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The relationship between pain and suicidal vulnerability in adolescence: A systematic review

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Summary

Leading suicide theories and research in adults suggest that pain may exacerbate an individual's suicidal risk. Although pain and suicidality both increase in prevalence during adolescence, their relationship remains unclear. We aimed to systematically review the empirical evidence for an association between pain and suicidality in adolescence (PROSPERO: CRD42018097226). In total, 25 observational studies, published between 1961 and December 2018, exploring the potential pain-suicidality association in adolescence (10-19 years) were included. Across various samples and manifestations of pain and suicidality, we found that pain approximately doubles adolescents' suicidal risk, with a few studies suggesting that pain may predict suicidality longitudinally. Although depression was an important factor, it did not fully explain the pain-suicidality association. Evidence on associations between pain characteristics and suicidality is sparse and inconclusive, potentially hiding developmental differences. Identification of psychological mediators and moderators is required to develop interventions tailored to the needs of adolescents in pain.

Introduction

Although suicide can affect people at all stages of life, it accounts for a major proportion of deaths amongst young people worldwide.[1,2] Death by suicide marks the fatal endpoint of the

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Contributors
VH, BG, and CC designed this study. VH, BG, CC, and TF reviewed the registered protocol. VH coordinated and performed the data searches, study selection, data extraction and quality assessments. LQ acted as second independent reviewer, performing the second data searches, study selection, and quality assessments. RB acted as second independent reviewer, performing the data extraction. BG oversaw the implementation and acted as a third independent reviewer to resolve conflicts. VH wrote the initial draft and RB checked the tables and numbers for accuracy. VH, BG, CC and TF contributed to revising the initial draft, leading to the final manuscript. All authors reviewed and approved the final manuscript before submission.

Declaration of Interests
We declare no competing interests.

Data Sharing
The corresponding study protocol and the EndNote libraries will be made available on the Open Science Framework at the time of publication (see https://osf.io/; project name: Pain and Suicidality in Adolescence).

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suicidality risk spectrum, which ranges from cognitions about suicide and self-harm (i.e., suicidal ideation) through suicidal behaviours (i.e., the actual act of harming oneself irrespective of suicidal intent and levels of medical severity) to death by suicide.[3] These non-fatal manifestations of suicidality are a common public health problem in adolescents (lifetime suicidal ideation: 29·9%; history of suicidal behaviour: 9·7%[4,5]), particularly between the ages of 12 and 17 years.[6,7] Thus, knowledge of the factors that promote risk and resilience to the development of suicidality and the transition from suicidal ideation to acts in adolescents is crucial.[8]

Leading theories of suicidality[9–12] and empirical research in adults[13–15] emphasize the role of pain in increasing an individual's suicidal risk. However, pain is a complex phenomenon and little is known about which aspects of the pain experience, including sensory (e.g., pain sensitivity), cognitive (e.g., pain catastrophizing) and affective-motivational components of pain (e.g., unpleasantness of pain[16,17]), confer an increased suicidal risk.[18] Alternative ways of describing pain are by its duration and/ or the impact of pain on functioning. Whilst 'acute pain' is short-lived (i.e., < 3 months) and caused by an identifiable disease or injury,[19] 'chronic pain' refers to an enduring primary health condition (i.e., ≥ 3 months) of persistent or recurrent pain that significantly impairs patients' wellbeing and functioning, despite treatment of an underlying medical condition.[20] In this review, '*pain*' refers to the presence of both acute and chronic pain conditions, aspects of the pain experience and functional impairment.

Although research has shown that prevalence rates of chronic pain tend to increase substantially from the age of 12 years onwards (median prevalence rate: 11-38%[21,22]), little is known about the pain-suicidality association in adolescents. In keeping with the definition proposed by the World Health Organisation,[23] we define adolescence as a distinct developmental period, ranging from 10 to 19 years of age. During these critical years of development, young people undergo marked physical, neuro-cognitive and social changes that may precipitate or protect against the emergence of various (mental) health outcomes in adulthood.[24,25] Pain during adolescence is predictive of pain in adulthood.[22,26] However, the manifestation of pain may vary between adolescents and adults,[21,27] and its effects may be particularly detrimental in adolescence, particularly by interfering with the adaptive development during this critical period.[28]

Given the growing support for a relationship between pain and suicidality in adults (see Racine[13], Rizvi et al.[14] and Tang et al.[15]), establishing whether a similar relationship exists in adolescents has the potential to enhance our understanding of the interplay between physical and mental suffering in this age group, and to inform the development of prevention strategies.[6,29]

In this paper, we report the findings of a systematic review designed to synthesise and critically evaluate the existing empirical evidence for an association between pain and suicidality in adolescence.

Methods

Search strategy and selection criteria

The protocol for the systematic review is compliant with the recommendations of the PRISMA statement[30] and was pre-registered in PROSPERO [CRD42018097226].

A comprehensive search strategy was used to identify candidate studies, developed in liaison with an information specialist and experts on pain and suicide research (see supplement 1). Literature searches were performed in Ovid Embase, Ovid PsycINFO, Ovid Medline, EBSCO CINAHL, PubMed, Web of Science, and Scopus, alongside checking of grey literature (ProQuest Dissertations and Theses; OpenGrey: opengrey.eu/), trial registers (ClinicalTrials.gov), conference proceedings (Web of Science and Embase), backward and forward citation screening and correspondence with authors of included studies, between June, 7th and December, 3rd, 2018. As the main database search yielded an additional key term (self-mutilation), the search was repeated on July, 3rd, 2018, focussing in the second round solely on self-mutilation as a measure of suicidality. An inclusive approach to eligibility assessment was taken. Studies were deemed eligible if they explored and provided data on the potential relationship between suicidality and pain in adolescence. No restrictions were placed on the type or the assessment of suicidality, pain or the research setting. In addition, studies (sampling both adolescents and adults) were included, provided data could be extracted for the subsample of adolescents (i.e., those aged 10 to 19 years[23]). In order to minimise between-study heterogeneity, only observational studies (i.e., cross-sectional, cohort and case-control studies) were included.

Studies were excluded if (1) the study did not allow to establish an association between pain and suicidality, (2) no data could be extracted for adolescents, (3) the study focussed on clearly distinct populations (e.g., animal studies, military studies, prison cohorts, and end-of-life care), (4) they did not provide original data (e.g., reviews, editorials, or opinion papers), (5) they did not use an observational study design (e.g., intervention studies, experimental studies and qualitative research), (6) they experimentally induced pain, (7) they used mixed measures of pain and suicidality (e.g., pain during self-harm) or measures of the perception of pain in comparison to other people, and (8) they were published in any other language than English. Furthermore, studies published before 1961 (the year of decriminalisation of suicide in England and Wales[31]) or after December 2018, and duplicates, were excluded from this review.

Using Covidence[32], two independent reviewers (VH and LQ) performed the eligibility assessments between June, 7th and December, 3rd, 2018. Title and abstract screening was followed by full-text screening. Inter-rater reliabilities were calculated, using the percentage agreement with a threshold of ≥ 0·8 indicating acceptable inter-tater reliability. Between-rater discrepancies were resolved through discussion and where necessary through involvement of a third independent reviewer (BG).

Data extraction and quality assessments

Two independent reviewers (VH & RB) performed the data extraction, using a standardised pre-piloted data extraction form (see supplement 2). Authors were contacted to provide

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missing (subsample) data where necessary. Two studies used the same dataset, as an already included study (Young-Hunt[33,34], Add Health[35,36]). We decided to treat all four studies separately, as data on different measures, subsamples[35,36] and follow-up waves[33,34] were reported, precluding a combined discussion of the study results.

Two independent reviewers (VH & LQ) performed the quality assessments, using the Newcastle-Ottawa Quality Assessment Scale ([NOS][37]) for nonrandomised studies.[38,39] Each study was evaluated on an item-basis to advance future research. Quality assessments were not used to determine eligibility, but to gauge the validity of the results and to generate guidelines for future research. Inter-rater reliabilities for the data extraction and quality assessments were calculated using the percentage agreement, and discrepancies between raters were resolved through discussion, and involvement of a third, independent reviewer (BG), if necessary.

Data synthesis

Given the large between-study heterogeneity in the exposure and outcome of interest, as well as in the population studied and statistics being used, a meta-analysis was considered to be inappropriate[40] and a narrative synthesis of aggregated and individual study findings was conducted, primarily using risk measures.

Role of the funding source

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Results

The comprehensive search strategy yielded 8217 references (figure 1). After deduplication, 3806 were retained for title and abstract screening, of which 557 studies were considered for full-text review. Independent review resulted in a total sample of 25 studies. Interrater agreement across the study selection phases and the data extraction phase was high (selection: percentage agreement=86·5-99·8%; data extraction: percentage agreement=97·7%).

The majority of selected studies had been published in the last decade (n=20[33,34,36,41–57]; 80% published after 2010; table 1). Studies were geographically diverse, and mainly based on community samples (n=17[33–36,43,44,46–51,53,55,57–59]), using cross-sectional designs (n=18[35,41,43,46,47,49–61]). Eighteen studies recruited participants aged 10 to 19 years, [33–36,42,45–48,50–53,57–61] whilst in 7 studies data on adolescents within a broader age sample were made available by the authors.[41,43,44,49,54–56]

Study quality was assessed (see supplement 3), with substantial interrater agreement (percentage agreement=77·7-83·3%). Although 17 studies scored positively on at least half of the assessment criteria,[33–36,42,44–48,50–53,58,59,61] study limitations became apparent in several domains, including the assessment of the exposure (i.e., pain; n=17[33–35,41,42,45,47–51,53,55–57,59,60]) and the outcome (i.e., suicidality; n=16[34–36,41,47,49–53,55–60]). Other major limitations involve the failure to justify sample size (n=9[41,43,49,54–57,60,61]), inappropriate use and reporting of statistical tests (n=7[41,43,49,54–57]), high number of non-respondents (n=7[35,43,49,52,56,58,60]) and failure to control for potential correlates, such as age, gender and/ or depression (n=6[41,43,49,54,56,60]).

Table 2 shows the individual study results, structured around the type of suicidality and the level of support provided for the potential pain-suicidality association. The majority of studies reviewed provided support for the hypothesised pain-suicidality association in adolescence. In three studies the relationship between pain and suicidality remained unclear, as no test statistics were available.[43,54,56]

Seven community-based studies[34–36,46,47,58,59] and four clinical studies[42,45,52,61] explored links between pain and suicidal ideation. In most of the community-based studies, pain increased the odds of suicidal ideation (e.g., see Halvorsen et al.[47]; Wang et al.[59]). Specifically, of the 4·5 to 17 percent of adolescents in community samples reporting suicidal ideation,[34–36,46,47,58,59] adolescents with pain reported significantly higher levels of suicidal ideation compared to those without pain (with pain: 7·2-23·9% vs. no pain: 3·5-6·2%).[46,47,59] However, probability estimates varied greatly between community samples (aOR=1·2-4·9; see table 2), and the statistical significance of the associations appeared to depend largely on the degree of control for covariates. All studies focussing on community samples accounted for demographics (n=7[34–36,46,47,58,59]), consistently showing that pain increased the odds of suicidal ideation. This association persisted when additionally controlling for health-related factors (n=3[34,35,46]), but inconsistencies appeared when studies also accounted for depression and other psychiatric symptoms (n=5[34,36,46,47,59]). In one study, pain was significantly associated with suicidal ideation after additionally controlling for psychiatric symptoms (aOR=1·8, 95%CI=[1·4-2·4]).[34] However, in other studies this association mostly diminished to non-significance after controlling for depression (see Halvorsen et al.[47]; Fuller-Thomson et al.[46]; Wang et al. [59]; Van Tilburg et al.[36]). When focussing on clinical samples of adolescents in pain (n=4[42,45,52,61]), three studies found significant associations between pain and suicidal ideation (aOR=1·0-7·8[45,52,61]; percentage with suicidal ideation: 20-22%[52,61], suicidal ideation with pain: 22% vs. without pain: 5·3%[45]), which were no longer apparent after controlling for demographics and depression.[52,61] One study did not reveal any association between pain and suicidal ideation (suicidal ideation with pain: 34·7% vs. without pain: 27·5%).[42]

Nine studies explored the association between pain and suicidal behaviour,[33,35,36,41,48,50,53,57,60] of which seven studies recruited community samples[33,35,36,48,50,53,57] and two studies focussed on adolescents in psychiatric services.[41,60] In community samples, pain increased the odds of suicidal behaviour, with large differences in probability estimates between community samples (aOR=1·2-9·0; see table 2), as a function of the degree of control for other correlates. Specifically, 1 to 21·4 percent of community adolescents

reported suicidal behaviour.[33,35,36,48,50,53,57] Adolescents with pain reported higher levels of suicidal behaviour than those adolescents without pain (with pain: 6-78% vs. without pain: 1·3-31·1%)[48,50,53] and adolescents with pain reported higher rates of suicidal behaviour than no suicidal behaviour (7.9-61.8 vs. 3.4-39.2).[33,57] All community-based studies (n=7[33,35,36,48,50,53,57]) accounted for demographics either in the study design[48] or through adding them as covariates (e.g., see Junker et al.[33]), and provided support for an association between pain and suicidal behaviour. In most studies, this association remained significant when adding behaviour- and health-related factors as covariates (n=4[35,48,53,57]). However additional control for psychiatric symptoms (n=4[36,48,50,53]), resulted in diminished associations. Of those studies that focussed on adolescents in psychiatric services (n=2[41,60]), one study found a significant association between pain and suicidal behaviour (OR=2·3-2·7).[60] Specifically, of the overall sample of adolescents in psychiatric services, 35·7 to 48·8 percent reported one type of suicidal behaviour. It remained unclear how many of those adolescents were also experiencing pain.[60] However, adolescents who showed aggressive compared to non-aggressive suicidal behaviours did not significantly differ in their report of pain (aggressive suicidal behaviour and pain: 11·8-17·6% vs. non-aggressive suicidal behaviour and pain: 9·4-34·4%).[41] Neither study accounted for other correlates.

Two studies examined the relationship between pain and death by suicide.[44,48] One identified an increased risk for death by suicide (HR=1·6; 95%CI=[1·2-2·3]) in a community sample of adolescents with pain, compared to adolescents without pain (i.e., percentage of suicides: 20·4%; of which 6-62% reported pain vs. 32% without pain), which was no longer apparent after accounting for behavioural factors and psychiatric symptoms.[48] Another large population-based cohort study explored the risk of death by suicide in opioid users with chronic non-cancer pain, showing that no deaths were recorded as suicides in this sample.[44]

Five studies explored longitudinal associations between pain and suicidality.[33,34,36,44,48] Two found pain to be longitudinally associated with suicidal ideation, controlling for demographics, health-related factors and psychiatric symptoms,[34,36] but only one of these measured and could thus control for suicidal ideation at baseline.[36] Three studies explored the pain-suicidal behaviour association longitudinally.[33,36,48] Pain was not found to predict suicidal behaviour over a one-year follow-up period,[36] but pain predicted suicidal behaviour over a 33-year[48], after controlling for demographics and psychiatric symptoms. Furthermore, pain was longitudinally associated with self-harm hospitalisation over a period of 12-years, controlling for demographics.[33] However, as self-harm was not measured at baseline, no interferences can be drawn about the direction of this relationship.[33] Finally, pain was not predictive of death by suicide after controlling for behavioural factors and psychiatric symptoms in two studies.[44,48]

One study showed that particularly comorbid pain, when three to five pain-sites were reported compared to fewer pain sites, increased the probability of suicidal ideation, after controlling for demographics and depression (aOR=1·8, 95%CI=[1·3-2·5]).[47] Specifically, 19·6 percent of adolescents with three to five pain sites reported suicidal ideation compared to 7·5 percent of adolescents with one or two pain site and 4·5 percent of adolescents without pain.[47] Four studies examined the relationship between pain frequency and suicidality.[33,50,59,60] Of these, one study explored suicidal ideation, showing that more,

compared to less, frequent pain, was significantly associated with suicidal ideation, after controlling for demographics and depression (aOR=1·7, 95%CI=[1·1-2·6]).[59] Specifically, the prevalence of suicidal ideation increased from 7·8 percent, for pain lasting less than one day, to 26·2 percent, for pain lasting between seven to 14 days, (overall 8·5% reported suicidal ideation in this sample).[59] Likewise, frequent pain was found to be associated with an increased risk of suicidal behaviour (OR=2·3-2·7),[60] and future self-harm hospitalisation, compared to individuals with less frequent pains ($aHR_{(sometimes/\ often\ headaches/\ stomach\ pain)}$=2·2).[33] Specifically, 41·3 to 64·2 percent of adolescents with frequent pains, compared to 35·8 to 58·8 percent with seldom/ never pain, reported self-harm hospitalisation at follow-up.[33] In keeping with these findings, recurrent pain was found to increase the odds of suicidal behaviour (aRR=1·4-1·8; recurrent pain: 6-20·5% with suicidal behaviour vs. no pain: 1·3-8·9% with suicidal behaviour), after controlling for demographics and psychiatric symptoms.[50] However, when exploring this relationship more thoroughly focussing on varying frequencies of suicidal behaviour and pain, the pain-suicidal behaviour association only remained significant for very frequent pain and up to three episodes of suicidal behaviour per year (aRR=1·6, 95%CI=[1·1-2·2]), and for specific pain locations, after controlling for demographics and psychiatric symptoms (see table 2).[50]

Three studies explored pain severity as a risk factor for suicidality.[48,52,53] One identified no association between severity and suicidal ideation after controlling for demographics and depression,[52] and two found partial support for an association with suicidal behaviour in community samples.[48,53]

One study explored the relationship between pain duration and suicidal ideation in a clinical sample of pain patients, showing that the association between pain duration and suicidal ideation severity (aOR=1·0, 95%CI=[1·0-1·0]) was mediated by depression.[52] Other pain characteristics (i.e., family history of pain disorders and pain intensity) were not associated with suicidal ideation in pain patients.[42,52]

Two studies explored the relationship between sensory (pain sensitivity and threshold) and affective (pain distress) components of the pain experience and suicidality in community samples.[49,55] One study found significant group differences for pain distress, with higher levels being reported by adolescents with suicidal ideation (Med=40·5) compared to suicidal behaviour (Med=39·0) or healthy controls (Med=30·5).[49] For pain sensitivity significant group differences only became apparent when comparing adolescents with suicidal behaviour to healthy controls (suicidal behaviour: M=6·6-2·3 vs. healthy: M=5·7-2·2).[49,55] Moreover, higher pain tolerance was reported by adolescents with ideation and behaviour, compared to healthy controls, with no significant differences between the suicidal groups (suicidal ideation: M=1·83 (SD=0·95), suicidal behaviour: M=1·80 (SD=1·05), healthy: M=1·60 (SD=0·82).[55]

Lastly, six studies examined the association between physical disability and suicidality.[35,42,46,51,52,59] In two community samples, the significant association between the amount of activities prevented by pain (aOR=2·0; 95%CI=[1·2-3·4]; suicidal ideation and some activities prevented by pain: 12·6% vs. no activities prevented: 3·5%),[46] as well as headache-

related disability and suicidal ideation (grade I disability=7·5% vs. grade IV=44·4% with suicidal ideation; $p < 0·001$) was no longer apparent after controlling for demographics, health-related factors and depression.[46,59] Likewise, two clinical samples showed that functional disability was not associated with suicidal ideation in pain patients,[52] and that functional disability and pain-bother did not differentiate between the presence of suicidal ideation in adolescents with and without chronic pain.[42] Finally, the level of mobility limitations did not moderate the relationship between pain and suicidal ideation or suicidal behaviour, in a community-based study controlling for demographics.[35] However, higher pain-related quality of life was significantly associated with lower levels of suicidality (aOR=0·97; 95%CI=[0·97-0·98]) in a community sample, after controlling for demographics.[51]

Figure 2 displays the results of this review, showing the different relationships between various manifestations of pain and suicidality in community and clinical samples of adolescents. Please note, that given the paucity of existing research and the large variety in the conceptualisation and measurement of each correlate, the evidence pertaining to specific correlates is rather limited and needs to be interpreted with caution (see supplement 4). Nevertheless, this systematic review has shown that the majority of studies reviewed provided support for the hypothesised pain-suicidality association in adolescence across the various manifestations of pain and suicidality, and the different samples being studied. Overall, we found higher prevalence rates of suicidality in community samples with pain compared to those without pain (suicidal ideation and pain: 7·6-17·7% vs. no pain: 3·6-6·2%; suicidal behaviour and pain: 6-63% vs. no pain: 1·3-39·2%), and in clinical samples (suicidal ideation and pain: 22% vs. no pain: 5·3%). Studies where the relationship was no longer apparent after control for other measured factors, were comparable to studies were this relationship remained in terms of their population, sample size and study designs, but those studies that provided only partial support generally explored more pain locations and types of suicidality, and controlled for more correlates, such as depression (n=9/11 vs. n=2/8, table 2). Across the different levels of support (full or partial support), similar associations have been found, namely around one- to two-fold increase in odds of suicidal ideation and suicidal behaviour, considering various pain locations. However, these associations became less robust and mostly reduced to non-significance after controlling for psychiatric symptoms (table 2).

Discussion

This systematic review synthesised and evaluated existing evidence across 25 studies, published between 2006 and 2018, on the hypothesised pain-suicidality association in adolescents. In keeping with our hypotheses derived from the adult literature,[13,15,18,62] we found evidence for an association between pain and suicidality in adolescents, across various samples and manifestations of pain and suicidality. Overall, we found higher prevalence rates of suicidality in community samples with pain compared to those without pain (suicidal ideation and pain: 7·2-23·9% vs. no pain: 3·5-6·2%; suicidal behaviour and pain: 6-78% vs. no pain: 1·3-31·1%), and in clinical samples (suicidal ideation and pain: 22% vs. no pain: 5·3%). In other words, pain doubles the risk of suicidality, with some studies suggesting that pain may predict suicidality longitudinally. Substantial between-study

heterogeneity in the operationalisation and assessment of exposures and outcomes, as well as in the population sampled, study designs used, and the degree of control for important correlates, led to inconsistent findings. These inconsistent findings are in keeping with research in adults,[18,62] and highlight the need for a systematic and consistent approach in research that aims to disentangle the complex relationship between pain and suicidality.

Studies in which the pain-suicidality association became non-significant after controlling for other variables, typically assessed the exposure and outcomes with validated tools (e.g., instead of single-item, non-validated questions), explored different pain locations and types of suicidality, thereby also providing a range of non-significant associations, and more rigorously controlled for psychiatric symptoms, such as depression, than studies that provided full support for this relationship. In keeping with the adult literature (see Hooley et al.[63]; Spiegel et al.[64]), depression stood out as an important factor in the relationship between pain and suicidality, as the association weakened after controlling for depression (e.g., see Fuller-Thomson et al.[46]). Yet, this systematic review shows that, even after adjustment for depression, the pain-suicidality association still remained significant for subgroups that are characterised by more frequent and severe pains (e.g., headaches; see Koenig et al. [50]; Hogstedt et al.[48]). This suggests that the relationship between pain and suicidality is complex, and at least partially depends on mechanisms other than depression (see Racine[13]). Additionally the cross-sectional nature of most studies means that research is still largely agnostic to the issue of whether depression acts as a confounder (increasing occurrence/reporting of both pain and suicidality), an intermediate mechanism (mediator) between pain and suicidality (e.g. pain > depression > suicidality), a moderator (e.g., the pain-suicidality association is stronger in the presence of co-morbid depression) or some complex interplay between these potential relationships. These proposed trajectories are consistent with a recent review, highlighting similar paths in which paediatric chronic pain and depression may co-occur and mutually maintain one another).[65] However, little is known about which of these trajectories are more likely and the respective correlates that may drive these associations of paediatric pain with depression, or indeed with suicidality.[65] Regarding suicidality, it is particularly relevant to explore these correlates to enhance our understanding of how changes in an initially adaptive state of acute pain may relate to maladaptive thoughts and behaviours. Feeling acute pain has a survival advantage, such that it signals harm and drives action to prevent future harm and promote recovery.[66] However, when pain becomes chronic it loses this advantage and is associated with increased distress and at its worst self-destructive behaviours.[66] In an attempt to better understand the complex pain-suicidality association in adults, a recent review has revealed psychological processes that are common to both conditions (e.g., psychological flexibility, future orientation and mental imagery).[67] However, it remains unknown whether these psychological processes may also drive the behavioural change that may explain the pain-suicidality relationship in adolescence. It is, therefore, essential to better understand the pain-suicidality trajectories and the potentially complex interplay with unique correlates in adolescence to identify these vulnerable youth.

Research in adults shows that common mental-health factors (e.g., depression and anxiety) mediate but do not fully account for the pain-suicidality association.[68–70] As pain and psychiatric symptoms are highly comorbid during adolescence,[71] it is crucial to better

understand the potentially complex interplay between physical and mental health when explaining the pain-suicidality association. To date, most studies have solely explored depression as a mental health factor underpinning the pain-suicidality association in adolescence, and little attention has been given to other potential mental health factors, such as anxiety or childhood trauma (see Spiegel et al.[64]), or psychological processes underpinning this association. Enhanced knowledge about and management of comorbid physical and mental-health risk factors may maximise treatment outcomes.[72]

Exploring different aspects of the pain experience, we found that more pain sites, frequent and recurrent pain and pain-related quality of life (i.e., people's perceived impact of their pain on their physical, mental and social well-being[51]), were associated with suicidality, which corroborates and extends existing research in adults.[13] In addition, longer pain duration was associated with suicidal ideation. In keeping with the adult literature, this relationship diminished after controlling for depression, suggesting that over time suicidal ideation may become more closely associated with comorbid psychological symptoms instead of the duration of the physical symptoms.[13] There are mixed findings for relationships with pain severity, pain sensitivity, distress and tolerance. Although physical disability has previously been found to be a predictor of suicidality in adult samples,[62] the current review detected inconsistent findings in adolescents. Even though some studies detected an association (see Lewcun et al.[52]), this relationship mostly diminished to non-significance, after controlling for psychiatric symptoms (see Fuller-Thomson et al.[46]). This finding is in keeping with research suggesting that the correlates of physical disability differ by age.[73] Specifically, physical disability was strongly associated with affective distress in younger patients, compared to elderly were physical disability was strongly associated with pain severity.[73] This finding suggests that in young people the association between physical disability and suicidality may be more strongly driven by the comorbid psychiatric symptoms than in older adults. That is, physical disability may increase suicidal vulnerability through its effect on mental health (e.g., emotional suffering[13]), or mental health problems may impact physical health and physical disability (e.g., due to fatigue, reduced activity or sleeping difficulties), leading to increased suicidal vulnerability. As most research to date is cross-sectional, the direction of the effects awaits further scrutiny. Furthermore, other aspects of the pain experience, namely family history of pain, pain intensity and opioid-use, were not found to be associated with suicidality in adolescents. As research on the relationship between aspects of the pain experience and suicidality in adolescence is very limited, mixed results, particularly when performing a range of subgroup analyses, may be attributable to a lack of power when exploring subgroups, adding moderators and controlling for various correlates. Hence, a systematic exploration of these factors and replication of existing research is warranted.

Research on the relationship between pain and suicidality during adolescence is emerging, with 18 studies that addressed the adolescent years specifically. However, the amount of evidence pertaining to the specific aspects of the pain experience that may exacerbate suicidal risk is rather limited and inconclusive (see supplement 5), which emphasizes the need for future research. Specifically, future research needs to address the above mentioned limitations by thoroughly assessing pain and suicidality, controlling for correlates other than depression, exploring aspects of the pain experience (e.g., pain frequency) and risk and

resilience factors underpinning this link more thoroughly across samples and study designs to elucidate under which conditions pain may be associated with suicidality during adolescence. As most research has been conducted with community samples, future research needs to explore how these findings translate to clinical samples of adolescents in pain. Most of the reviewed research aligns with findings from similar studies in adults, which suggest a two- to three-times increased risk of suicidality in adults with chronic pain (see Racine[13]), compared to the doubled risk identified here. This challenges the proposed developmental profile underlying the pain-suicidality association, although the presence of a similar associations may hide different underlying mechanisms. Research to date has explored the pain-suicidality association in adolescence based on hypotheses derived from the emerging research in adults without acknowledging and exploring potential developmental differences between adolescents and adults. Moreover, as the current systematic review elucidates, the existing literature is limited by the superficial exploration of the pain-suicidality association in adolescents, mainly focussing on the overall relationship rather than specific pain characteristics. This superficial investigation may hide developmental differences that may become apparent when considering different lifetime periods and aspects of the pain experience. Chronic pain is a stressful experience that is frequently perceived as uncontrollable and functionally impairing.[74] Hence, exposure to chronic pain during the sensitive adolescent period[75] may interfere with adaptive neuro-cognitive development (e.g., acquisition of self-regulatory skills) and social maturation (e.g., independence), making adolescents more susceptible to prolonged emotional difficulties and at its worst suicidality.[28,75] However at the same time, adolescents are shielded from some of the harsher socioeconomic effects of chronic disabling pain that may be experienced in adulthood (e.g., inability to work), and they are likely to be living in a social context which provides support for daily tasks. These highly speculative hypotheses await further scrutiny, and a systematic exploration of developmental similarities and differences underpinning the pain-suicidality association in adolescents and adults is warranted to tailor early interventions to patients' needs.

There are several limitations pertaining to the current systematic review. First, as we focused on literature published in English, we cannot generalise these findings to research published in any other language. Second, the direction of the effects between pain and suicidality remains unclear, given the small number of cohort studies that allow a consideration of direction of causality in observed associations. In addition, the existing cohort studies were limited by the single assessment of the outcome at follow-up, which precludes conclusions to be drawn about the direction of the effects. By assessing pain and suicidality at multiple times throughout development, future studies should ideally enable stronger statements to be made concerning the likely direction of effects. Third, the identified support for the pain-suicidality association during adolescence may be due to publication bias (see also supplement 4), which we were unable to formally test, because of the large between-study heterogeneity that precludes the use of forest plots as part of a meta-analysis. Finally the findings are limited by the covariates used in existing studies (mostly depression), and it is unclear whether other unmeasured and uncontrolled factors could fully or partially explain the pain-suicidality association during adolescence.

Despite these limitations, this is the first review that systematically explored the relationship between pain and suicidality during the critical years of adolescence – a distinct developmental period with marked increases in the report of pain[22] and suicidality.[6,7] This review is characterised by methodological rigor, including double data search, eligibility and quality assessments, and data extraction with substantial inter-rater reliability. Moreover, unpublished subsample data has been obtained for seven studies. Across studies, we found evidence to suggest that adolescents suffering from pain are at an increased risk of suicidal ideation and behaviour. Although depression was identified as an important factor in this association, the pain-suicidality association could not be fully explained by the presence of comorbid depression. Evidence on associations between pain characteristics and suicidality is sparse and inconclusive, potentially hiding developmental differences. Interventions are warranted that target key psychological mechanisms underpinning the pain-suicidality association in adolescence to prevent or intervene with the progression along the suicide spectrum in adolescents suffering from pain. In addition, routine screening for suicidal risk needs to be facilitated to provide timely help and support.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Panel: Key Messages

- Leading suicide theories and research in adults suggest that pain may exacerbate an individual's suicidal risk. Although pain and suicidality both increase in prevalence during adolescence, their relationship remains unclear.
- Across various manifestations of pain and suicidality, we found that pain approximately doubles the risk of suicidality in community samples (suicidal ideation and pain: 7·2-23·9% vs. no pain: 3·5-6·2%; suicidal behaviour and pain: 6-78% vs. no pain: 1·3-31·1%) and clinical samples (suicidal ideation and pain: 22% vs. no pain: 5·3%) of adolescents.
- Although depression was found to play an important role in this association, the pain-suicidality association cannot solely be explained by the presence of comorbid depression. Furthermore, we identified a small number of studies that explored and found inconsistent evidence for associations between pain characteristics and suicidality.
- By identifying a final sample of 25 studies, this review further underscores the paucity of research with adolescents. In addition, the existing studies were limited by the assessment of pain and suicidality (e.g., single-item questions) and the degree of control for other correlates. Future research needs to address these limitations by thoroughly assessing pain and suicidality, controlling for correlates other than depression, as well as exploring aspects of the pain experience (e.g., pain frequency) and risk and resilience factors underpinning this link more thoroughly across samples and study designs. These studies may build on, but should not be restricted to, factors identified in the adult literature, in order to allow for a systematic exploration of potential developmental differences.
- These findings have important clinical implications, such that interventions need to be developed that target key psychological mechanisms underpinning the pain-suicidality link in adolescence to prevent or intervene with the progression along the suicide spectrum in adolescents with pain. In addition, routine screening for suicidal risk needs to be facilitated in order to provide timely help and support.

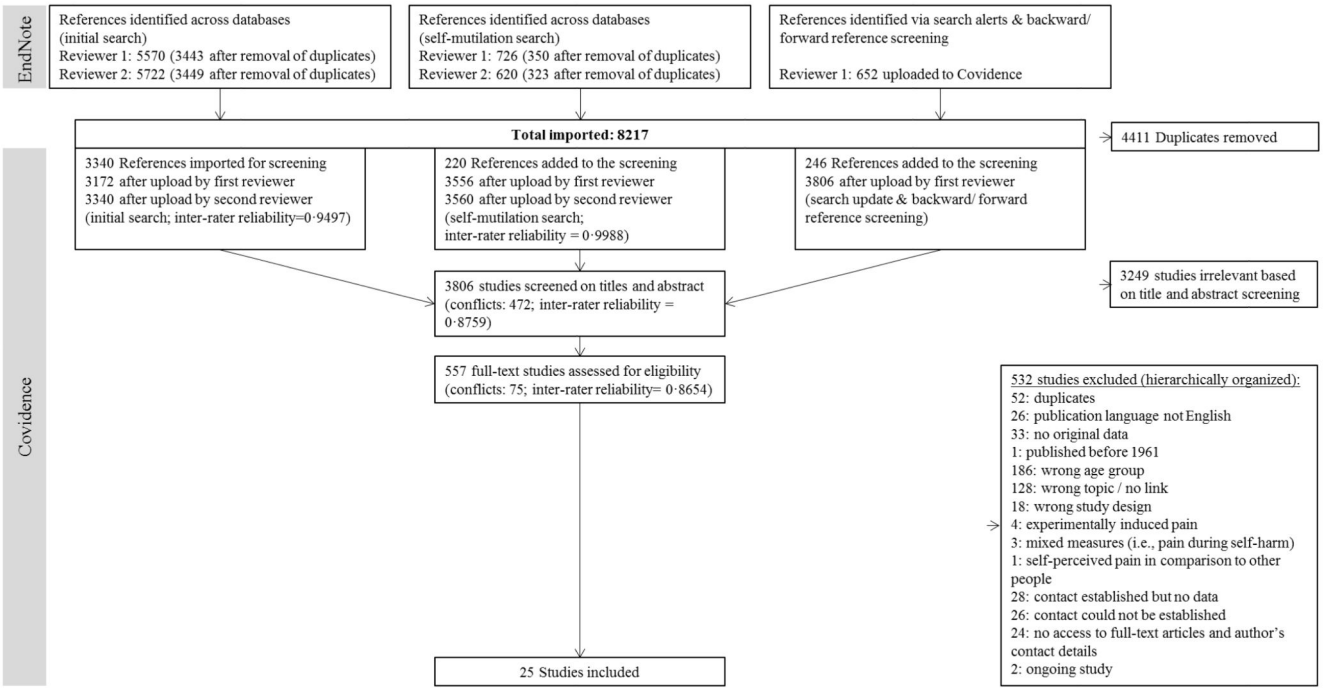

Figure 1. PRISMA flow-chart of the data search and eligibility assessment.

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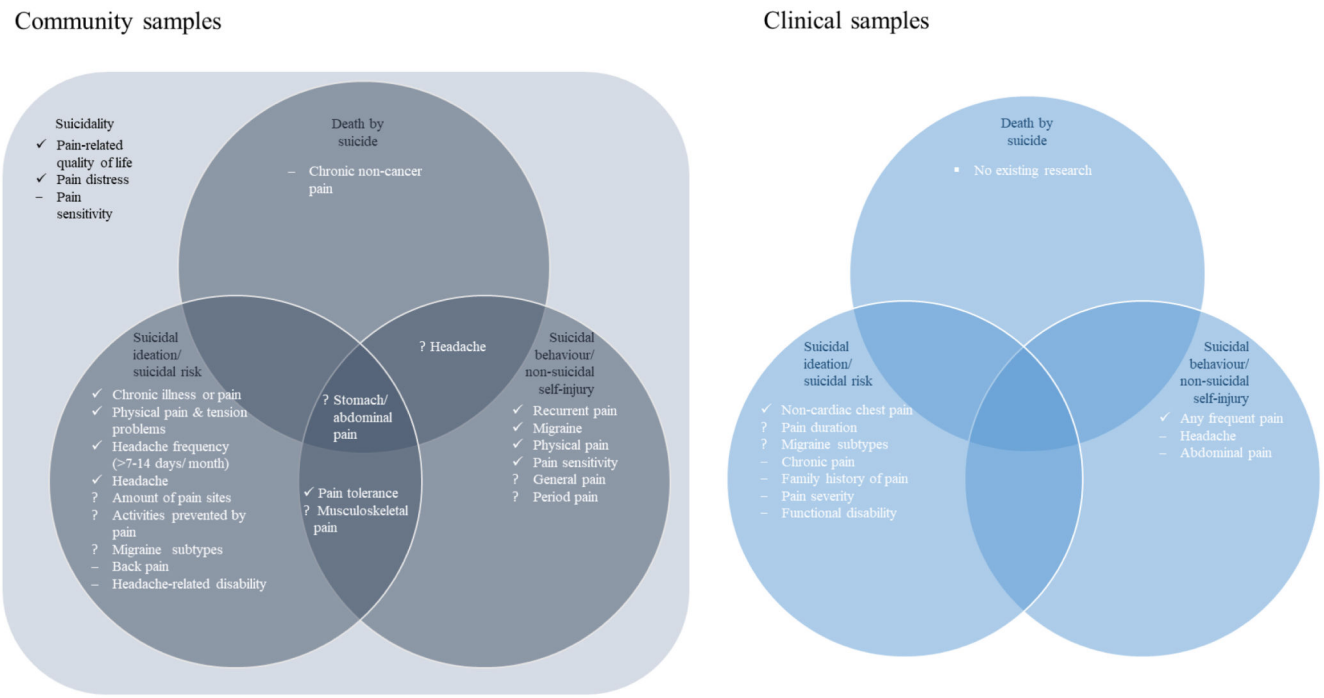

Figure 2. Schematic representation of the complex relationship between pain and suicidality in community and clinical sample of adolescents, respectively.

Note. The symbol '✓' indicates correlates that were fully supported by existing research, the symbol '?' shows correlates for which we found mixed findings (e.g., significance of the association depended on specific subtypes and the level of control for other factors e.g., depression; see also supplement 4 for an overview of an conditions under which this correlates were found to be significant), and the symbol '–' indicates correlates that were not found to be related to suicidality. Please note, that given paucity of existing studies and the large variety in the conceptualisation and measurement of each correlate, the evidence pertaining to the specific correlates is rather limited.

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Table 1

Study characteristics (N=25)

Study	Country	Population	Age range (years)	Sample size (number of adolescents if different)	Type of pain	Method of pain assessment [a]	Type of suicidality	Method of suicidality assessment [a]
Suicidal ideation [SI] / suicidal risk (n=9)								
Cross-sectional study								
Fuller-Thomson et al., 2013[46]	Canada	Community sample	15-19	5.788	Migraine headache, back problems, activities prevented by pain	Interview (–)	Suicidal ideation (past 12 months)	Interview (–)
Halvorsen et al., 2012[47]	Norway	Community sample	18-19	3.775	Pain sites (composed of pain in the head, neck/ shoulder, arms/legs, stomach and back; past 12 month)	Self-report (–)	Suicidal ideation (past week)	Self-report (/)
Chan et al., 2009[58]	China	Community sample	15-19	511	Chronic illness or pain	Interview (–)	Suicidal ideation (composed of lifetime & past year)	Self-report (/)
Wang et al., 2009[59]	Taiwan	Community sample	13-15	3.963	Migraine diagnosis (with/ without aura), headache frequency, headache disability (past 3 months)	Self-report (+)	Suicidal ideation (past month)	Self-report (/)
Lewcun et al., 2018[52]	USA	Adolescents diagnosed with amplified musculoskeletal pain syndrome (AMPS)	11–17	453	Family history of pain disorder Pain severity Pain duration (months) Functional disability	Patient registries (+), self-report (+), & interview (–)	Suicidal ideation (past two weeks)	Self-report (/)
Wang et al., 2007[61]	Taiwan	Adolescents diagnosed with chronic daily headache	12-15	122	Migraine diagnosis (yes/ no, with/ without aura)	Interview (+)	Suicidal risk (past month)	Interview (+)
Cohort study								
Strandheim et al., 2014[b,34]	Norway	Community sample	T0: 13-15 T1: 17-19	2.399	Physical pain & tension problems (past year)	Self-report (/)	Suicidal ideation (past month)	Self-report (–)
Case-control study								
Eliacik et al., 2017[45]	Turkey	Adolescents with vs. without non-cardiac chest pain	13–18	176	Non-cardiac chest pain	Diagnostic evaluation (+)	Suicidal ideation	Interview (–)
Bromberg et al., 2017[42]	USA	Adolescents with vs. without chronic pain [CP]	12-18	186	Chronic pain; pain intensity & pain bother (past 3 months)	Self-report (+)	Suicidal ideation	Self-report (+)
Suicidal behaviour [SB] / self-harm (n=6)								
Cross-sectional study								
Liu et al., 2018[53]	China	Community sample	12–18	5.813	Period pain (no, mild, moderate, severe)	Self-report (–)	Non-suicidal self-injury ([NSSI], lifetime & past year)	Self-report (/)

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Study	Country	Population	Age range (years)	Sample size (number of adolescents if different)	Type of pain	Method of pain assessment [a]	Type of suicidality	Method of suicidality assessment [a]
Koenig et al., 2015[50]	Germany	Community sample	13-18	5.504	General pain (aches or pains), recurrent pain headache, abdominal pain/ stomach ache	Self-report (+)	Frequency of self-injury per year & suicidal attempt ([SA]; ever)	Self-report (+)
Tsai et al., 2011[57]	Taiwan	Community sample	15-18	742	Headache	Self-report (–)	Self-harm (ever)	Self-report (–)
Bayramoglu et al., 2015[41]	Turkey	Adult suicide attempts	14-88	533 (n=145)	Chief complaint: Headache & Abdominal pain	Interview (–)	Type of suicide attempt (aggressive vs. non-aggressive)	Interview (–)
Reigstad et al., 2006[60]	Norway	Adolescents attending the child & adolescent psychiatric services	12–18	129	Any frequent pain (composed of headaches, stomach pain, back pain & limb pain)	Self-report (–)	Self-harm (ever) & suicide attempt ([SA]; ever)	Self-report (–)
Cohort study								
Junker et al., 2017[b,33]	Norway	Community sample	T0 to T1: 13-19	T0: 8.965 T1: 5.152	Migraine (≥6 months), frequent headache, stomach pain (past year)	Self-report (–)	Self-harm hospitalisation	Interview (+) & Patient records (+)
Death by suicide (n=1)								
Cohort study								
Ekholm et al., 2014[44]	Denmark	Community sample	16-65+	13.127 (n=unclear)	Chronic non-cancer pain (past 6 months)	Self-report (–)	Death by suicide	Patient registries (+)
Suicidality (mixed assessments; n=9)								
Cross-sectional study								
Ren et al., 2019[55]	China	Community sample	15-21	930 (n=926)	Pain tolerance & Pain sensitivity	Self-report (/)	Suicidal ideation & attempts (past year)	Self-report (+; / ; –)
Lee et al., 2017[51]	Taiwan	Community sample	11–18	6.150	Pain-related quality of life (past 2 weeks)	Self-report (+)	Suicidality (composed of four types of suicidal ideation & suicide attempts; past year)	Self-report (+)
Campbell et al., 2015[43]	Australia	Community sample	16-85	8.841 (n=706)	Any chronic pain (composed of arthritis, migraines, back/neck problems; past 6 months) vs. no pain	Interview (/)	Suicidal ideation, plans & attempts (past 12 months)	Interview (/)
Kirtley et al., 2015[49]	Scotland	Student sample	M_{age}=19·8 (SD=4·2)	351 (n=234)	Pain distress & sensitivity	Self-report (+)	Suicidal ideation & behaviour	Self-report (/)
Alriksson-Schmidt, 2008[c,35]	USA	Community sample	M=15·96 (SE = 0·11)	22.261.000 (n=6.357 available for SI analyses; n=6.400 available for SA analyses)	Physical pain (composed of headache, stomach aches, joint pain; past 12 months)	Self-report (/)	Suicidal ideation [SI] & attempts ([SA]; past year)	Self-report (–)

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Study	Country	Population	Age range (years)	Sample size (number of adolescents if different)	Type of pain	Method of pain assessment [a]	Type of suicidality	Method of suicidality assessment [a]
Park et al., 2015[54]	Republic of Korea	Hospital-based study of migraine patients	15-75	220 (n=23)	Migraine (composed of ever & now)	Self-report (+) & Interview (+) & Patient records (+)	Suicidality	Interview (+)
Rozen et al., 2012[56]	USA	Patients, diagnosed with cluster headache, from the community	<20-61+	1.134 (n=7)	Cluster headache	Self-report (–)	Suicidality	Self-report (–)
Cohort study								
Hogstedt et al., 2018[48]	Sweden	Swedish males, who were conscripted for compulsory military service in 1969 and 1970.	18-20	49.321 (suicide: N=619; Suicide attempt: N=1.102)	Headache, stomach pain, both symptoms collapsed as general pain	Self-report (–)	Death by suicide & suicidal attempts during follow-up	Patient registries (+)
Van Tilburg et al., 2011[c],36	USA	Community sample	11–18	T0: 9.970 T1: 9.925	(a) headache, (b) stomach ache/upset stomach, (c) aches, pains/ soreness in muscles or joints (past year)	Self-report (–)	Suicidal ideation & attempt (past year)	Self-report (–)

Note. Studies are grouped by the type of suicidality being measured and the study design being used. Furthermore, they are grouped by the study population, with the most recent studies being presented first. Community samples: Depending on the scale of the study, some of the samples represent large-scale national or regional surveys.

[a]Validated tools are marked with (+) Validated single items/ questions taken, or single items/ questions taken from validated tools are marked with (/) and non-validated single items/ questions are marked with (-)

[b]Junker et al., 2017[33] and Strandheim et al., 2014[34] are partially based on the same dataset: Young Hunt.

[c]Alriksson-Schmidt, 2008[35] and van Tilburg et al., 2011[36] are partially based on the same dataset: Add Health.

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Table 2

Study results, structured around the type of suicidality

Variables used to establish the pain-suicidality association						Results			
Study	**Study design**	**Population**	**Type of pain**	**Type of suicidality**	**Control for covariates**	**Significant crude probability estimates [95%CI]; otherwise frequencies**	**Significant adjusted probability estimates [95%CI]**	**Number of tested and non-significant pain-suicidality associations**	**Study quality**
Suicidal ideation/ suicidal risk (n=9)									
Full support									
Chan et al., 2009[58]	CS	Community sample	Chronic illness or pain	Suicidal ideation (composed of lifetime & past year)	Demographics	OR=6·4 [2·5-16·2]	aOR=4·9, [1·7-14·3]	0	**5/8**
Strandheim et al., 2014[c,34]	CH	Community sample	Physical pain & tension problems (past year)	Suicidal ideation (past month)	Demographics psychiatric symptoms & health-related factors	OR=2·7 [2·1-3·4]	aOR=1·8, [1·4-2·4]	0	**6/9**
Eliacik et al., 2017[45]	CC	Adolescents with vs. without non-cardiac chest pain	Non-cardiac chest pain	Suicidal ideation	Demographics	Cases = 22% (n=22/100) vs. controls = 5·26% (n=4/76), p < 0·001	Not reported	0	**6/9**
Partial support [a]									
Halvorsen et al., 2012[47]	CS	Community sample	Pain sites (composed of pain in the head, neck/ shoulder, arms/legs, stomach and back; past 12 month)	Suicidal ideation (past week)	Demographics & depression	$OR_{(1\text{-}2\ pain\ sites)}$=1·5 [1·0–2·2]; $OR_{(3\text{-}5\ pain\ sites)}$=4·7; [3·2–6·8]	$aOR_{(3\text{-}5\ pain\ sites)}$=1·8, [1·3-2·5]	1: aOR non-sig for 1-2 pain sites	**6/8**
Fuller-Thomson et al., 2013[46]	CS	Community sample	Migraine headache, back problems, activities prevented by pain	Suicidal ideation (past 12 months)	Demographics, depression & health-related factors	Migraine: Yes = 7·2% (n=425/5788) vs. no = 3·6% (n=5363/5788), p < 0·001 Back pain: Yes = 7·6% (n=482/ 5788) vs. no = 3·5% (n=5306/5788), p < 0·001 Activities prevented: Yes = 12·6% (n=216/ 5783) vs. no = 3·5% (n=5567/5783), p < 0·001	$a_1OR_{(activities)}$=2·0, [1·2-3·4]	5: $a_1OR_{(controlling\ for\ demographics\ \&\ health)}$ non-sig for migraines & back pain; $a_2OR_{(controlling\ for\ depression)}$ non-sig for migraines & back pain; activities prevented by pain	**8/8**
Wang et al., 2009[59]	CS	Community sample	Migraine diagnosis (with/ without aura), headache frequency, headache	Suicidal ideation (past month)	Demographics & depression	$OR_{(migraine\ diagnosis\ vs.\ no\ migraine)}$= 2·9 [2·3-3·6]; $OR_{(migraine\ no\ aura/\ probable\ migraine\ vs.\ no\ migraine)}$= 2·4 [1·9-3·1]; $OR_{(migraine\ with\ aura\ vs.\ no\ migraine)}$=4·6 [3·0-7·0]; $OR_{(migraine\ with\ aura\ vs.\ no\ aura/\ probable\ migraine)}$=1·8 [1·2-2·8]; higher headache frequency (3·6+-4·4 vs.	$aOR_{(migraine\ with\ aura)}$=1·8 [1·1-3·0]; $aOR_{(frequency\ >7\text{-}14\ days/month)}$= 1·7 [1·1-2·6]	2: aOR non sig. for migraine without aura/ probable migraine and headache-related disability	**6/8**

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Variables used to establish the pain-suicidality association						Results			
Study	**Study design**	**Population**	**Type of pain**	**Type of suicidality**	**Control for covariates**	**Significant crude probability estimates [95%CI]; otherwise frequencies**	**Significant adjusted probability estimates [95%CI]**	**Number of tested and non-significant pain-suicidality associations**	**Study quality**
			disability (past 3 months)			1·6 +-2·8 days/month; p< 0·001) headache-related disability (8·0+-19·7 vs. 2·5 +-7·9 p< 0·001)			
Lewcun et al., 2018[52]	CS	Adolescents diagnosed with amplified musculoskeletal pain syndrome (AMPS)	Family history of pain disorder Pain severity Pain duration (months) Functional disability	Suicidal ideation (past two weeks)	Demographics & depression	Not reported	$a1OR_{(pain\ duration)}$=1·0 [1·0-1·0] $a2OR_{(pain\ duration)}$= non-sig.	4: a1OR $_{(controlling\ for\ demographics)}$ non-sig for family history of pain; pain severity; functional disability a2OR $_{(controlling\ for\ depression)}$: pain duration non-sig	**5/8**
Wang et al., 2007[61]	CS	Adolescents diagnosed with chronic daily headache	Migraine diagnosis (yes/ no, with/ without aura)	Suicidal risk (past month)	Demographics & depression/ anxiety	Migraine: OR=4·3 [1·2-15·5]	$aOR_{(migraine\ with\ aura\ vs.\ no\ migraine)}$=7·8 [1·4-44·6]	1: aOR non-sig for migraine without aura vs. no migraine	**7/8**
No support									
Bromberg et al., 2017[42]	CC	Adolescents with vs. without chronic pain [CP]	Chronic pain; pain intensity & pain bother (past 3 months)	Suicidal ideation	Demographics & depression	none	Not reported	1: Cases 34·7% (33/95) vs. controls 27·5% (25/91), p >0·05	**6/9**
Suicidal behaviour / non-suicidal self-injury (n=6)									
Full support									
Tsai et al., 2011[57]	CS	Community sample	Headache	Self-harm (ever)	Gender & behaviour/ health-related factors	OR=6·5, [3·7-11·5]	aOR=9·0, [4·6-17·6]	0	3/8
Reigstad et al., 2006[60]	CS	Adolescents in child & adolescent psychiatric services	Any frequent pain (composed of headaches, stomach pain, back pain & limb pain)	Self-harm (ever) & suicide attempt ([SA]; ever)	N/A	$OR_{(self\text{-}harm)}$=2·7, [1·3-5·6]; $OR_{(SA)}$=2·3, [1·1-5·0]	N/A	0	2/8
Junker et al., 2017 c,[33]	CH	Community sample	Migraine (≥6 months), frequent headache, stomach pain (past year)	Self-harm hospitalisation	Demographics	$HR_{(migraine)}$=2·7, [1·3-5·9]; $HR_{(headache)}$=2·7, [1·7-4·2]; $HR_{(stomach\ pain)}$=2·7, [1·8-4.3]	$aHR_{(migraine)}$=2·3, [1·1-5·1]; $aHR_{(headache)}$=2·2, [1·4-3·5]; $aHR_{(stomach\ pain)}$=2·2, [1·4-3·5]	0	**6/9**
Partial support [a.]									

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Variables used to establish the pain-suicidality association						Results			
Study	**Study design**	**Population**	**Type of pain**	**Type of suicidality**	**Control for covariates**	**Significant crude probability estimates [95%CI]; otherwise frequencies**	**Significant adjusted probability estimates [95%CI]**	**Number of tested and non-significant pain-suicidality associations**	**Study quality**
Liu et al., 2018[53]	CS	Community sample	Period pain (no, mild, moderate, severe)	Non-suicidal self-injury ([NSSI], lifetime & past year)	Demographics psychiatric symptoms & BMI & impulsivity	NSSI lifetime: $OR_{(mild\text{-}severe)}$= 1·3-2·0 [f.] NSSI past year: $OR_{(mild\text{-}severe)}$= 1·3-2·1 [f.]	NSSI lifetime: $a2OR_{(mild\text{-}moderate)}$= 1·2-1·3 [f.] NSSI past $year_{(mild\text{-}moderate)}$: a2OR=1·2-1·3 [f.]	2: a2OR (adjusting for all covariates): non-sig for severe pain and NSSI lifetime & past year	**6/8**
Koenig et al., 2015[50]	CS	Community sample	Recurrent pain, as well as general pain (aches or pains), headache, abdominal pain/ stomach ache (for general, headache and abdominal pain: sometimes vs. very often)	Frequency of self-injury per year (1-3x/year vs. <3x/year) & suicidal attempt ([SA]; 1 SA vs. multiple SAs, ever)	Demographics & psychiatric symptoms	Self-injury 1-3x/year: $RR_{(recurrent\ vs.\ no\ pain)}$=3·0 [2·4–3·6]; $RR_{(general)}$=1·7-2·6 [e.] $RR_{(headache)}$=1·3-1·9 [e.] $RR_{(abdominal)}$=1·7-2·7 [e.] Self-injury >3x/year: $RR_{(recurrent)}$= 6·0 [4·4–8·2]; $RR_{(general)}$=2·0-3·2 [e.]; $RR_{(headache\ –\ very\ often)}$= 2·5 [1·5-4·1]; $RR_{(abdominal)}$=2·0-5·1 [e.] One SA: $RR_{(recurrent)}$= 3·6 [2·8–4·6]; $RR_{(general)}$=1·8-2·7 [e.]; $RR_{(headache\ –\ very\ often)}$= 2·6 [1·7–3·9]; $RR_{(abdominal)}$=2·2-2·3 [e.] Multiple SA: $RR_{(recurrent)}$= 5·5 [3·8–7·8]; $RR_{(general)}$=2·0-2·8 [e.]; $RR_{(abdominal)}$=1·7-5·8 [e.]	Self-injury 1-3x/year: $a2RR_{(recurrent)}$=1·4, [1·2-1·8] $a2RR_{(general\ pain\ –\ very\ often)}$= 1·6, [1·1-2·2]; Self-injury >3x/year: $a2RR_{(recurrent)}$=1·8, [1·3-2·6]; One SA: $a2RR_{(recurrent)}$=1·4, [1·1-1·8]; $a2RR_{(headache\ –\ very\ often)}$=1·6, [1·0-2·3]; $a2RR_{(abdominal\ pain\text{-}sometimes)}$=1·5, [1·1-2·1]; Multiple SA: $a2RR_{(recurrent)}$=1·8, [1·2-2·6]; $a2RR_{(abdominal\ pain\ –\ very\ often)}$=2·0, [1·1-3·5]	30: OR non-sign. for self-injury > 3x/year & $headaches_{(sometimes)}$; one SA & $headaches_{(sometimes)}$; multiple SA & $headaches_{(sometimes\ \&\ very\ often)}$; a1OR (controlling for demographics) non-sig for self-injury 1-3x/year & $headaches_{(sometimes)}$; self-injury >3 & $headaches_{(sometimes)}$; one SA & $headaches_{(sometimes)}$; multiple SA & $headaches_{(sometimes\ \&\ very\ often)}$ & abdominal pain $_{(sometimes)}$; a2OR (all covariates): non-sig for self-injury 1-3x/year & general pain $_{(sometimes)}$ & $headaches_{(sometimes\ \&\ very\ often)}$ & abdominal $pain_{(sometimes\ \&\ very\ often)}$; self-injury >3 & general $pain_{(sometimes\ \&\ very\ often)}$ & $headaches_{(sometimes\ \&\ very\ often)}$ & abdominal pain $_{(sometimes\ \&\ very\ often)}$; one SA & general $pain_{(sometimes\ \&\ often)}$ & $headaches_{(sometimes)}$; abdominal pain $_{(often)}$; multiple SA & general $pain_{(sometimes\ \&\ often)}$ & $headaches_{(sometimes\ \&\ often)}$ & abdominal pain $_{(sometimes)}$	**6/8**
No support									
Bayramoglu et al., 2015[41]	CS	Adult suicide attempts	Chief complaint: Headache & Abdominal pain	Type of suicide attempt (aggressive vs. non-aggressive)	N/A	none	Not reported	2: Headache: 11·8% (2/17) vs. 9·4% (12/128), p=0·60 Abdominal pain: 17·6% (3/17) vs. 34·4% (44/128), p=0·37	2/8
Death by suicide (n=1)									
No support									
Ekholm et al., 2014[44]	CH	Community sample	Chronic non-cancer pain (past 6 months)	Death by suicide	N/A	none	Not reported	1: Death by suicide: n=0	**7/9**
Suicidality (overall) & mixed assessments (n=9)									

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	Variables used to establish the pain-suicidality association					Results			
Study	**Study design**	**Population**	**Type of pain**	**Type of suicidality**	**Control for covariates**	**Significant crude probability estimates [95%CI]; otherwise frequencies**	**Significant adjusted probability estimates [95%CI]**	**Number of tested and non-significant pain-suicidality associations**	**Study quality**
Full support									
Lee et al., 2017[51]	CS	Community sample	Pain-related quality of life (past 2 weeks)	Suicidality (composed of four types of suicidal ideation & suicide attempts; past year)	Demographics	Not reported	aOR=0·97 [0·97-0·98]	0	**5/8**
Alriksson-Schmidt, 2008 d,[35]	CS	Community sample	Physical pain (composed of headache, stomach aches, joint pain; past 12 months)	Suicidal ideation [SI] & attempts ([SA]; past year)	Demographics & severity of mobility limitations	Not reported	$aOR_{(SI)?}$=1·2, [1·2-1·3]; $aOR_{(SA)}$=1·2, [1·1-1·3]	0	**5/8**
Partial support [a]									
Ren et al., 2019[55]	CS	Community sample	Pain tolerance & Pain sensitivity	Suicidal ideation & attempts (past year)	Gender	Not reported	Suicidal ideation [SI] vs. control $aOR_{(pain\ tolerance)}$=1·4, [1·1-1·8] Suicidal behaviour [SA] vs. control $aOR_{(pain\ sensitivity)}$= 0·63, [0·42-0·96]; $aOR_{(pain\ tolerance)}$=1·9, [1·2-3·1]	3: aOR non sign. for SI vs. control & pain sensitivity; for SB vs. SI & pain sensitivity/ pain tolerance	2/8
Kirtley et al., 2015[49]	CS	Community sample	Pain distress & sensitivity	Suicidal ideation & behaviour	N/A	Pain distress: z=2·4, p=0·018	Not reported	1: Pain sensitivity: z=1·0, p=0·300	0/8
Hogstedt et al., 2018[48]	CH	Swedish males, who were conscripted for compulsory military service in 1969 and 1970.	Headache, stomach pain, both symptoms collapsed as general pain (categorised based on limited and severe symptoms)	Death by suicide & suicidal attempts [SA] during follow-up	Demographics, psychiatric diagnosis & other symptoms	Death by suicide: $HR_{(severe\ headache)}$= 1·4 [1·0–2·0]; $HR_{(severe\ stomach\ pain)}$= 1·5 [1·1–2·1]; $HR_{(sever\ headache\ \&\ stomach\ pain)}$=1·6 [1·2-2·3] Suicide attempt: $HR_{(limited\text{-}severe\ headache)}$=1·1-1·9 [e]; $HR_{(severe\ stomach\ pain)}$= 2·1 [1·7-2·6]; $HR_{(severe\ headache\ \&\ stomach\ pain)}$=1·1-2·3 [e]	Suicide attempt: $aHR_{(severe\ headache)}$=1·5, [1·1-2·2]	24: OR non-sig. for suicide & $headache_{(limited)}$, $stomach\ pain_{(limited)}$ & headache/stomach pain $_{(limited)}$; for suicide attempts & $stomach\ pain_{(limited)}$ $a1OR_{(controlling\ for\ psychiatric\ diagnosis)}$ non sig. for suicide & $headache_{(limited\text{-}severe)}$, stomach problems $_{(limited\text{-}severe)}$, & headache/stomach problems $_{(limited\text{-}severe)}$; for SA & $headache_{(limited)}$, stomach problems $_{(limited)}$, & headache/ stomach problems $_{(limited)}$ $a2OR_{(controlling\ for\ other\ symptoms)}$ non sig. for suicide & $headache_{(limited\text{-}severe)}$, stomach problems $_{(limited\text{-}severe)}$ & headache/ stomach problems $_{(limited\text{-}severe)}$; for SA & $headache_{(limited)}$,stomach problems $_{(limited\ severe)}$ & headache/ stomach problems $_{(limited\text{-}severe)}$	**6/9**

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Variables used to establish the pain-suicidality association						Results			
Study	**Study design**	**Population**	**Type of pain**	**Type of suicidality**	**Control for covariates**	**Significant crude probability estimates [95%CI]; otherwise frequencies**	**Significant adjusted probability estimates [95%CI]**	**Number of tested and non-significant pain-suicidality associations**	**Study quality**
Van Tilburg et al., 2011[d],[36]	CH	Community sample	(a) headache, (b) stomach ache/ upset stomach, (c) aches, pains/ soreness in muscles or joints (past year)	Suicidal ideation & attempt (past year)	Demographics & depression	Suicidal ideation: $OR_{(headache\text{-}wave\ 1\&2)}$=1·5-1·7 [e]; $OR_{(stomach\ pain\text{-}wave\ 1\&2)}$=1·6-1·9 [e]; $OR_{(musculoskeletal\ pain\text{–}wave\ 1\&2)}$=1·5-1·4 [e]. Next-year suicidal ideation (excl. wave 1 SI): $OR_{(headache)}$=1·2 [1·0-1·5] $OR_{(stomach\ pain)}$=1·4 [1·1-1·7]; Suicide Attempt [SA]: $OR_{(headache\text{-}wave\ 1\&2)}$=1·4-2·1 [f]; $OR_{(stomach\ pain\text{-}wave\ 1\&2)}$=1·8 [e]. $OR_{(musculoskeletal\ pain\text{–}wave\ 2)}$=1·5 [1·1–2·1] Next-year SA (excl. wave 1 SA): $OR_{(stomach\ pain)}$=1·6 [1·2-2·1]; $OR_{(musculoskeletal\ pain)}$=1·5 [1·1-2·1]	Suicidal ideation: $aOR_{(headache\text{-}wave\ 1\&2)}$=1·3-1·4 [e]; $aOR_{(stomach\ pain\ –\ wave\ 2)}$=1·4 [1·2-1·7]; $aOR_{(musculoskeletal\ pain\ –\ wave\ 1)}$=1·3 [1·1-1·5]; Next-year suicidal ideation: $aOR_{(headache)}$=1·2 [1·1-1·5] Suicide Attempt: $aOR_{(headache\text{-}wave\ 2)}$=1·6, [1·2-2·2]; $aOR_{(musculoskeletal\ pain\text{–}wave\ 2)}$=1·1 [0·8-0·9]	14: OR non sig. for next-year suicidal ideation (excl. wave 1 SI) & musculoskeletal pain; for SA & musculoskeletal $pain_{(wave\ 1);}$ for Next-year SA (excl. wave 1 SA) & headache; aOR non sig. for SI & stomach $pain_{(wave\ 1)}$/ musculoskeletal $pain_{(wave\ 2);}$ for Next-year SI (excl. wave 1 SI) & stomach pain/ musculoskeletal pain; for SA & $headache_{(wave\ 1)}$ /stomach $pain_{(wave\ 1\&2)}$/ musculoskeletal $pain_{(wave\ 1);}$ for next-year SA (excl. wave 1 SA) & headache/ stomach pain/ musculoskeletal pain	**7/9**
Pain-suicidality association unclear [b]									
Campbell et al., 2015[43]	CS	Community sample	Any chronic pain (composed of arthritis, migraines, back/ neck problems; past 6 months) vs. no pain	Suicidal ideation, plans & attempts (past 12 months)	N/A	Suicidal $ideation_{(chronic\ pain)}$: 11·1% (10/90) vs. 3·2% (20/616) Suicidal $plan_{(chronic\ pain)}$: 7·8% (7/90) vs. 0·8% (5/616); Suicidal $attempt_{(chronic\ pain)}$: 6·7% (6/90) vs. 0·9% (6/616)	Not reported	Unclear	3/8
Park et al., 2015[54]	CS	Hospital based study of migraine patients	Migraine (composed of ever & now)	Suicidality	N/A	Suicidal risk: yes=30·4% (7/23) vs. no=69·6% (16/23)	Not reported	Unclear	3/8
Rozen et al., 2012[56]	CS	Patients, diagnosed with cluster headache	Cluster headache	Suicidality	N/A	Suicidal ideation: 71% (5/7); Suicidal behaviour: 14% (1/7); No suicidality: 29% (2/7)	Not reported	Unclear	0/8

Note. CS = Cross-sectional Studies; CH = Cohort studies; CC = Case-control studies; OR = crude odds ratio; aOR = adjusted odds ratio. Within the table outcomes are further structured around the level of support and the population.

[a]Results did not remain (or only partially remain) significant when controlling for covariates (e.g., depression) in multivariate models. Hence, results are reported for most significant outcomes: crude odds ratios (OR) or adjusted odds ratios (aOR), depending on whether or not the adjusted odds ratio still remained significant

[b]The results are unclear, as no test statistics were available and only frequencies were reported.

[c]Junker et al., 2017[33] and Strandheim et al., 2014[34] are partially based on the same dataset: Young Hunt.

[d]Alriksson-Schmidt, 2008[35] and van Tilburg et al., 2011[36] are partially based on the same dataset: Add Health.

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[e] In these cases, pain has been divided into subcategories of varying severity levels and frequencies. To keep the table as concise a possible, we present the range of odds ratios over the different pain severity levels/ frequencies, instead of individual odds ratios. Therefore, confidence intervals are omitted.