The Course of Chronic Pain With and Without Psychiatric Disorders: A 6-Year Follow-Up Study From Childhood to Adolescence and Young Adulthood

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ABSTRACT

Objective: Psychiatric disorders are common in children with chronic pain, but their course and impact when children grow up are unknown. This study examines the 6-year clinical outcome of children referred for chronic pain with and without comorbid psychiatric disorders.

Method: In 91 children and adolescents (aged 8 to 17 years) referred to a university outpatient clinic for chronic pain, child psychiatric disorders were assessed using the Diagnostic Interview Schedule for Children-parent version (DISC-P) between 2000 and 2002. Participants (aged 13 to 24 years) were reassessed on average 6-years later. Outcome measures were chronic pain and psychiatric disorders assessed with the Diagnostic Interview Schedule for Children-children version (DISC-C) or the Composite International Diagnostic Interview (CIDI) and Diagnostic Interview Schedule IV (DIS).

Results: After 6 years, 75% of the participants still experienced chronic pain and 15% were in complete remission of both chronic pain and psychiatric disorder. The prevalence of psychiatric disorders (both persistent and new onset disorders) at follow-up was 32%. Baseline psychiatric disorder was a predictor of psychiatric disorder at follow-up (OR = 2.6, 95% CI = 1.1–6.5, $P = .04$; adjusted OR = 2.8, 95% CI = 1.1–7.1, $P = .03$) but did not predict persistence of chronic pain.

Conclusions: Children referred for chronic pain frequently continue to suffer from chronic pain and psychiatric disorders in adolescence and young adulthood. In this population, comorbid psychiatric disorder at study entry was a predictor of psychiatric disorder, but not of persistent chronic pain, in adolescence and young adulthood.

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Chronic pain is a common problem in children and adolescents[1] and leads to substantial impairments in daily life, especially in children referred for clinical care.[2,3] Short-term follow-up studies have shown that child chronic pain is persistent in 20%–65% of cases,[4–8] despite treatment in specialized clinics.[4] The few studies that have investigated long-term persistence of child chronic pain reported that 34%–73% of various pain conditions are persistent.[9–12] Furthermore, chronic pain in childhood has been found to predict chronic pain in adulthood[13] and adult psychiatric disorders.[14]

A considerable number of children with chronic pain suffer from comorbid psychiatric disorders[15–18]; not only anxiety disorders and mood disorders, but also externalizing disorders such as attention-deficit/hyperactivity disorder (ADHD) and oppositional defiant disorder are associated with child chronic pain.[15–18] Several studies on the impact of internalizing disorders on daily life functioning show a relation with increased functional disability.[19–22] Studies of the course and predictive value of comorbid psychopathology in children with chronic pain are scarce and also have been restricted to the assessment of internalizing psychiatric symptoms.[6,23] Perquin et al[6] found that baseline self-reported anxiety and depressive symptoms predicted persistent chronic pain in children at 2-year follow-up. Mulvaney et al[23] observed that self-reported anxiety and depressive symptoms in patients with abdominal pain were related to persistence of pain after 5 years. Depressive and anxiety symptoms are common in children with chronic pain, but the clinical significance of these findings is unclear. The question remains whether comorbid psychiatric disorders influence the course of the pain. If so, psychiatric interventions might improve the clinical outcome of these patients.

The aim of this study was to examine the impact of baseline comorbid psychiatric disorders on the clinical outcome in adolescents and young adults 6 years after pediatric referral for chronic pain to an outpatient university clinic. Two clinical outcome measures were used: persistence of chronic pain complaints and the presence of psychiatric disorders as measured by structured psychiatric interviews. It was predicted that children with baseline comorbid psychiatric disorders would be at risk for persistence of chronic pain and psychiatric disorders at follow-up.

METHOD

Participants

In this study, we reexamined the participants of the Pain of Unknown origin in Children (PUC1) study.[2,15,18,24] The PUC1 study included children and adolescents referred for the first time with unexplained pain to the Wilhelmina Children's Hospital University Medical Centre Utrecht, (Utrecht, The Netherlands). Additional inclusion criteria were pain lasting at least 3 months, being at least 8 years old, and sufficient knowledge of the Dutch language. The Dutch health care system is organized such that a general practitioner first evaluates a child. If further specialized care is necessary, the child can be referred to a regional or a university hospital. If specialists in the regional hospital need a second opinion, children can be

referred to a university hospital. In The Netherlands, therefore, children in a university hospital are either referred by general practitioners or referred by medical specialists in regional pediatric clinics. One hundred forty-nine children were assessed between 2000 and 2002, and of these children, 134 (37 boys, 97 girls), aged 8 to 18 years, completed the whole baseline assessment and a psychiatric interview with the parent version of the Diagnostic Interview Schedule for Children (DISC-P).[25] Further details about the patient selection and procedures, baseline analyses, diagnostic approach, and comorbid psychiatric disorder can be found in previous studies.[2,18,24]

Clinical Points

- Chronic pain in most children in pediatric care is not self-limiting and is often accompanied by psychiatric disorders when they grow up.
- Psychiatric care alongside standard medical care should be made available for children with chronic pain and impairing comorbid psychiatric disorders.

Procedure

After a minimum of 5 years of follow-up, adolescents, young adults, and their parents were invited to participate in the Pain of Unknown origin in Children 2 (PUC2) study. They were approached by phone to ask whether they would be willing to receive written information about the study. If so, adolescents (up to 18 years) and their parents and young adults (18 years and above) received separate leaflets explaining the procedures and aims of the study. A week later, they were contacted by phone and invited to participate. After explanation of the procedure, all adolescents and their parents (up to 18 years) and young adults (18 years and above) who were willing to participate gave their written informed consent. Between November 2006 and May 2007, participants completed a semistructured inquiry and questionnaires, and a psychiatric interview was performed. The Medical Ethics Committee of the University Medical Centre Utrecht approved the study protocol.

Outcome Measures

Pain. At follow-up, participants were asked if they had suffered from pain in the previous years. If they answered yes, they were asked whether they still suffered from pain today. If both questions were answered positively, the participants were regarded as suffering from persisting chronic pain and completed questions on pain intensity and pain localization. Pain intensity was assessed using the Visual Analog Scale (VAS) derived from the Pediatric Pain Questionnaire (PPQ).[26,27] The VAS has demonstrated validity for use in school-aged children and adults with chronic pain.[26–30] Participants were asked if their pain was primarily located in (1) the head, (2) the abdomen, (3) muscles or joints, or (4) other locations.

Psychiatric disorder. The Diagnostic Interview Schedule for Children (DISC),[25] the Composite International Diagnostic Interview (CIDI)[31] version 2.1, and the Diagnostic Interview Schedule IV (DIS)[32] were used to diagnose psychiatric disorders. The DISC and CIDI are comprehensive fully structured respondent-based interviews assessing a broad range of psychiatric disorders according to *DSM-IV* diagnostic criteria.[25,31,32] Both interviews have demonstrated good to excellent validity and reliability.[25,33,34]

We used the child version of the DISC for children from 12 years up to 18 years (n = 40) and the CIDI for participants aged 18 years and older (n = 51). The following diagnostic sections of the DISC were used: Anxiety Disorders, Mood Disorders, Disruptive Disorders, Substance-Use Disorders, Schizophrenia, and Miscellaneous Disorders (Eating, Tic disorder). All anxiety disorders sections, mood disorder sections, substance use disorder sections, and the sections Psychosis and Eating disorders of the CIDI were used. In addition, the DIS section L[32] was used to specifically assess ADHD, oppositional defiant disorder, and conduct disorder in participants aged 18 years and older. The time frame of the DISC, CIDI, and DIS for current disorders is the past 12 months.

The DISC, CIDI, and DIS questions are highly structured. They are designed to be read exactly as written. In each section, questions are asked about specific symptoms during the past year, and then follow-up questions in case of positive endorsement. If enough symptoms have been endorsed, and these symptoms occur in a pattern that suggests a diagnosis might be present, respondents are asked about the onset of the particular cluster of symptoms that they have endorsed. An example of a question from the CIDI is, "The next questions are about longer periods of feeling worried, tense, or anxious. In the past 12 months, did you have a period of a month or more when most days you felt worried or tense or anxious about everyday problems such as work or family?" Each diagnosis is "self-contained," so that information from other diagnostic modules is not necessary in order to assign a diagnosis.

The administration time for the whole DISC is 70 minutes to 120 minutes per informant. For the CIDI, the administration time is, on average, 75 minutes. Two trained interviewers (L.M.E.K. and B.T.) conducted the interviews. The adolescent psychiatric interviews were completed in person and the adult interviews in person (n = 49) or by phone (n = 2). Clinically significant psychiatric disorder was defined as a positive psychiatric diagnosis in combination with a Children's Global Assessment Scale (CGAS)[35,36] or Global Assessment of Functioning Scale (GAF)[37] score lower than 61. The CGAS and GAF are clinician-scored scales of adaptive functioning that are useful for incorporating a measure of impairment in the classification of psychiatric disorders.[35–38] A CGAS score of 61 is the best cutoff for definite psychiatric cases, identifying children who have received mental health services.[38]

Data Analysis

Cross-sectional differences between groups were tested with 2-sided *t* tests for continuous variables and χ^2 tests for

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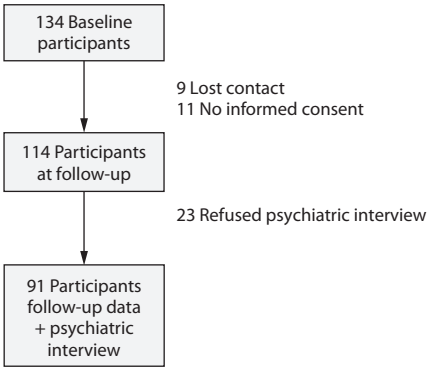
Figure 1. Flowchart Follow-Up Study on Clinical Outcome of Children With Chronic Pain



dichotomous variables. Differences between baseline and follow-up variables were tested with paired-samples *t* tests for continuous variables and McNemar test for dichotomous variables. Differences in subgroups of clinical outcome were tested with χ^2 analysis. In case of a non-normal distribution, nonparametric tests were used. Univariate logistic regression analysis was performed to examine independent predictors of persisting pain, remission, and psychiatric disorders at follow-up.

Results are expressed as odds ratios with corresponding 95% confidence intervals. Adjusted odds ratios were calculated using a backward stepwise multivariate logistic regression model entering possible confounding factors as covariates (age and gender of the child, socioeconomic status). For statistical analyses, the Statistical Package for Social Sciences (SPSS Inc, Chicago, Illinois) version 17.0 was used. Statistical significance was considered for P values ≤ .05.

RESULTS

Characteristics

Of the 134 participants in PUC1, 9 lost contact, 11 refused to participate, and 23 completed the questionnaires, but refused a psychiatric interview, leaving 91 participants with a median age of 18 years (range, 13–24) in this study (Figure 1). Reported reasons for not consenting to participate in the follow-up study were "bad experience in your hospital" (n = 1), "dislike psychological character of the study" (n = 2), "pain remission" (n = 3), "cannot participate because of autism" (n = 1), "diagnosis changed to chronic fatigue syndrome" (n = 1), and "too busy" (n = 3). The study group consisted of 40 adolescents and 51 adults (≥ 18 years). Comparison of the baseline parameters (demographic, pain, psychiatric disorder) of the present study population and the PUC1 cohort did not reveal differences apart from a higher proportion of males in nonparticipants (42% vs 21% in participants, P = .011).

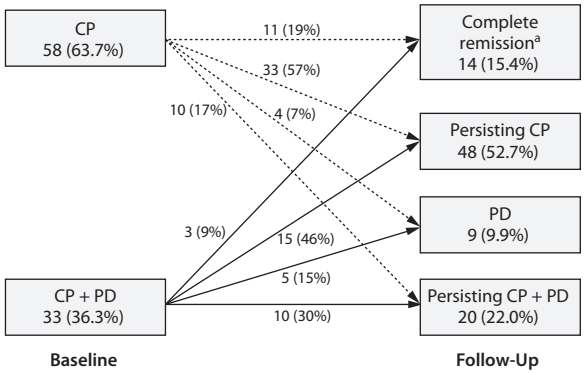
Table 1 presents the baseline characteristics of participants (N = 91). It shows that females were predominant (n = 72, 79%) and that the median duration of pain at the time of referral was 12 months (range, 3–144). The median follow-up time was 6 years (range, 5–8). Eighty-six participants (95%) had at least a minimal education level of lower-level vocational training, indicating that at least 86 participants had an IQ above 70.

Table 1. Demographic Characteristics of the Participants (N = 91)

Characteristic	Value
Age at referral, y, mean (SD)	12.1 (2.6)
Age at follow-up, y, mean (SD)	17.9 (2.6)
Sex, n (%) female	72 (79.1)
Pain duration at referral, mo, mean (SD)	23.4 (26.1)
Referred by, n (%)	
General practitioner	28 (30.8)
Medical specialist	63 (69.2)
Follow-up time, y, mean (SD)	5.9 (0.8)
Current living arrangement, n (%)	
With parents	73 (80.2)
Alone, with peers, or with partner	18 (19.8)
Current education level, n (%)[a]	
Low	9 (9.9)
Middle	41 (45.1)
High	36 (39.6)
Other	5 (5.5)
Socioeconomic status, n (%)[b]	
Low	19 (20.9)
Middle	38 (41.8)
High	30 (33.0)
Unknown	4 (4.4)

[a]Low = lower level vocational training; middle = intermediate level vocational training, intermediate professional training; high = higher secondary school levels, higher professional education, university; other = finished primary school, secondary school level unknown.
[b]Based on the father's occupation at baseline. Classification according to the Statistics Netherlands; Standaard Beroepenclassificatie (Dutch Standard Classification of Occupations); Voorburg, Heerlen (1992).

Figure 2. Development of Chronic Pain (CP) and Psychiatric Disorder (PD) in Individuals (n, %) With and Without Comorbid Psychiatric Disorder 6 Years After Referral for Chronic Pain



[a]Absence of chronic pain and psychiatric disorder.

Clinical Outcome of Chronic Pain and Psychiatric Disorder

There were 4 main outcomes of baseline chronic pain with or without comorbid psychiatric disorder (Figure 2). At follow-up, 14 participants (15%) had neither chronic pain nor a psychiatric disorder, 48 participants (53%) had chronic pain, 9 participants (10%) had a psychiatric disorder, and 20 participants (22%) had both chronic pain and a psychiatric

Table 2. Persistent Pain and Psychiatric Disorders 6 Years After Referral for Chronic Pain

Pain and Disorder	Baseline	Follow-Up	*P* Value[a]
Chronic pain, n (%)	91 (100)	68 (74.7)	
VAS current pain, mean (SD)[b]	4.8 (3.0)	4.0 (2.8)	*.05*
VAS worst pain past week, mean (SD)[b]	7.2 (2.8)	5.4 (3.2)	*< .001*
Pain localization, n (%)			
No pain	0 (0)	23 (25.3)	
Abdominal	27 (29.7)	14 (15.4)	
Headache	20 (22.0)	14 (15.4)	
Musculoskeletal	44 (48.4)	38 (41.8)	
Unknown		2 (0.02)	
Any psychiatric disorder, n (%)	33 (36.3)	29 (31.9)	.60
Any anxiety disorder	29 (31.9)	12 (13.2)	*.001*
Any mood disorder	7 (7.7)	8 (8.8)	1
Any externalizing disorder[c]	6 (6.6)	6 (6.6)	1
Any substance use disorder	…	12 (13.2)	
No. of psychiatric diagnoses, median (range)	1 (1–9)	2 (1–5)	.13

[a]Paired samples *t* test was used to compare baseline and follow-up pain levels (Visual Analog Scale [VAS]); McNemar test was used to compare dichotomous variables. Italic values show significance.
[b]If persistent pain was present.
[c]Attention-deficit/hyperactivity disorder, oppositional defiant disorder.
Symbol: … = substance use disorders were not evaluated at baseline.

Table 3. Comorbid Baseline Child Psychiatric Disorder as Predictor of Clinical Outcome at 6-Year Follow-Up[a]

Outcome	OR	95% CI	*P* Value	Adjusted OR[b]	95% CI	*P* Value
Persistence of symptoms[c]	2.3	0.6–9.1	.22	1.9	0.5–7.9	.38
Chronic pain	1.1	0.4–2.9	.86	0.8	0.3–2.3	.68
Psychiatric disorder	2.6	1.1–6.5	*.04*	2.8	1.1–7.1	*.03*
Anxiety disorder	4.3	1.2–15.7	*.03*	4.1	1.0–16.5	*.05*
Mood disorder	1.8	0.4–8.0	.40	1.7	0.4–8.0	.48
Disruptive disorder	1.8	0.3–9.7	.47	1.6	0.2–10.5	.63
Substance use disorder	1.0	0.3–3.2	.96	2.2	0.5–9.5	.31

[a]Groups with persistent pain and psychiatric disorder overlapped for cases in which both were present at follow-up. Italic values show significance.
[b]Adjusted by age, gender, and socioeconomic status.
[c]Presence of chronic pain and/or psychiatric disorder at follow-up.

disorder. Of the 58 children with only chronic pain at baseline, 14 were diagnosed with a psychiatric disorder at follow-up. Of the 33 children with comorbid psychiatric disorder at baseline, 18 no longer had a psychiatric disorder at follow-up. Three (9%) of the 33 participants with baseline psychiatric disorder, compared to 11 (19%) of 58 participants without baseline psychiatric disorder, were in complete remission of symptoms at follow-up ($\chi^2 = 1.6$, $P = .21$).

Comparison of baseline and follow-up data showed that 75% (n = 68) of the adolescents and young adults still experienced chronic pain (Table 2), although the current and worst pain intensity VAS results were significantly lower than 6 years earlier ($P = .05$ and $P < .001$, respectively). The prevalence of psychiatric disorder at follow-up was 31.9%, comparable with that at baseline (Table 2). The prevalence of any anxiety disorder decreased significantly from 31.9% (n = 29) to 13. 2% (n = 12, $P = .001$, Table 2). The elaborate psychiatric assessment at follow-up resulted in a diagnosis of substance use disorder in 12 participants with 1 substance use disorder or more (alcohol misuse [n = 9], alcohol dependence [n = 1], cannabis misuse [n = 2], and cannabis dependence [n = 2]). Neither eating disorders nor psychotic disorders were diagnosed at follow-up.

If cases with merely substance use disorder were excluded, the prevalence of psychiatric disorder at follow-up decreased to 23.1% (n = 21). Taking into account only those psychiatric disorders with a CGAS/GAF score below 61 (clinical significance), prevalence rates decreased to 17.6% (n = 16) at baseline and 15.4% (n = 14) at follow-up.

Psychiatric Disorder as Independent Predictor of Clinical Outcome

The presence of any psychiatric disorder at baseline did not predict the persistence of chronic pain at follow-up ($P = .86$, see Table 3). However, a psychiatric disorder at baseline significantly predicted the persistence of any psychiatric disorder at follow-up (OR = 2.6, 95% CI = 1.1–6.5, $P = .04$, Table 3), anxiety disorders in particular (OR = 4.3, 95% CI = 1.2–15.7, $P = .03$, Table 3). These associations sustained after correcting for age, gender, and socioeconomic status (for any psychiatric disorder, adjusted OR = 2.8, 95% CI = 1.1–7.1, $P = .03$; for any anxiety disorder, adjusted OR = 4.1, 95% CI = 1.0–16.5, $P = .05$ [see Table 3]). Psychiatric disorder at baseline also predicted psychiatric disorder without substance use disorders at follow-up (OR = 3.1, 95% CI = 1.1–8.5, $P = .03$; adjusted OR = 3.3, 95% CI = 1.2–9.1, $P = .02$). The presence of clinically significant psychiatric disorder at baseline predicted clinically significant psychiatric disorder at follow-up (OR = 3.3, 95% CI = 0.9–11.8, $P = .06$; adjusted OR = 4.0, 95% CI = 1.1–14. 5, $P = .04$).

DISCUSSION

In this longitudinal study of children referred for chronic pain, we found that 75% of the individuals still experienced chronic pain and 32% suffered a psychiatric disorder 6 years later. By combining pain and psychiatric disorder in the clinical outcome, we found that merely 15% of all children referred were free of pain and psychiatric symptoms at follow-up. Furthermore, we showed that comorbid child psychiatric disorder at baseline did not predict chronic pain persistence but did predict the presence of a broad range of psychiatric disorders in adolescence and young adulthood.

The prevalence rate of persistent pain found in this study exceeds prevalences reported in previous follow-up studies,[9,11,12] with the exception of a study reporting on the prevalence of chronic headache after 10 years.[10] Since a presenting chronic pain site might relocate over time,[6] lower prevalence rates in other follow-up studies might be due to investigating pain at one localization only. Moreover, our referred sample was previously found to be characterized by considerable impairment.[2] This might indicate that these children are at greater risk for persistence of pain. As previous studies reported higher chronic pain persistence in females than in males,[4,6,12] a female predominance in

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our sample may account for a higher pain persistence rate than previous studies. Although the greater proportion of females is similar to demographic patterns in other clinical samples,[3,39] we used multiple regression analysis to control for a possible confounding gender effect.

New onset and persistent psychiatric disorders diagnosed at follow-up included internalizing psychiatric disorders, externalizing psychiatric disorders (ADHD), and substance use disorders. These findings are in line with previous studies on the co-occurrence of chronic pain and psychiatric disorders in children[15–18] and adults.[40–42] This co-occurrence is reported to be common in families with chronic pain.[43–45] It is likely to be the result of a genetic predisposition,[46] and often develops in both directions.[40,47]

We found that children with any psychiatric disorder at referral, compared to those who merely suffered from chronic pain, had a 3 times higher risk of psychiatric disorder 6 years later. Narrowing the definition of psychiatric disorder by including impairment strengthened the predictive value for future clinically significant psychiatric disorders. In contrast with the general finding that chronic pain in children predicts future psychiatric disorders,[13,14] our results show that it is particularly those children who already experienced psychiatric disorder in childhood who suffer from psychiatric disorders later on. Our findings are in line with those studies in general child psychiatry showing that psychiatric disorders in childhood and adolescence predict adult psychiatric disorders.[48–50] As in general child psychiatry, treatment of psychiatric disorder in children with chronic pain might prevent future psychopathology.[51,52]

Although the prevalence of anxiety disorders significantly decreased at follow-up, baseline psychiatric disorder in our sample seemed to predict anxiety disorders in particular. This relation sustained after adjusting for potential confounders such as gender and age. Given the high prevalence of baseline child anxiety disorders, it is possible that we studied the predictive value of comorbid anxiety disorders instead of comorbid child psychiatric disorders in general. However, this result is in contrast with studies showing that child anxiety disorders predict a broad range of psychiatric disorders in adolescence[49] instead of solely anxiety disorders.

Our results should be considered in the light of the strengths and limitations of the study. Strengths are the prospective longitudinal design by which children were followed up into adolescence and young adulthood and the use of a broad standardized psychiatric assessment. However, there are some limitations. First, our dataset comes from a sample recruited at a pediatric outpatient department. Therefore, generalizability to other chronic pain populations is unknown. Yet, our sample does reflect daily pediatric practice and our findings could therefore have clinical implications with regard to the need for treatment of children referred for chronic pain. Second, because the participants became adolescents and adults, different psychiatric diagnostic interview instruments had to be used. At baseline, the parent version of the DISC was used, while at follow-up, the child version of the DISC and the CIDI and DIS were used. Different instruments and informants may lead to different results,[53] which might explain the change in prevalence of, for example, anxiety disorders. However, there are many similarities between the DISC, CIDI, and DIS: all instruments are fully structured diagnostic psychiatric interviews based on the *DSM-IV* and have the same outline in assessing these disorders. Third, in our small sample, we detected that more children with than without comorbid psychiatric disorder had persistence of clinical symptoms (a negative clinical outcome) as we hypothesized, but this result was not statistically significant due to the lack of power. At last, since persisting symptomatology does not necessarily mean persisting disability, longitudinal studies that include disability could examine to what extent persisting symptoms influence daily functioning of children growing up with chronic pain. Furthermore, longitudinal studies are needed that include potential moderators or mediators such as catastrophizing[54,55] and positive affect[56] when studying the association between comorbid psychopathology and the outcome of children with chronic pain.

In conclusion, chronic pain in most children who seek outpatient care is not self-limiting and is often accompanied by psychiatric disorder in adolescence and young adulthood. This poor clinical outcome suggests that in addition to a standard clinical assessment, early intervention should be available for all children who are referred for chronic pain. Comorbid psychiatric disorder at entry predicted the persistence of psychiatric disorder later on, but did not predict persistence of chronic pain. The prevalence of a broad range of new onset and persisting psychiatric disorders justifies psychiatric assessment alongside standard medical care of these patients. Should impairing psychiatric disorders be diagnosed, additional psychiatric intervention is warranted to improve daily functioning and to prevent future psychopathology.

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