large number of identifiable factors is promising, since they can be amenable to change through a chronic pain management program. Additionally, it appears that sociodemographic factors, pain characteristics and physical factors were not found to predict, at least directly, suicidality in individuals with chronic pain. The aforementioned risk factors stress the importance of comprehensively assessing patients with chronic pain for suicidality, while also incorporating a suicide prevention component as part of chronic pain management programs.

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The authors declare no financial or other relationships that might lead to a conflict of interest related to this study.

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