General Hospital Psychiatry xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

General Hospital Psychiatry

journal homepage: www.elsevier.com/locate/genhospsych

Pain as a risk factor for suicidal ideation. A population-based longitudinal cohort study

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ARTICLE INFO

Keywords:
Pain
Pain severity
Interference due to pain
Suicidal ideation
Mental disorders
General population

ABSTRACT

Objective: To examine the longitudinal association between pain and suicidal ideation in the general adult population.
Method: Data were used from two waves (baseline and three-year follow-up) of the Netherlands Mental Health Survey and Incidence Study-2. Persons without prior 12-month suicidal ideation at baseline were included in this study ($N = 5242$). Pain severity and interference due to pain in the past month were measured using the 36-item Short Form Health Survey. Suicidal ideation and DSM-IV mental disorders were assessed using the Composite International Diagnostic Interview. Logistic regression analyses were performed.
Results: Moderate to very severe pain (OR 3.39, $p < .001$) and moderate to very severe interference due to pain (OR 2.35, p .01) were associated with a higher risk for incident suicidal ideation at follow-up after adjustment for baseline sociodemographic variables and mental disorders. No interaction effects were found between pain severity or interference due to pain and mental disorders.
Conclusion: Moderate to severe pain and interference due to pain are risk factors for suicidal ideation independently of concomitant mental disorders. We suggest taking assessment and management of suicidal ideation in patients with pain into account both in clinical treatment as well as in suicide prevention action plans.

1. Introduction

Every year, approximately 800,000 people die by suicide worldwide [1], and is thus a major public health problem. A suicide attempt is preceded by suicidal ideation, and the risk of a suicide attempt is highest in the first year after ideation [2,3]. Understanding which factors contribute to suicidal ideation might, therefore, help in improving suicide prevention plans.

Although chronic pain is mentioned as an important risk factor for suicidal behavior (including ideation) in a WHO report [4], many European countries have developed suicide prevention plans that only take mental disorders into account [5], and not pain. Pain occurs in 19% of the adult European population [6]. In severe cases [7–10], if treatment is no longer effective, one of the choices to end pain might be to commit suicide [11]. Hence, the association of pain with suicidal ideation is a relevant public health problem. However, the current evidence on the size of this association is limited and is mostly based on clinical, retrospective or cross-sectional studies [7,10]. More importantly, these studies did not control for concomitant mental disorders, that have a known association with suicidal ideation. Several other, cross-sectional, studies did control for the presence of common mental disorders, and demonstrated a significant link between pain and suicidal ideation [12–14]. Unfortunately, data regarding the longitudinal association of pain with suicidal ideation in the general population is more scarce.

One longitudinal, population-based study, investigating the association between headache and suicidal ideation in adults, shows a 1.5-fold increased risk of suicidal ideation in those reporting headache,

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https://doi.org/10.1016/j.genhosppsych.2018.11.005
Received 20 January 2018; Received in revised form 17 November 2018; Accepted 20 November 2018

after adjustment for menal disorders (i.e. depressive, anxiety and substance use disorders [15]. A more recent longitudinal, population-based study, found similar results in a population sample of adolescents, in which those reporting headache had a 1.5-fold increased risk of subsequent suicidal ideation, after adjustment of depression [16]. As these studies focused only on headaches in the adult population [15] and on chronic pain in the adolescent population [16], the association of pain in general with subsequent suicidal ideation in the general adult population, over and above common mental disorders, still needs further exploration. To gain insight into the interplay of physical pain and suicidal ideation we need longitudinal population-based research, exploring the role of pain in the development of suicidal ideation, taking mental disorders into account that have a known association with suicidal ideation.

We will explore the influence of pain characteristics in general (pain severity and interference with normal activities due to pain) on subsequent suicidal ideation in the adult general population, using data of the Netherlands Mental Health Survey and Incidence Study-2 (NEMESIS-2). Although it would be of interest to study the influence of pain on a wider range of suicidal behavior (including plans and attempts), the most frequent suicidal behavior endorsed in this population sample was suicidal ideation, which is, therefore, the focus of this study. We hypothesize that subjects with more severe pain and subjects with more interference due to pain are at increased risk for suicidal ideation compared to subjects without pain, in an adult general population sample. Furthermore, we hypothesize that this association will be stronger in subjects with a mental disorder compared to subjects without a mental disorder.

2. Material and methods

2.1. Study design and participants

Data were used from the first two waves of NEMESIS-2, a psychiatric epidemiological cohort study among the Dutch general population aged 18–64 years at baseline [17]. Design and methods of the NEMESIS-2 study are described elsewhere [17], but a brief summary is given here. The NEMESIS-2 study is based on a multistage, stratified random sampling of households, with one respondent randomly selected in each household. The sample was nationally representative, although younger subjects were somewhat under-represented. The Medical Ethics Committee for Institutions on Mental Health Care (METIGG) approved the study. After having been informed about the study objective, respondents provided written informed consent.

See Fig. 1 for a flowchart of the inclusion procedure. In the first wave (T0), performed from November 2007 to July 2009, a total of 6646 persons were interviewed (response rate 65.1%; average interview duration 95 min). The interviews were laptop computer assisted and almost all were held at the respondent's home. All T0 respondents were approached for follow-up (T1) three years after T0, from November 2010 to June 2012. Of this group, 5303 persons were re-interviewed (response rate 80.4%, excluding those deceased; average interview duration 84 min). The mean period between both interviews was three years and seven days. Baseline psychopathology was not significantly associated with attrition at follow-up, after controlling for sociodemographics [18], compared to other studies that did find such an association [19–21]. Furthermore, in the cohort used for this study (i.e. those without 12-month suicidal ideation at baseline), pain characteristics at baseline were not significantly associated with attrition at follow-up, after controlling for demographics.

For this study, those persons without 12-month suicidal ideation at T0 were selected ($N = 5242$). Lifetime previous suicidal ideation was not an exclusion criterion if in the last 12 months at baseline no suicidal ideation was reported.

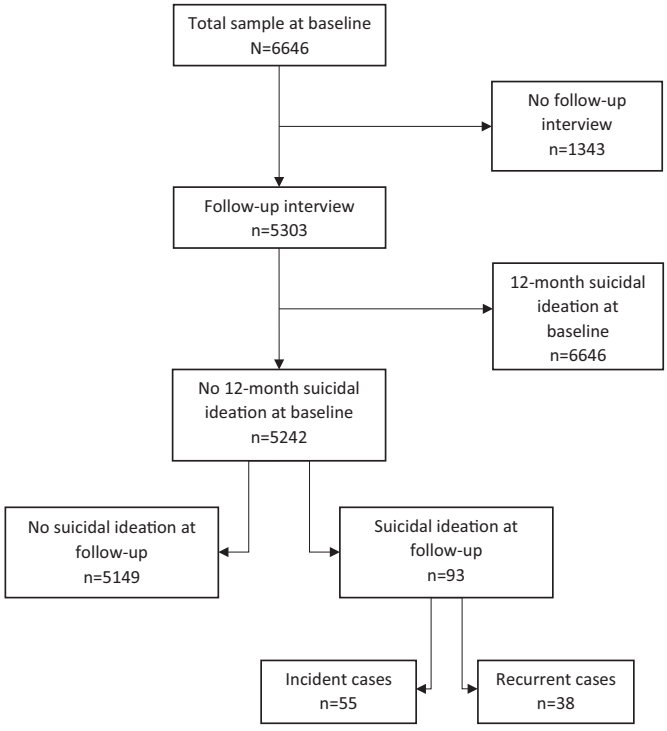

Fig. 1. Flowchart of inclusion procedure.

2.2. Outcome

2.2.1. Suicidal ideation

Suicidal ideation was assessed using the Suicidality Module of the Composite International Diagnostic Interview (CIDI) version 3.0, a fully structured lay-administered diagnostic interview of mental disorders and suicidality [22]. The CIDI was developed and adapted for use in the World Mental Health Survey Initiative. In the Netherlands, the CIDI 3.0 was first used in ESEMeD [23], which is part of this initiative. The CIDI 3.0 version used in NEMESIS-2 was an improvement of the one used in the Dutch ESEMeD study. At baseline, respondents were asked about previous experiences of suicidal ideation ("Have you ever seriously thought about committing suicide?"), suicide plans ("Have you ever made a plan for committing suicide?") and suicide attempts ("Have you ever attempted suicide?"). The respondents received a 'respondent booklet', in which these suicidal experiences were listed as A (suicidal ideation), B (suicidal plans), and C (suicidal attempt). Subsequently, if a respondent answered with yes, it was asked how old that person was when they first had such an experience, and whether they had this experience in the last 12 months. At T1, respondents were asked the same questions about suicidal ideation, but then the time period referred to suicidal ideation they had experienced since the baseline interview.

2.2.2. Pain assessments

At baseline, pain severity was assessed using a question from the SF-36-item Short Form Health Survey [24,25]: "How much pain did you experience in the past four weeks?" Respondents could choose between "no pain", "very little pain", "little pain", "moderate pain", "severe pain" and "very severe pain". Due to the small number of subjects in the moderate, severe, and very severe pain categories, grouping these categories together into one answer category was needed to create more equal groups. Therefore, the categories used in this study were: 0 = no pain, 1 = very little pain, 2 = little pain, 3 = moderate to very severe pain.

Interference due to pain was measured with the SF-36 question: "How much interference did you experience with normal activities

Table 1
Sociodemographics, pain characteristics (severity and interference), and mental disorders in the general population among the total sample, those without 12-month suicidal ideation, and those with suicidal ideation, at baseline.

		Total sample (N = 5242)	No suicidal ideation at follow-up (n = 5149)	Suicidal ideation at follow-up (n = 93)
		n (%)	%	%
Gender	Male	2351 (50.6)	50.6	48.5
	Female	2891 (49.4)	49.4	51.5
Age	18–24	349 (11.9)	11.9	13.5
	25–34	843 (20.0)	19.9	21.4
	35–44	1361 (24.5)	24.7	18.5
	45–54	1290 (23.3)	23.1	31.6
	55–64	1399 (20.3)	20.4	15.1
Education	Primary	222 (7.1)	6.8	19.5
	Lower secondary	1370 (22.3)	22.2	26.9
	Higher secondary	1707 (41.8)	42.0	30.4
	Higher professional/university	1943 (28.9)	29.0	23.2
Living situation	Without partner	1595 (32.0)	31.8	39.7
	With partner	3647 (68.0)	68.2	60.3
Working situation	No job	1257 (23.1)	22.7	42.3
	Job	3985 (76.9)	77.3	57.7
Pain severity[a]	None	3071 (59.2)	59.7	35.0
	Very little	618 (12.0)	12.0	11.8
	Little	777 (14.0)	14.0	13.9
	Moderate to very severe	775 (14.8)	14.3	39.2
Pain interference[b]	None	4010 (77.7)	78.1	55.6
	Little	794 (14.2)	14.1	23.6
	Moderate to very severe	436 (8.1)	7.8	20.8
12-month (mood, anxiety or substance use) disorder	No 12-month (mood, anxiety or substance use) disorder	4408 (83.2)	83.9	47.4
	Any 12-month (mood, anxiety or substance use) disorder	834 (16.8)	16.1	52.6
12-month mood disorder	No 12-month mood disorder	4954 (94.5)	95.0	69.4
	Any 12-month mood disorder	288 (5.5)	5.0	30.6
12-month anxiety disorder	No 12-month anxiety disorder	4731 (90.0)	90.5	63.5
	Any 12-month anxiety disorder	511 (10.0)	9.5	36.5
12-month substance use disorder	No 12-month substance use disorder	5024 (94.7)	94.8	91.7
	Any 12-month substance use disorder	281 (5.3)	5.2	8.3

[a] n = 5241 due to missing data of 1 person on pain severity.
[b] n = 5240 due to missing data of 2 persons on pain interference.

(including work outside household, and domestic work) in the past four weeks as a consequence of pain?". Respondents could choose between "no interference", "little interference", "moderate interference", "much interference" and "very much interference". Due to the small number of subjects in the moderate, much, and very much interference categories, we grouped these categories into one answer category to create more equal groups. Therefore, the categories used in this study were: 0 = no interference, 1 = little interference, 2 = moderate to very much interference.

2.2.3. Covariates

The covariates included in this study are: 1) sociodemographic variables (including sex, age in categories (18–24, 25–34, 35–44, 45–54, 55–64), education (primary, lower secondary, higher secondary, higher professional/university), living situation (with partner or not), and working situation (having a paid job or not)); 2) twelve-month prevalence of mental disorders at baseline (as measured with the CIDI version 3.0 [22], including any mood disorder (major depression, dysthymia, bipolar disorder), any anxiety disorder (panic disorder, agoraphobia, social anxiety disorder, generalized anxiety disorder, specific disorder), and any substance use disorder (alcohol/drug abuse and dependence)); and 3) prior suicidal ideation (> 12 months prior to baseline). Research has demonstrated acceptable reliability and validity for assessing the common mental disorders [26].

2.3. Statistical methods

First, univariate analyses were performed to describe the sample at baseline, regarding sociodemographics, mental disorders, pain severity and interference due to pain. Second, logistic regression analyses were performed with four models to examine both the risks of pain severity and pain interference on suicidal ideation at follow-up: model 1 shows the unadjusted odds ratios (OR); model 2 shows the ORs adjusted for demographics; model 3, shows the ORs adjusted for demographics, any 12-month mood disorder, any 12-month anxiety disorder, and any 12-month substance use disorder at baseline; model 4 shows the ORs adjusted for all the covariates as in model 3, and for lifetime suicidal ideation. In all models, persons with no pain and persons with no interference due to pain were selected as the reference category. To test for linear trends, potential determinants (i.e. pain severity and interference due to pain) were also modelled separately as continuous variables in all models (p for trend test). In order to detect modifying or interaction effects, an additive model was used (guided by previous work, see e.g.: [27,28]). Additive interaction exists if the combined effect of pain and a common mental disorder on suicidal ideation is stronger than the sum of the separate effects. Additive interaction effects were estimated by comparing the ORs of pain and the common mental disorder combined with the expected value in case of no interaction. If the expected OR, that is $OR(AB) \approx OR(A) + OR(B) - 1$, lays below the lower limit of the confidence interval of the combined effect, additive interaction is assumed [29,30]). In total, we tested six interaction effects: pain severity by mood disorder, by anxiety disorder and by substance use disorder as well as interference due to pain by mood disorder, by anxiety disorder and by substance use disorder on suicidal ideation. For these analyses, pain severity was dichotomized into moderate to very severe pain (1) versus no to little pain (0).

Interference due to pain was dichotomized into moderate to very much interference (1) versus no to little interference (0). Two-tailed testing procedures were used in all analyses with 0.05 alpha levels, except the interaction analyses, where an alpha of 0.001 was used. All statistical analyses were performed with Stata version 12.1, using weighted data (weighted with the variables sex, age, partner status (living with or without partner), educational level, degree of urbanization, working situation, and country of birth) to ensure they were representative of the national population. Robust standard errors were calculated to obtain correct 95% confidence intervals and p values [31].

3. Results

Table 1 describes the baseline characteristics of the 5242 persons in this cohort. In all, 50.6% were men and most of the participants were 35 years of age or older. Of the total participant group, 68% had a partner and 76.9% had a job. Most subjects (41.8%) attended higher secondary school, whereas 7.1% of the subjects had only attended primary school. Most subjects (83.1%) did not have any 12-month mood, anxiety or substance use disorders, whereas 5.5% reported any mood disorder, 10.0% any anxiety disorder and 5.3% any substance use disorder in the past 12 months. Of the cohort, 14.8% experienced moderate to very severe pain, 26.0% reported very little to little pain and 59.2% reported having no pain in the past month. Regarding interference due to pain in the month before baseline, 8.1% had moderate to very severe interference, 14.2% reported little interference and 77.7% reported no interference.

Data are presented in unweighted numbers and weighted percentages for the total sample ($N = 5242$), and in weighted percentages for those reporting no suicidal ideation at follow-up ($n = 5149$) and those reporting suicidal ideation at follow-up ($n = 93$).

At follow up, 93 subjects (1.8%) reported suicidal ideation. Of these 93 subjects, 17 made a suicide plan and of these 17 subjects who made a plan 9 also made a suicide attempt. Table 2 shows the odds ratios (OR) of pain severity at baseline with suicidal ideation three years later. In all models of pain severity, only the category of moderate to very severe pain was significantly associated with incident suicidal ideation three years later. In the unadjusted model (model 1), individuals with moderate to very severe pain had almost a five times higher OR for suicidal ideation than individuals without pain (OR 4.68, 95% CI 2.65–8.23). When controlling for demographics (model 2), the OR slightly decreased to a four times higher OR for suicidal ideation (OR 4.00, 95% CI 2.08–7.70), and when also controlling for any 12-month mood disorder, any 12-month anxiety disorder, and any 12-month substance use disorder (model 3), the OR for suicidal ideation was still more than three times higher (OR 3.39, 95% CI 1.74–6.61) for those with moderate to very severe pain compared to individuals without pain. The p for trend showed that with higher pain severity, the risk of suicidal ideation significantly increased (models 1, 2, and 3: $p < .001$; model 4: $p < .01$).

Little interference due to pain (Table 3) was significantly associated with suicidal ideation compared to the reference category in the unadjusted model (model 1: OR 2.35, 95% CI 1.17–4.72)) and when adjusted for demographics only (model 2: OR 2.22, 95% CI 1.14–4.34). When also adjusted for mental disorders (model 3) and prior suicidal ideation (model 4), the association became non-significant (model 3: OR 1.74, 95% CI 0.81–3.74; model 4: OR 1.57). The category of moderate to very severe interference due to pain was significantly associated with suicidal ideation in all models: the OR was highest in the unadjusted model (model 1: OR 3.76; 95% CI 2.07–6.82) and lowest in the fully adjusted model (model 4: OR 1.90, 95% CI 1.00–3.59). With more interference due to pain at baseline, the risk of suicidal ideation three years later significantly increased (p for trend in models 1 and 2: < 0.001; in model 3: < 0.01; in model 4: < 0.05).

No interaction effects were found for any mood disorder with pain, any anxiety disorder with pain, and any substance use disorder with pain on the risk of suicidal ideation. These effects applied for both pain severity and interference due to pain. This implies that the association between pain and suicidal ideation did not significantly differ between subjects with and subjects without a mental disorder.

4. Discussion

The aim of this study was to explore the longitudinal influence of pain severity and interference due to pain occurring in the last month on subsequent suicidal ideation in the general adult population. We found that the risk of incident suicidal ideation was significantly higher for persons with more severe pain and for those who experience more interference due to pain, which confirm our first hypothesis. These results did not change when adjusting for demographics and, more importantly, for concurrent mental disorders. In accordance with previous studies [16,32], adjusting for mental disorders did not significantly attenuate the observed risk of suicidal ideation.

Our second hypothesis, that the association between pain and suicidal ideation would be stronger in subjects with a mental disorder, was not confirmed. The effect of pain on suicidal ideation did not differ between subjects with a mental disorder and subjects without a mental disorder. Our findings, therefore, show that pain is an important and unique risk factor for suicidal ideation, independent of mental disorders, and extend previous research by showing that more severe pain and more interference due to pain are risk factors for suicidal ideation at three-year follow-up in the general population, even when mental disorders are taken into account. Pain and suicidal ideation may share similar biological pathways that can explain our results. For example, a dysfunction in serotonin transmission, also implicated in pain, might ultimately lead to suicidal ideation [33,34]. More research on shared biological pathways between pain and mental disorder is needed to shed light on this issue.

Our study found a higher OR than Calati et al. in their meta-analysis [7]; this may be related to the fact that the current study used a large nationally representative sample and had a longitudinal design, whereas Calati et al. [7] also included cross-sectional studies. This allows us to look at the incident suicidal ideation in persons with and without pain over time.

4.1. Strengths and limitations

Major strengths of this study are the longitudinal design and the large representative sample of the general population. Moreover, this is the first study to examine pain severity and interference due to pain as a risk factor for suicidal ideation in a large sample of the general population. This sample is representative of the general adult population (age 18–64 year), but might not be generalizable to other age categories, although comparable results were found in adolescents [16]. However, several limitations need to be noted as well. This study was based on self-reports, and suicidal ideation might therefore have been underreported. Furthermore, because we excluded individuals who experienced suicidal behavior > 12 months prior to baseline, we could not report on the recurrence of suicidal ideation. Whether pain might play a more important role in new onset or in recurrent suicidal ideation remains unknown. Future longitudinal research should take this into account, but this requires much larger samples with subjects reporting (new onset and recurrent) suicidal ideation at follow up. Additionally, it remains unknown whether pain also has an influence on other forms of suicidal behavior, such as plans and attempts. In the population sample of our study, suicidal ideation was the most frequent suicidal behavior endorsed, which prohibited us to study the influence of pain on other forms of suicidal behavior. A need exists, therefore, for studies which take these other forms of suicidal behavior into account. Regarding pain, we measured this with two items from the pain subscale of the SF36. A more comprehensive measurement of pain is preferred, in which more aspects of pain are distinguished, such as

Table 2
Odds ratios with 95% confidence intervals for the association between pain severity at baseline and suicidal ideation three years later among those without 12-month suicidal ideation at baseline.

		Model 1		Model 2		Model 3		Model 4	
		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Pain severity									
0 (none) *(ref)*									
1 (very little)		1.70 (0.68–4.21)	0.25	1.68 (0.70–3.99)	0.24	1.69 (0.72–4.00)	0.23	1.67 (0.68–4.10)	0.26
2 (little)		1.70 (0.83–3.45)	0.14	1.73 0.91–3.31)	0.10	1.43 (0.74–2.79)	0.29	1.57 (0.82–2.99)	0.17
3 (moderate to very severe)		4.68 (2.65–8.23)	< 0.001	4.00 (2.08–7.70)	< 0.001	3.39 (1.74–6.61)	< 0.001	2.69 (1.40–5.18)	0.003
Covariates									
Gender	Male *(ref)*								
	Female			0.76 (0.36–1.61)	0.47	0.59 (0.26–1.33)	0.20	0.68 (0.34–1.38)	0.28
Age	18–24 *(ref)*								
	25–34			1.77 (0.46–6.87)	0.40	1.71 (0.42–6.90)	0.45	1.70 (0.52–5.63)	0.38
	35–44			2.66 (1.04–6.83)	0.04	2.34 (0.86–6.37)	0.09	2.57 (0.94–7.04)	0.07
	45–54			1.77 (0.82–3.79)	0.14	1.47 (0.65–3.35)	0.35	1.49 (0.68–3.24)	0.32
	55–64			2.69 (1.15–6.31)	0.02	2.25 (0.92–5.57)	0.07	2.11 (0.92–4.84)	0.08
Education	Primary *(ref)*								
	Lower secondary			2.38 (0.77–7.34)	0.13	2.65 (0.89–7.88)	0.08	2.28 (0.87–5.98)	0.09
	Higher secondary			1.21 (0.50–2.90)	0.67	1.08 (0.45–2.62)	0.86	1.20 (0.50–2.90)	0.68
	Higher professional/university			0.80 (0.38–1.68)	0.56	0.75 (0.35–1.60)	0.45	0.79 (0.37–1.68)	0.54
Living situation	With partner *(ref)*								
	Without partner			1.21 (0.74–1.98)	0.44	0.91 (0.53–1.58)	0.75	0.79 (0.45–1.39)	0.41
Working situation	Job *(ref)*								
	No job			2.27 (1.13–4.57)	0.02	1.84 (0.86–3.95)	0.12	1.58 (0.78–3.19)	0.20
12-month mood disorder	None *(ref)*								
	Any					4.78 (2.17–10.52)	< 0.001	3.52 (1.81–6.82)	< 0.001
12-month anxiety disorder	None *(ref)*								
	Any					3.08 (1.29–7.35)	0.01	2.25 (0.98–5.17)	0.06
12-month substance use disorder	None *(ref)*								
	Any					0.58 (0.18–1.84)	0.35	0.58 (0.18–1.85)	0.35
Prior suicidal ideation	No (*ref*)								
	Yes							6.48 (3.34–12.60)	0.001
P for trend		1.63 (1.35–1.98)	< 0.001	1.56 (1.25–1.93)	< 0.001	1.47 (1.17–1.84)	0.001	1.37 (1.11–1.69)	0.004

Model 1: unadjusted odds ratios.
Model 2: adjusted for demographics (gender, age, education, living situation, working situation) and time between measurements (T0–T1).
Model 3: adjusted for demographics (gender, age, education, living situation, working situation), any mood disorder, any anxiety disorder, any substance use disorder, and time between measurements (T0–T1).
Model 4: adjusted for demographics (gender, age, education, living situation, working situation), any mood disorder, any anxiety disorder, any substance use disorder, prior suicidal behavior, and time between measurements (T0–T1).

Table 3
Odds ratios with 95% confidence intervals for the association between pain interference at baseline and suicidal ideation three years later among those without 12-month suicidal ideation at baseline.

		Model 1		Model 2		Model 3		Model 4	
		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Pain interference									
0 (none) (*ref*)									
1 (little)		2.35 (1.17–4.72)	0.02	2.22 (1.14–4.34)	0.02	1.74 (0.81–3.74)	0.15	1.57 (0.72–3.43)	0.26
2 (moderate to very severe)		3.76 (2.07–6.82)	< 0.001	2.87 (1.64–5.02)	< 0.001	2.35 (1.22–4.53)	0.01	1.90 (1.00–3.59)	0.05
Covariates									
Gender	Male (*ref*)								
	Female			0.78 (0.38–1.68)	0.56	0.62 (0.28–1.35)	0.23	0.71 (0.36–1.40)	0.32
Age	18–24 *(ref)*								
	25–34			1.75 (0.44–6.97)	0.42	1.62 (0.39–6.71)	0.51	1.59 (0.46–5.51)	0.46
	35–44			2.66 (1.03–6.77)	0.04	2.33 (0.84–6.50)	0.11	2.57 (0.91–7.31)	0.08
	45–54			1.76 (0.79–3.70)	0.17	1.45 (0.64–3.31)	0.37	1.47 (0.68–3.19)	0.33
	55–64			2.70 (1.14–6.27)	0.03	2.24 (0.91–5.50)	0.08	2.18 (0.94–5.05)	0.07
Education	Primary *(ref)*								
	Lower secondary			2.54 (0.87–7.34)	0.09	2.76 (0.95–8.00)	0.06	2.38 (0.96–5.93)	0.06
	Higher secondary			1.26 (0.55–2.84)	0.60	1.12 (0.48–2.62)	0.79	1.21 (0.51–2.86)	0.67
	Higher professional/university			0.81 (0.40–1.65)	0.56	0.77 (0.37–1.61)	0.49	0.79 (0.37–1.68)	0.54
Living situation	With partner *(ref)*								
	Without partner			1.19 (0.72–1.93)	0.51	0.89 (0.51–1.57)	0.69	0.75 (0.42–1.35)	0.34
Working situation	Job *(ref)*								
	No job			2.29 (1.15–4.42)	0.02	1.87 (0.90–3.88)	0.09	1.62 (0.84–3.13)	0.15
12-month mood disorder	None *(ref)*								
	Any					4.54 (2.10–9.80)	< 0.001	3.33 (1.73–6.42)	< 0.001
12-month anxiety disorder	None *(ref)*								
	Any					3.17 (1.26–7.95)	0.01	2.32 (0.97–5.54)	0.06
12-month substance use disorder	None *(ref)*								
	Any					0.63 (0.22–1.83)	0.40	0.61 (0.20–1.88)	0.39
Prior suicidal ideation	No (*ref*)								
	Yes							6.92 (3.52–13.61)	< 0.001
P for trend		1.98 (1.51–2.61)	< 0.001	1.75 (1.35–2.27)	< 0.001	1.56 (1.14–2.13)	0.006	1.40 (1.02–1.93)	0.04

Model 1: unadjusted odds ratios.
Model 2: adjusted for demographics (gender, age, education, living situation, working situation) and time between measurements (T0–T1).
Model 3: adjusted for demographics (gender, age, education, living situation, working situation), any mood disorder, any anxiety disorder, any substance use disorder, and time between measurements (T0–T1).
Model 4: adjusted for demographics (gender, age, education, living situation, working situation), any mood disorder, any anxiety disorder, any substance use disorder, prior suicidal behavior, and time between measurements (T0–T1).

frequency/chronicity and cause or origin of pain. Regarding frequency/chronicity, the subjects in this study were asked to report pain severity and interference due to pain in the month before baseline, and although our results show a significant association of these pain variables with suicidal ideation in the following three years, a measurement of a longer duration of pain (e.g. chronic pain vs. acute pain) might result in stronger association with suicidal ideation [10,35]. Moreover, pain is not time independent and severity can change over time, affecting our results. For example, previous literature suggests that a change in severity of pain is associated with the course and severity of mental disorders [36,37], and it is therefore not unlikely that a change in pain severity could lead to a change in the risk of suicidal ideation (e.g. less severe pain over time might decrease the risk of suicidal ideation). However, in the present study, measurement of pain referred to pain in the four weeks prior to baseline. As the course of pain was not assessed in detail in NEMESIS-2 in the period between baseline and first follow-up, no inferences could, therefore, be made whether changes in the course of pain affected suicidal ideation. To differentiate pain trajectories, associated with suicidal ideation, we need to measure pain more comprehensively in future studies. The effect of this limitation is that we probably underestimate associations between pain and suicidality. It is conceivable that if we had restricted ourselves to a longer duration of pain at baseline or a measurement of increasing pain over time, we would have found even stronger associations with suicidal ideation at follow-up [10,35]. Regarding the cause or the origin of the pain, pain itself, of course, can be the trigger for a mental disorder, such as in a somatic symptom disorder [38]. However, there is a recent debate on whether this new DSM-5 diagnosis might lead to overpsychologizing and mislabeling pain [39]. Therefore, instead of making statements whether the experienced pain is part of a mental disorder, this study only focused on how severe the individual experienced the pain and how much interference due to pain there was. The experienced pain might also be explained as part of a more 'somatic' disease, such as cancer [40], cardiovascular disease [41], and rheumatoid arthritis [42]. It is often clinically difficult to tease out primary and secondary factors. In the present study, however, we did not know whether the experienced pain originated from a somatic disease. Furthermore, pain is highly associated with a variety of somatic diseases, and controlling for somatic diseases would then lead to overcorrection of the statistical model. An area of further study would be to consider to what extent pain is 'mentally' or 'somatically' attributable, and if so, to examine whether the risk of suicidal ideation differs from non-attributable pain. Other factors, such as social support and poor pain-related coping (e.g. catastrophizing), might also play a mediating role in the link between pain and suicidal ideation, [43,44], but these were not studied here. In a study among 360 patients with rheumatic disease, less social support was associated with an increased risk for suicidal ideation [44], and in a sample of 1512 pain patients, catastrophizing was an important predictor of both the presence and severity of suicidal ideation, even after controlling for measures of affective function (e.g. depression, anxiety) [43]. In future research and treatment of pain, social support and catastrophizing as pain-related coping should be considered, as this may explain why pain predicts suicidality and can help designing strategies to prevent suicidal ideation. Furthermore, the course of mental disorders is diverse [45–47], and can be described as an incident, remitted, or chronic course. The literature shows that these different courses are associated with different courses of the severity of pain [36,37], making it of interest to study how different trajectories of mental disorders, next to different trajectories of pain, are associated with subsequent suicidal ideation. However, in the present study, no information was available on the exact time of onset of suicidal ideation. Therefore, we could not take interval mental disorders into account, as we could not tell whether suicidal ideation or a newly developed mental disorder between baseline and follow-up came first.

4.2. Implications

Our finding that pain has a significant impact on suicidal ideation may be important for developing and customizing suicide prevention plans for patients suffering from pain [48]. To date, such plans mainly focus on mental disorders [5]. Patients with pain might also benefit from psychotherapeutic interventions, with a focus on building distress tolerance skills, challenging catastrophic thoughts, and instilling hope in the future. Pain medication can be an effective treatment for reducing pain symptoms and, therefore, might protect against developing suicidal ideation. However, caution is necessary, especially with opioid therapy: opioid deaths (including intentional suicides) are rising [49], and a higher dose of opioids increases the risk of suicide [50]. Two longitudinal studies [16,32] reported the increased risk of headaches and migraines on suicidal ideation/attempt versus controls. Our findings broaden this finding by including pain of any form – if severe or significant interference is experienced due to pain – as a risk factor for suicidal ideation. Therefore, the risk of suicidal ideation may need further discussion, even in the absence of common mental disorders when persons present themselves with severe pain or significant interference due to pain. More longitudinal research is needed that focuses on the role of pain in suicidal ideation, in which pain is measured more comprehensively, including pain location, origin of pain, and pain-related coping.

Acknowledgments

NEMESIS-2 is conducted by the Netherlands Institute of Mental Health and Addiction (Trimbos Institute) in Utrecht. Financial support has been received from the Dutch Ministry of Health, Welfare and Sport, with supplementary support from the Netherlands Organisation for Health Research and Development (ZonMw) and the Genetic Risk and Outcome of Psychosis (GROUP) investigators. The funding sources had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication. The views expressed are those of the author and not necessarily those of the Ministry of Health, Welfare and Sport.

Conflict of interests

Prof. van der Feltz-Cornelis reports grants from Eli Lilly, non-financial support from GGz inGeest and Arkin outside the submitted work; Prof. Beekman reports personal fees from Lundbeck, outside the submitted work; all other authors have nothing to disclose.

Contributors

MtH and RdG are part of the NEMESIS-2 research team and obtained funding for the NEMESIS-2 study. EdH, MtH, RdG and CvdFC conceived the initial idea for the present study and all authors contributed to its planning, including defining the aims, variables of interest, and analysis strategy. Analyses were done by MtH, but all authors had access to the statistical outputs. EdH drafted the article and all authors contributed to revisions. All authors approved the final manuscript.

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