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Complete List of Authors:	Elander, James; University of Derby, Duarte, Joana Maratos, Frances Gilbert, Paul
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Predictors of painkiller dependence among people with pain in the general population

James Elander,[1] Joana Duarte,[2] Frances A. Maratos[1] and Paul Gilbert[1]

1. University of Derby, UK
2. Coimbra University, Portugal

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Correspondence: James Elander, Centre for Psychological Research, University of Derby, Kedleston Road, Derby DE22 1GB, UK. Email j.elander@derby.ac.uk

Abstract

Aims: Self-medication with painkillers is widespread and increasing, and evidence about influences on painkiller dependence is needed to inform efforts to prevent and treat problem painkiller use.

Design: Online questionnaire survey.

Participants: People in the general population who had pain and used painkillers in the last month (n=112).

Measurements: Pain frequency and intensity, use of over-the-counter and prescription painkillers, risk of substance abuse (SOAPP scale), depression, anxiety, stress, alexithymia, pain catastrophizing, pain anxiety, pain self-efficacy, pain acceptance, mindfulness, self-compassion, and painkiller dependence (Leeds Dependence Questionnaire).

Findings: In multiple regression, the independent predictors of painkiller dependence were prescription painkiller use (ß 0.21), SOAPP score (ß 0.31), and pain acceptance (ß -0.29). Prescription painkiller use mediated the influence of pain intensity. Alexithymia, anxiety and pain acceptance all moderated the influence of pain.

Conclusions: The people most at risk of developing painkiller dependence are those who use prescription painkillers more frequently, who have a prior history of substance-related problems more generally, and who are less accepting of pain. Based on these findings, a preliminary model is presented with three types of influence on the development of painkiller dependence: a) pain leading to painkiller use, b) risk factors for substance-related problems irrespective of pain, and c) psychological factors related to pain. The model could guide further research among the general population and high risk groups, and acceptance-based interventions could be adapted and evaluated as methods to prevent and treat painkiller dependence.

Introduction

Increasing access to over the counter (OTC) and prescription medicines is national policy in many countries including the UK [1], and painkillers are the most frequently used type of medication [2–4]. One review concluded that, "on balance, OTC pain relievers have provided a profound benefit to American consumers. After literally billions of doses, their record of safety and efficacy – when used as directed – is extremely favourable from a risk-benefit viewpoint" [5, p. 534]. However, painkiller misuse (when painkillers are used to relieve pain, but are used in an incorrect manner) is common [3], and painkiller abuse (when they are used for reasons other than to relieve pain) has increased steadily in both the US and UK in recent years [6–8].

Evidence is needed to inform early detection and management of painkiller misuse and abuse, but research with chronic pain patients has not identified consistently reliable predictors of painkiller misuse [9], and the most reliable predictors of painkiller abuse are measures that focus mainly on prior history of substance abuse, such as the Screener and Opioid Assessment for Patients with Pain (SOAPP) [10, 11]. Much less attention has been given to understanding the development of psychological dependence on painkillers, which might be more amenable to early intervention. Psychological dependence does not mean the same as addiction or a diagnosable substance use disorder, but it could influence the development of one of those outcomes. Evidence about behavioural and/or psychological risk factors for painkiller dependence could therefore be used to develop and target preventative or treatment interventions for painkiller-related problems including misuse, abuse, addiction or other substance use disorders. Evidence about risk factors for painkiller dependence could also be used to address excessive or unfounded concerns about painkillers, which can lead to pain being inadequately treated [12].

Psychological drug dependence is operationalized by the Leeds Dependence Questionnaire (LDQ) which captures the graded severity of dependence by focusing on psychological symptoms mapping onto ICD-10 and DSM-IV criteria, such as preoccupation, compulsion and planning [13]. The LDQ has been used successfully to measure painkiller dependence among people with headache, migraine and rheumatic disease [14, 15].

A number of psychological factors would be expected to influence painkiller dependence, either directly or by moderating the effects of pain. These include constructs derived from the fear-avoidance model of chronic pain [16], such as pain catastrophising, pain anxiety and pain self-efficacy, which have been shown to affect

adjustment, disability and medication use among people with pain [17–19], and factors associated with emotional regulation and metacognition, such as alexithymia, pain acceptance, mindfulness, and self-compassion.

Alexithymia involves impaired ability to think about and verbalize emotions, especially negative emotions, leading to poor emotional self-regulation and chronic sympathetic hyperarousal, physiological sensations, somatosensory amplification, and complaints of physical symptoms. Alexithymia is a possible risk factor for a variety of psychiatric and physical disorders, including chronic pain [20, 21] and substance use disorders [22, 23].

Pain acceptance is "willingness to experience continued pain without needing to reduce, avoid or otherwise change it" [24, p. 93]. Acceptance-oriented interventions may be more effective than coping-oriented interventions in terms of improving functioning and adjustment in chronic pain [25, 26], and greater pain acceptance was associated with less use of pain medication [27].

Mindfulness involves awareness of and attention to experience and reality in the present or current moment. It is flexible, self-regulated, and does not involve conceptual processing [28]. Mindfulness-based interventions for chronic pain have been effective [29], and one study showed that more mindful behaviour patterns predicted better physical, social and emotional functioning, and less medication use, among people seeking treatment for chronic pain [30].

Self-compassion involves "being kind and understanding toward oneself in instances of pain or failure rather than being harshly self-critical" [31, p. 223]. Self-compassion was associated with improved psychological wellbeing [32], including among people with chronic pain [33].

In the present study, we used a cross-sectional survey to examine those psychological factors, as well as severity of pain and frequency of painkiller use, as influences on painkiller dependence among people with pain.

Methods

Participants

The participants were 112 members of the general population who completed an online survey and were aged over 18 years, had pain in the last month, and used over the counter or prescription painkillers in the last month. Participants were recruited by dissemination of an email invitation to employees of a University and a large hospital, with instructions to pass the invitation on to other individuals or groups who might be interested in taking part. The survey was not associated with any specific website, and participants were not compensated or rewarded in any way.

The aim was to obtain a non-clinical sample with frequently occurring types of pain, which would be broadly representative of people with pain in the general population.

Measures

Pain

Pain frequency was rated on a 5-point scale labelled 'once or twice', 'about once a week', 'more than once a week', 'almost every day', and 'every day'. Pain intensity in the last month was measured as the average of four ratings of pain in the last month: at its worst, on average, at its least, and right now, each with 0-10 response scales labelled 'no pain' to 'worst pain possible', in the same way as in the Brief Pain Inventory [34]. Participants also indicated the types and causes of their pain, and whether their pain was caused by a diagnosed medical condition.

Risk of substance abuse

The 14-item Screener and Opioid Assessment for Patients with Pain (SOAPP) measures 'risk of opioid abuse for patients on opioid medication' [35, p. 287). There are 14 items about 'aberrant' drug-related behaviour, including seven items about substance abuse history, three about medication-related behaviors, and one each about psychiatric history, neurobiologic need for medicine, doctor-patient relationship, and antisocial behaviour [10]. Each item is rated on a 5-point scale ranging from 'never' (0) to 'very often' (4). A review of measures noted that "the SOAPP probably has the best psychometrics of any of the measures designed to predict aberrant drug-taking behaviour prior to the initiation of opioid therapy" [36, p. S154].

Depression, anxiety and stress

The Depression Anxiety and Stress Scale – 21 (DASS-21) consists of 21 items all referring to experiences in the past week, with 4-point response scales ranging from 0 ('did not apply to me at all') to 3 ('applied to me very much, or most of the time'). There are three subscales of seven items each. Subscale scores are obtained by summing across the seven items, then doubling to allow comparison with the 42-item version. The DASS-21 has good internal consistency, excellent convergent validity, and good discriminative validity [37].

Alexithymia

The Toronto Alexithymia Scale (TAS) assesses difficulties identifying and describing feelings. Respondents rate 20 statements using 5-point response scales

ranging from 1 ('strongly disagree') to 5 ('strongly agree'). A total score is computed by summing across all 20 items. The TAS-20 has good internal consistency and test-retest reliability [38], and has been used successfully with the general population [38] as well as clinical samples of people with musculoskeletal problems [39] and substance use or eating disorders [40].

Pain catastrophizing

The Pain Catastrophizing Scale (PCS) assesses frequency of catastrophic thoughts about pain, with particular emphasis on rumination, helplessness and magnification. Each of 13 items is rated on a 5-point scale ranging from 0 ('not at all') to 4 ('all the time'). A total score is computed as the total across items [41]. There was good evidence of reliability and validity in an adult community sample [42].

Pain anxiety

The Pain Anxiety Symptoms Scale-20 (PASS-20) measures fear, avoidance, and other anxiety responses in relation to chronic pain, with 20 items rated on a 6-point scale from 0 ('never') to 5 ('always'). A total score is computed as the sum across items [43]. The PASS-20 has been shown to have good reliability and validity [44].

Pain self-efficacy

The Pain Self-efficacy Questionnaire (PSEQ) measures confidence in ability to function despite pain. Each of 10 items is rated on a 7-point scale from 0 ('not at all confident') to 6 ('completely confident'). A total score is obtained by summing across items. Principal components analysis showed a single factor with good internal reliability and test-retest reliability, and validity was indicated by associations with a range of other measures, including medication use [19].

Pain acceptance

The Chronic Pain Acceptance Questionnaire (CPAQ) measures ability and willingness to continue with everyday activities despite pain and to desist from attempts to avoid or reduce chronic pain, with 20 items scored on a 6-point scale from 'never true' (0) to 'almost always true' (5). Two subscale scores are obtained by summing across items, and a total score is obtained by adding one subscale score to the other. Internal reliability was good among people with chronic pain conditions, and relationships with other measures of functioning supported scale validity [45].

Mindfulness

The Mindful Attention Awareness Scale (MAAS) measures the general tendency to be attentive to and aware of present-moment experiences in daily life. Item content reflects the opposite of the construct of mindfulness, or 'mindlessness', and items are rated on a 6-point scale ranging from 1 ('almost always') to 6 ('almost never'). A total score is computed as the mean of all 15 items, with higher scores indicating greater mindfulness. A single factor was indicated with good internal reliability in student and general adult samples [46].

Self-compassion

The Self-Compassion Scale – Short Form (SCS-SF) measures accepting, understanding and kind attitudes to oneself at difficult times. There are 12 items with 5-point response scales ranging from 1 ('almost never') to 5 ('almost always'). Certain items are reverse-coded and a total score is computed as the mean across items. The original 26-item Self-Compassion Scale has been shown to be reliable and valid [31], and the short form produces scores with a near-perfect correlation with those produced by the 26-item version [47].

Painkiller use and misuse

Frequency of over the counter and prescription painkiller use in the last month were rated on 5-point scales labelled 'once or twice', 'about once a week', 'more than once a week', 'almost every day', and 'every day'. Participants also indicated how often they took more than the recommended dose and used painkillers for longer than recommended, using four-point scales labelled 'never', 'sometimes', 'usually' and 'always'. Painkiller misuse was recorded as present for participants who reported usually or always taking more than the maximum recommended dose of either OTC or prescription painkillers, or usually or always taking OTC or prescription painkillers for longer than recommended, consistent with the definition of misuse as using medication "for a legitimate medical reason but in higher doses or for a longer period than recommended" [48, p. 170].

Painkiller dependence

The Leeds Dependence Questionnaire (LDQ) measures the graded severity of psychological dependence, with 10 items based on ICD-10 and DSM-IV criteria for substance dependence: preoccupation, salience, compulsion to start, planning, maximizing effect, narrowing of repertoire, compulsion to continue, primacy of effect, constancy of state, and cognitive set. The items have 4-point response scales

labelled 'never' (0), 'sometimes' (1), 'often' (2) and 'always' (3), and a single score is computed as the total across the 10 items [13].

The scale has been used in research on analgesic dependence among people with headaches [14, 49], migraine and rheumatic disease [15], as well as on substance dependence among students and juvenile delinquents [50] and people being treated for alcohol and opiate dependence [13, 51]. In its original form, the scale asks respondents to nominate their drug of concern, and the items refer to 'drink or drugs'. In an adaptation very similar to that made in a study of painkiller use among people with headaches [14], we replaced the words 'drink and drugs' in each item with 'painkillers' (eg., 'do you find yourself thinking about when you will next be able to take painkillers?').

Factor analysis showed that the scale comprised a single factor and had good internal consistency and test-retest reliability, and there was evidence for content, concurrent, discriminant and convergent validity [13]. No cut-off score has been identified, for the LDQ was designed "to be sensitive through the range from mild to severe dependence" [13, p. 563], and "users of the scale are encouraged to see dependence as a continuum" [13, p. 570].

Data analysis

We used t-tests to examine group differences, and Pearson correlations to examine associations among measures. To identify independent predictors of painkiller dependence and assess the moderation of pain by psychological factors, we conducted a hierarchical multiple linear regression analysis with predictor variables added using the stepwise method in four blocks: 1) demographic and clinical factors (age, gender, employed vs. not employed, married/cohabiting vs. single/other, diagnosis vs. no diagnosis); 2) pain frequency and intensity, over the counter and prescription painkiller use; 3) psychological factors; and 4) terms for interactions between pain frequency/intensity and psychological factors, computed as products of standardized scores. Significant interactions were explored using the slopes calculator provided by Jeremy Dawson (http://www.jeremydawson.co.uk/slopes.htm).

In cases where the regression coefficient for one predictor variable was substantially reduced when other predictors were added, we assessed potential mediation with Sobel tests [52], using the SPSS macro provided by Preacher and Hayes [53]. This tests the extent to which one variable mediates, or accounts for, the relationship between a predictor and the outcome or criterion variable.

The t-tests and correlations were conducted using unstandardized scores. For the regression and mediation analyses, standardized scores with means of zero and standard deviations of 1.0 were used for all the predictor variables because some of the measures were non-normally distributed, and because interaction terms had to be computed as the products of standardized scores.

Results

There were 208 respondents to the survey, of whom 135 met the inclusion criteria, and 112 had complete study data and comprised the study sample. Demographic information was provided by almost all those who began but did not complete the survey, so we compared the study sample with the remainder in terms of demographics. The study sample had a higher proportion of females [82% (92/112), compared with 69.5% (66/95); χ^2 (1) = 3.89, p = 0.049], and a higher proportion of people with a medical diagnosis [54.5% (61/112) compared with 20% (19/96); χ^2 (1) = 24.81, $p < 0.001$], but there were no differences in mean age or proportions married or cohabiting.

Among the study sample, ages ranged from 19 to 76 years, with a mean of 44.5 years (SD 13.5). There were 92 females (82%) and 20 males (18%). There were 75 (67%) who were married or cohabiting and 37 (33%) who were single, separated or divorced. There were 88 (78.6%) who reported being employed, eleven (9.8%) studying, seven (6.3%) retired, and one each who described themselves as 'disabled', 'retired through ill health', 'freelance/temping', 'volunteer', 'student placement', and 'housewife'. There were 61 (54.5%) who reported a diagnosed medical condition causing pain, most commonly arthritis, migraine or fibromyalgia, but also including a wide range of other conditions in which pain was a primary or secondary feature.

The most common type of pain in the last month was headache, which was reported by 64% (72/112). Back pain was reported by 46% (51/112), joint pain by 44% (49/112), menstrual pain by 33% of females (30/92), migraines by 15% (17/112), and pain from sports or other injuries by 9% (10/112). There were also 17% (19/112) who reported a range of other types of pain (some people reported more than one type of pain, so percentages add to more than 100%).

Pain frequency in the last month varied quite evenly, with 22% (25/112) reporting pain just once or twice, 17% (19/112) once a week, 20.5% (23/112) more than once a week, 18% (20/112) almost every day, and 22% (25/112) every day.

Duration of pain was less variable, and 81% (91/112) reported pain that had lasted over a year.

More people reported using over the counter painkillers than prescription painkillers in the last month. For over the counter painkillers, there were 9% (10/112) who reported not using in the last month, 29% (32/112) using once or twice, 18% (20/112) about once a week, 28% (31/112) more than once a week, 9% (10/112) almost every day, and 8% (9/112) every day. For prescription painkillers, there were 58% (65/112) who reported not using in the last month, 15% (17/112) using once or twice, 4.5% (5/112) about once a week, 5% (6/112) more than once a week, 2% (2/112) almost every day, and 15% (17/112) every day. Of those who had used prescription painkillers, 79% (37/47) had also used over the counter painkillers.

The most frequently used over the counter painkillers were ibuprofen, which was used by 44% (49/112), followed by paracetamol (acetaminophen), which was used by 38% (43/112). Products combining paracetamol and codeine were used by 12.5% (14/112). Aspirin was used by 4.5% (5/112), and products combining aspirin and paracetamol by 3.5% (4/112). Products combining paracetamol and dihidrocodeine were used by 2% (2/112).

The most frequently used prescription painkillers were non-steroidal anti-inflammatory drugs, which were used by 16% (18/112). Products with opioids were used by 12% (13/112). Products with codeine were used by 9% (10/112) and those with dihydrocodeine by 3% (3/112). Products with 5HTI receptor agonists were used by 4.5% (5/112). Anti-epileptic drugs were used by 3% (3/112). One person each reported using prescribed antidepressants, antifibrinolytics, anxiolytics, non-opioid analgesics (benzoxazocine), and paracetamol.

The rate of painkiller misuse (exceeding recommended doses or using for longer than recommended) was 22% (25/112) for over the counter painkillers and 4% (4/112) for prescription painkillers. There were two individuals who reported misusing both over the counter and prescription painkillers, so the overall rate of painkiller misuse was 24% (27/112).

Tables 1 and 2 about here

Descriptive data for the psychological measures are given in table 1. In a small number of cases where data points were missing but more than half the values per scale were present, scale scores were computed based on the items for which values were present. Scores for pain intensity, alexithymia, pain self-efficacy, pain acceptance, mindfulness, and self-compassion were all normally distributed, but

those for SOAPP, depression, anxiety, stress, pain anxiety, pain catastrophizing, and painkiller dependence were all negatively skewed, with more scores at the lower end of the range.

Males had greater alexithymia (t = 3.50, p = 0.001) and painkiller dependence (t = 2.30, p = 0.023), but did not differ from females on other measures. Participants with painkiller misuse had more frequent pain (t = 2.42, p = 0.017) and used over the counter painkillers more frequently (t = 2.37, p = 0.020), but did not differ on any other measures.

Pearson correlations among measures are given in table 2. Pain frequency and intensity were positively correlated, and both were correlated with depression, catastrophizing, pain anxiety, pain acceptance (negatively) and prescription painkiller use. Over the counter and prescription painkiller use were not correlated (r = -0.09). Painkiller dependence was positively correlated with pain frequency and intensity, SOAPP score, depression, anxiety, stress, alexithymia, pain catastrophizing, pain anxiety and prescription painkiller use, and negatively correlated with pain self-efficacy and pain acceptance.

The results of the regression analysis are given in table 3. SOAPP score was the strongest single predictor in the final model, followed by pain acceptance. Higher SOAPP score and lower pain acceptance predicted greater painkiller dependence. Prescription painkiller use was also a significant predictor, but the regression coefficient was more than halved in the final model compared with on entry. Gender and pain intensity were significant predictors on entry, but not in the final model.

Table 3 about here

There were three significant interactions: pain frequency was moderated by alexithymia and anxiety, and pain intensity was moderated by pain acceptance. More frequent pain increased painkiller dependence when alexithymia was high but decreased it when alexithymia was low (Fig 1). More frequent pain increased painkiller dependence when anxiety was low, but decreased it when anxiety was high (Fig 2). More intense pain increased painkiller dependence when pain acceptance was low, but decreased it when pain acceptance was low (Fig 3).

Figs. 1-3 about here

Because the regression coefficients for gender, pain intensity and prescription painkiller use were reduced when other predictors were added, we assessed the

mediation of those factors by other significant independent predictors. Gender differences were not mediated by other factors. The influence of pain intensity was mediated by prescription painkiller use (Sobel = 0.7894, 95% CIs 0.3252 to 1.2536, p = .0009). The influence of prescription painkiller use was mediated by the pain acceptance x pain intensity interaction (Sobel = 0.2796, 95% CIs 0.0017 to 0.5575, p = .0486).

Discussion

Prescription painkiller use, SOAPP score and pain acceptance all independently predicted painkiller dependence. Prescription painkiller use mediated the influence of pain intensity. Alexithymia, anxiety and pain acceptance all moderated the influence of pain.

The mediation of pain intensity by prescription painkiller use suggests a process in which more intense pain leads to more frequent use of stronger (prescription) painkillers, which increases the risk of dependence. That is consistent with evidence from interviews with people with prescription opioid dependence, which also suggested a process in which regular use led to dependence [54].

SOAPP scores are generally interpreted as measuring risk potential for substance abuse among people with pain [10, 35]. Of the 14 items in the version we used, seven items deal with past problems with alcohol and drugs generally [10], and in our data, SOAPP scores were uncorrelated with pain frequency and intensity, so this measure probably reflects factors that increase the risk of substance-related problems irrespective of pain.

Greater pain acceptance reduced painkiller dependence, and less acceptance increased dependence, but only when pain was more intense. To put the interaction another way, more intense pain increased dependence when acceptance was low, and reduced dependence when acceptance was high (Fig. 3). The pain intensity x pain acceptance interaction also partly mediated, or accounted for, the influence of prescription painkiller use on painkiller dependence. These findings suggest that acceptance-based interventions could potentially help people reduce their reliance on prescribed painkillers and avoid becoming dependent on painkillers. Interventions for painkiller dependence could potentially be based on existing acceptance-based interventions for people with both chronic pain and substance dependence [55], which could potentially be adapted for other target groups of painkiller users, such as those who are not yet dependent but have been identified as at risk of future dependence.

The moderation of pain frequency by alexithymia is unsurprising considering that pain is an unpleasant emotional experience and that alexithymia involves difficulties processing negative emotions. This finding is also consistent with research suggesting the effects of alexithymia on substance use disorders are not straightforward [56, 57], so more research is needed on how alexithymia influences how people respond to pain.

The moderation of pain frequency by anxiety perhaps seems counterintuitive, but the DASS-21 measures generalized rather than pain-related anxiety, and anxiety is one of a cluster of psychiatric symptom types that are frequently associated with substance-related problems in the absence of pain. It is possible that anxiety increases the risk of dependence for people with less frequent pain in the same way as for people without pain, whereas for people with more frequent pain, anxiety could translate into concerns about medication and fears about becoming addicted to painkillers, making dependence less likely. The interaction between pain frequency and anxiety is also consistent with a typology of opioid-using chronic pain patients in which an 'addictive behaviors' group had increased mental health problems and increased opioid problems, but not increased pain [58].

Fig 4 about here

The findings from the final regression model are useful for understanding mechanisms in the development of dependence and for informing interventions. They suggest that individuals most at risk of developing painkiller dependence are those who use prescription painkillers more frequently, who have a prior history of substance-related problems, and who are less accepting of pain, but that other psychological factors can moderate the effects of pain. Fig. 4 presents a preliminary model of influences on painkiller dependence, with three pathways. In pathway A, the effect of pain is mediated by painkiller use, so more severe pain leads to more frequent use of stronger painkillers, which increases dependence. In pathway B, risk factors for substance-related problems more generally, such as a personal or family history of such problems, increase the risk of painkiller dependence irrespective of pain. In pathway C, psychological factors such as acceptance, alexithymia or anxiety moderate the effects of pain. The factors in pathways B and C could increase the risk of painkiller dependence directly, or have influences that are mediated by greater painkiller use, or both.

The unadjusted associations with painkiller dependence are also potentially informative from a clinical point of view, for one cannot 'adjust' for an individual

patient's gender, pain intensity or relevant psychological characteristics. From this perspective, depression, stress, pain catastrophizing, pain anxiety and pain self-efficacy were all correlated with painkiller dependence, although they were not independently predictive, whereas mindfulness and self-compassion were not correlated with painkiller dependence.

Painkiller misuse was also not associated with dependence, and was associated only with pain frequency and over the counter painkiller use. The survey did not ask about misuse of specific medications, so it was not possible to estimate the influence of misuse of specific pain medications on painkiller dependence. The measure of misuse combined over the counter and prescription painkillers because there was some overlap in the medications obtained over the counter and by prescription, and many participants reported using more than one type of painkiller. However, because there are potentially separate concerns associated with misuse of different classes of pain medication, we ran the regression analysis two more times, with the overall misuse measure replaced as a predictor first by a measure of over the counter painkiller misuse, then by a measure of prescription painkiller misuse. In each case the results were identical; just as for the overall misuse measure, neither of the alternative measures were retained in the regression model.

The sample size was modest so the findings should be regarded as preliminary, and it is possible that future analyses with larger samples would produce different final models, possibly including factors with smaller effects than the present study had power to detect. Future research could also improve on the representativeness of the present sample, which was composed predominantly of married or cohabiting working women. Participants reported a wide range of causes of pain, with no single condition or cause predominating, and only 40% (45/112) reported pain almost or every day, so the sample included people with episodic as well as chronic pain. The sample also included relatively few opioid painkiller users.

We should therefore be cautious about the extent to which the study findings represent other groups of painkiller users, or could be used prospectively to predict more severe future painkiller dependence. Mean LDQ scores were similar to those of patients with episodic headaches but lower than those with diagnosed substance dependence [14], so the sample represents people with only mild to moderate levels of dependence. Different factors might well influence the development of more severe painkiller dependence, although predicting mild to moderate dependence could also be important for interventions designed to prevent dependence reaching diagnosable levels.

The LDQ measures the graded severity of behavioral and psychological aspects of dependence, which is arguably a more important and useful outcome for behavioral research than painkiller misuse, abuse, addiction, or substance use disorder, because the behavioural and psychological processes involved in the development of *psychological* dependence may be more amenable to change and could be targeted by preventative and treatment interventions.

To conclude, the study showed that painkiller dependence is influenced both by risk of substance-related problems irrespective of pain, and by psychological factors closely associated with the experience of pain. We hope that this preliminary study will lead to further research that could include larger scale national surveys and studies of specific groups of painkiller users, like those who may be at high risk of dependence, or people using or misusing specific categories of painkillers, like prescribed opioids. Research on painkiller dependence might also employ methods with less reliance on self-report measures, so as to avoid the possibility of responder biases, considering that the socially desirable responses to questions about painkiller use, misuse and dependence are generally fairly apparent. Further research could also focus on the development and evaluation of acceptance-based approaches to preventing and treating painkiller addiction. Considering that problematic painkiller use is a global problem, international, cross-cultural studies could also help to understand ways that social and contextual as well as individual factors influence painkiller use.

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References

1. Department of Health (2000). *Pharmacy in the Future — Implementing the New NHS Plan: A programme for pharmacy in the National Health Service.* London: The Stationery Office. Available from http://www.publications.doh.gov.uk/pdfs/pharmacyfuture.pdf
2. Goh, L.Y., Vitry, A.I., Semple, S.J., Esterman, A., & Lusczc, M.A. (2009). Self-medication with over-the-counter drugs and complementary medications in South Australia's elderly population. *BMC Complementary and Alternative Medicine,* 9,

42. Available from: http://www.biomedcentral.com/1472-6882/9/42. DOI:10.1186/1472-6882-9-42

3. Porteous, T., Bond, C., Hannaford, P. & Sinclair H. (2005). How and why are non-prescription analgesics used in Scotland? *Family Practice,* 22, 78–85. DOI: 10.1093/fampra/cmh719
4. Proprietary Association of Great Britain (2005). *Self care: realising the vision (PAGB annual review 2005)*. London: Proprietary Association of Great Britain.
5. Hersh, E.V., Moore, P.A., & Loss, G.L. (2000). Over-the-counter analgesics and antipyretics: a critical assessment. *Clinical Therapeutics*, 22, 500–548. DOI: 10.1016/S0149-2918(00)80043-0
6. Compton, W.M. & Volkow, N.D. (2006). Abuse of prescription drugs and the risk of addiction. *Drug and Alcohol Dependence*, 83 Suppl 1, S4–S7. DOI: 10.1016/j.drugalcdep.2005.10.020
7. Lessenger, J.E. & Feinberg, S.D. (2008). Abuse of prescription and over-the-counter medications. *Journal of the American Board of Family Medicine*, 21, 45–54. DOI: 10.3122/jabfm.2008.01.070071
8. National Treatment Agency for Substance Misuse (2011). *Addiction to Medicine: An investigation into the configuration and commissioning of treatment services to support those who develop problems with prescription-only or over-the-counter medicine.* Available online: http://www.nta.nhs.uk/uploads/addictiontomedicinesmay2011a.pdf
9. Turk, D. C., Swanson, K.S. & Gatchel, R.J. (2008). Predicting opioid misuse by chronic pain patients - A systematic review and literature synthesis. *Clinical Journal of Pain*, 24, 497–508. DOI: 10.1097/AJP.0b013e31816b1070
10. Butler, S.F., Budman, S.H., Fernandez, K. & Jamison, R.N. (2004). Validation of a screener and opioid assessment measure for patients with chronic pain, *Pain*, 112, 65–75. DOI:10.1016/j.pain.2004.07.026
11. Butler, S.F., Fernandez, K., Benoit, C., Budman, S.H., & Jamison, R.N. (2008). Validation of the revised screener and opioid assessment for patients with pain (SOAPP-R). *The Journal of Pain*, 9, 360-372. doi:10.1016/j.jpain.2007.11.014
12. National Collaborating Centre for Cancer (2012). *Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults*. National Institute for Health and Clinical Excellence (NICE). Available from http://guidance.nice.org.uk/CG140/Guidance/pdf/English
13. Raistrick, D. S., Bradshaw, J., Tober, G., Weiner, J., Allison, J., & Healey, C. (1994). Development of the Leeds Dependence Questionnaire. *Addiction*, 89, 563−572. DOI: 10.1111/j.1360-0443.1994.tb03332.x

14. Ferrari, A., Cicero, A.F.G., Bertolini, A., Leone, S., Pasciullo, G. & Sternieri, E. (2006). Need for analgesics/drugs of abuse: a comparison between headache patients and addicts by the Leeds Dependence Questionnaire (LDQ). *Cephalagia*, 26, 187–193. DOI: 10.1111/j.1468-2982.2005.01020.x
15. Ferrari, A., Leone, S., Tacchi, R., Ferri, C., Gallesi, D., Giuggioli, D. & Bertolini, A. (2009). The link between pain patient and analgesic medication is greater in migraine than in rheumatic disease patients. *Cephalalgia*, 29, 31–37. DOI: 10.1111/j.1468-2982.2008.01697.x
16. Leeuw, M., Goossens, M., Linton, S.J., Crombez, G., Boersma, K. & Vlaeyen, J.W.S. (2007). The fear-avoidance model of musculoskeletal pain: current state of scientific evidence. *Journal of Behavioral Medicine*, 30, 77–94. DOI: 10.1007/s10865-006-9085-0
17. McCracken, L.M., Faber, S.D. & Janeck, A.S. (1998). Pain-related anxiety predicts non-specific physical complaints in persons with chronic pain. *Behaviour Research and Therapy*, 36, 621–630. DOI: 10.1016/S0005-7967(97)10039-0
18. McCracken, L.M., Spertus, I.L., Janeck, A;C., Sinclair, D. & Wetzel, F.T. (1999). Behavioral dimensions of adjustment in persons with chronic pain: pain-related anxiety and acceptance. *Pain*, 80, 283–289. DOI: 10.1016/S0304-3959(98)00219-X
19. Nicholas, M.K. (2007). The pain self-efficacy questionnaire: taking pain into account. *European Journal of Pain*, 11, 153–163. DOI: 10.1016/j.ejpain.2005.12.008
20. Cox, B.J., Kuch, K., Parker, J.D., Shulman, I.D. & Evans, R.J. (1994). Alexithymia in somatoform disorder patients with chronic pain. *Journal of Psychosomatic Research*, 38, 523–527. DOI: 10.1016/0022-3999(94)90049-3
21. Lumley, M.A., Stettner, L. & Wehmer, F. (1996). How are alexithymia and physical illness linked? A review and critique of pathways. *Journal of Psychosomatic Research*, 41, 505–518. DOI: 10.1016/S0022-3999(96)00222-X
22. El Rasheed, A.H. (2009). Alexithymia in Egyptian substance abusers. *Substance Abuse*, 22, 11–21. DOI: 10.1080/08897070109511442
23. Speranza, M., Corcos, M., Stephan, P., Loas, G., Perez-Diaz, F., Lang, F., Venisse, J.L., Bizouard, P., Flament, M., Halfon, O., and Jeammet, P. (2004). Alexithymia, depressive experiences, and dependency in addictive disorders. *Substance Use & Misuse*, 39, 551–579. DOI: 10.1081/JA-120030058
24. McCracken, L.M. (1999). Behavioural constituents of chronic pain acceptance: Results from factor analysis of the Chronic Pain Acceptance Questionnaire. *Journal of Back and Musculoskeletal Rehabilitation*, 13, 93–100.

25. McCracken, L.M. & Eccleston, C. (2003). Coping or acceptance: what to do about chronic pain? *Pain*, 105, 197–204. DOI: 10.1016/S0304-3959(03)00202-1
26. Vowles, K.E. & McCracken, L.M. (2008). Acceptance and values-based action in chronic pain: A study of treatment effectiveness and process. *Journal of Consulting and Clinical Psychology*, 76, 397–407. DOI: 10.1037/0022-006X.76.3.397
27. McCracken, L.M. & Eccleston, C. (2005). A prospective study of acceptance of pain and patient functioning with chronic pain. *Pain*, 118, 164–169. DOI: 10.1016/j.pain.2005.08.015
28. Bishop, S.R., Lau, M., Shapiro, S., Carlson, L., Anderson, N.D., Carmody, J., Segal, Z.V., Abbey, S., Speca, M., Velting, D. & Devins G. (2004). Mindfulness: a proposed operational definition. *Clinical Psychology*, 11, 230–241. DOI: 10.1093/clipsy/bph077
29. Kabat-Zinn, J., Lipworth, L. & Burney, R. (1985). The clinical use of mindfulness meditation for the self-regulation of chronic pain. *Journal of Behavioral Medicine*, 8, 163–190. DOI: 10.1007/BF00845519
30. McCracken, L.M., Gauntlett-Gilbert, J. & Vowles, K.E. (2007). The role of mindfulness in a contextual cognitive-behavioral analysis of chronic pain-related suffering and disability. *Pain*, 131, 63–69. DOI: 10.1016/j.pain.2006.12.013
31. Neff, K. (2003). The development and validation of a scale to measure self compassion: the Self Compassion Scale. *Self and Identity, 2*, 223–250. DOI: 10.1080/15298860390209035
32. Neff, K, Kirkpatrick, K. & Rude, S. (2007). Self- compassion and adaptative psychological functioning. *Journal of Research in Personality, 41*, 139–154. DOI: 10.1016/j.jrp.2006.03.004
33. Wren, A.A., Somers, T.J., Wright, M.A., Goetz, M.C., Leary, M.R., Fras, A.M., Huh, B.K., Rogers, L.L., and Keefe, F.J. (2012). Self-compassion in patients with persistent musculoskeletal pain: relationship of self-compassion to adjustment to persistent pain. *Journal of Pain and Symptom Management*, 43, 759–770. DOI: 10.1016/j.jpainsymman.2011.04.014
34. Tan, G., Jensen, M.P., Thornby, J.I., and Shanti, B.F. (2004). Validation of the Brief Pain Inventory for chronic nonmalignant Pain. *The Journal of Pain*, 5, 133–137. DOI:10.1016/j.jpain.2003.12.005
35. Akbik, H., Butler, S.F., Budman, S.H., Fernandez, K., Katz, N.P., and Jamison, R.N. (2006). Validation and clinical application of the Screener and Opioid Assessment for patient with pain. Journal of Pain and Symptom Management, 32, 287–293. DOI: 10.1016/j.jpainsymman.2006.03.010

36. Passik, S.D., Kirsh, K.L., & Caspar, D. (2008). Addiction-related assessment tools and pain management: instruments for screening, treatment planning, and monitoring compliance. *Pain Medicine*, 9, S145–S166. DOI:10.1111/j.1526-4637.2008.00486.x

37. Gloster, A.T., Rhoades, H.M, Novy, D. Klotsche, J., Senior, A., Kunik, M., Wilson, N., Stanley, M.A. (2008). Psychometric Properties of the Depression Anxiety and Stress Scale-21 in Older Primary Care Patients. *Journal of Affective Disorders*, 110, 248–259. DOI:10.1016/j.jad.2008.01.023

38. Bagby, R.M., Parker, J.D.A. & Taylor, G.J. (1994). The twenty-item Toronto Alexithymia Scale: I. Item selection and cross-validation of the factor structure. *Journal of Psychosomatic Research*, 38, 23–32. DOI: 10.1016/0022-3999(94)90005-1

39. Swift, L., Stephenson, R., & Royce, J. (2006). The 20-item Toronto Alexithymia Scale: Validation of factor solutions using confirmatory factor analysis on physiotherapy out-patients. *Psychology and Psychotherapy: Theory, Research and Practice*, *79*, 83–88. DOI:10.1348/147608305X42875

40. Loas, G., Corcos, M., Stephan, P., Pellet, J., Bizouard, P., Venisse, J.L., Perez-Diaz, F., Guelfi, J.D., Flament, M., Jeammet., P., and the Reseau INSERM no. 494013 (2001). Factorial structure of the 20-item Toronto Alexithymia scale : confirmatory factor analyses in clinical and non-clinical samples. *Journal of Psychosomatic Research*, 50, 255–261.

41. Sullivan, M.J.L., Bishop, S.R., Pivik, J. (1995). The Pain Catastrophising Scale: Development and Validation. *Psychological Assessment*, 7, 524–532.

42. Osman, A., Barrios, F.X., Guttierez, P.M., Kopper, B.A., Merrifield, T., & Grittmann, L. (2000). The Pain Catastrophizing Scale: further psychometric evaluation with adult samples. *Journal of Behavioral Medicine,* 23, 351–365. DOI: 10.1023/A:1005548801037

43. McCracken, L.M. & Dhingra, L. (2002). A short version of the pain anxiety symptoms scale (PASS-20): Preliminary development and validity. *Pain Research and Management*, 7, 45–50.

44. Roelofs, J., McCracken, L., Peters, M.L., Crombez, G., van Breukelen, G., and Vlaeyen, J.W.S. (2003). Psychometric evaluation of the Pain Anxiety Symptoms Scale (PASS) in chronic pain patients. *Journal of Behavioral Medicine*, 27, 167-183. DOI: 10.1023/B:JOBM.0000019850.51400.a6

45. McCracken, L.M., Vowles, K.E. & Eccleston, C. (2004). Acceptance of chronic pain: component analysis and a revised assessment method. *Pain*, 107, 159–166. DOI: 10.1016/j.pain.2003.10.012

46. Brown, K.W. & Ryan, R.M. (2003) The benefits of being present: mindfulness and its role in psychological well-being. *Journal of Personality and Social Psychology*, 84, 822–848. DOI: 10.1037/0022-3514.84.4.822

47. Raes, F., Pommier, E., Neff, K.D., and Van Gucht, F (2011). Construction and factorial validation of a short form of the self-compassion scale. *Clinical Psychology and Psychotherapy,* 18, 250–255. DOI: 10.1002/cpp.702

48. Wazaify, M., Shields, E., Hughes, C.M. & McElnay, J.C. (2005). Societal perspectives on over-the-counter (OTC) medicines. *Family Practice*, 22, 170–176. doi:10.1093/fampra/cmh723

49. Corbelli, I., Caproni, S., Eusebi, P., & Sarchielli, P. (2012). Drug-dependence behaviour and outcome of medication-overuse headache after treatment. *The Journal of Headache and Pain*, 13, 653–60. DOI: 10.1007/s10194-012-0492-z

50. Lennings, C.J. (1999). An evaluation of the Leeds Dependence Questionnaire. *Journal of Child and Adolescent Substance Abuse*, 8 (3), 73–87. DOI: 10.1300/J029v08n03_05

51. Kelly, J.F., Magill, M., Slaymaker, V., and Kahler, C. (2010). Psychometric validation of the Leeds Dependence Questionnaire (LDQ) in a young adult clinical sample. *Addictive Behaviors*, 35, 331–336. DOI:10.1016/j.addbeh.2009.11.005

52. Sobel, M.E. (1982). Asymptotic confidence intervals for indirect effects in structural equation models. In S. Leinhart (Ed.), *Sociological methodology* (pp. 290-312). San Francisco, CA: Jossey-Bass.

53. Preacher, K.J., & Hayes, A. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behavior Research Methods, Instruments, and Computers*, *36*, 717–731. DOI: 10.3758/BF03206553

54. Back, S.E., Lawson, K.M., Singleton, L.M., and Brady, K.T. (2011). Characteristics and correlates of men and women with prescription opioid dependence. *Addictive Behaviors,* 36, 829–834. DOI: 10.1016/j.addbeh.2011.03.013

55. Ilgen, M.A., Haas, E., Czyz, E., Webster, L., Sorrell, J.T., and Chermack, S. (2011). Treating chronic pain in veterans presenting to an addictions treatment Program. *Cognitive and Behavioral Practice*, 18, 149–160. DOI: 10.1016/j.cbpra.2010.05.002

56. Bonnet, A., Bejaoui, M., Brejard, V., and Pedinielli, J. -L.). (2011). Physiological dependence and emotional functioning in young adults: Affectivity, alexithymia and emotional intensity in the consumption of psychoactive substances. *Annales Medico-Psychologiques*, 169, 92–97. DOI: 10.1016/j.amp.2010.04.022

57. Thorberg, F.A., Young, R.M., Sullivan, K.A., and Lyvers, M. (2009). Alexithymia and alcohol use disorders: A critical review. *Addictive Behaviors*, 34, 237–245. DOI: 10.1016/j.addbeh.2008.10.016

58. Banta-Green, C.J., Merrill, J.O., Doyle, S.R., Boudreau, D.M., and Calsyn, D.A. (2009). Opioid use behaviors, mental health and pain – development of a typology of chronic pain patients. *Drug and Alcohol Dependence*, 104, 34–42. DOI: 10.1016/j.drugalcdep.2009.03.021

Table 1. Descriptive statistics for study measures

	Mean (SD)	Range	Alpha[1]
Pain intensity	4.94 (1.63)	1.75-9.50	0.82
SOAPP score	4.31 (5.12)	0-41	0.81
Depression	10.48 (10.93)	0-42	0.92
Anxiety	6.95 (7.61)	0-34	0.80
Stress	14.76 (10.66)	0-40	0.90
Alexithymia	50.99 (10.80)	20-80	0.79
Pain catastrophizing	12.13 (11.12)	0-50	0.94
Pain anxiety	29.87 (17.03)	1-84	0.92
Pain self-efficacy	38.54 (14.50)	2-60	0.94
Pain acceptance	78.04 (19.78)	10-120	0.89
Mindfulness	4.22 (1.00)	1.2-6.00	0.92
Self-compassion	3.03 (0.80)	1.33-5.00	0.86
Painkiller dependence	4.32 (4.24)	0-23	0.82

Note to table 1:

1. Cronbach's alpha, a coefficient of internal consistency

Table 2. Correlations among study measures

1. Age	1.00										
2. Pain frequency	0.40**	1.00									
3. Pain intensity	0.11	0.47**	1.00								
4. SOAPP score	-0.05	-0.04	0.14	1.00							
5. Depression	0.09	0.29*	0.20*	0.27*	1.00						
6. Anxiety	-0.07	0.17	0.31*	0.40**	0.64**	1.00					
7. Stress	-0.12	0.15	0.27*	0.34**	0.69**	0.66*	1.00				
8. Alexithymia	-0.06	0.10	0.13	0.29*	0.58**	0.46**	0.56**	1.00			
9. Pain catastrophizing	0.08	0.34**	0.52**	0.19*	0.46**	0.45**	0.48**	0.25*	1.00		
10. Pain anxiety	0.05	0.20*	0.39**	0.25*	0.50**	0.57**	0.45**	0.36**	0.80**	1.00	
11. Pain self-efficacy	-0.16	-0.18	-0.31*	-0.05	-0.29*	-0.38**	-0.27*	-0.09	-0.53**	-0.68**	1.00
12. Pain acceptance	-0.23*	-0.44**	-0.40**	-0.18	-0.39**	-0.45**	-0.32*	-0.25*	-0.63**	-0.70**	-0.67**
13. Mindfulness	0.09	-0.02	-0.14	-0.07	-0.54**	-0.49**	-0.62**	-0.40*	-0.24*	-0.26*	0.18
14. Self-compassion	0.24*	-0.19*	-0.14	-0.14	-0.57**	-0.45**	-0.57**	-0.39**	-0.27*	-0.26*	0.15
15. OTC painkiller use	0.17	0.38**	0.07	-0.11	-0.09	-0.10	-0.09	-0.21*	-0.17	-0.13	0.02
16. Prescription painkiller use	0.28*	0.52**	0.40**	0.10	0.23*	0.23*	0.17	0.18	0.44**	0.41**	-0.34**
17. Painkiller dependence	0.16	0.37*	0.35**	0.38**	0.31*	0.36**	0.35**	0.38**	0.45**	0.49**	-0.34**
	1	2	3	4	5	6	7	8	9	10	11

* $p <= .05$; ** $p <= .001$

Table 2 continued

12. Pain acceptance	1.00				
13. Mindfulness	0.16	1.00			
14. Self-compassion	0.17	0.56**	1.00		
15. OTC painkiller use	-0.01	0.11	-0.02	1.00	
16. Prescription painkiller use	-0.55**	0.02	0.05	-0.09	1.00
17. Painkiller dependence	-0.54**	-0.14	-0.11	-0.03	0.51**
	12	13	14	15	16

* $p <= .05$; ** $p <= .001$

Table 3. Proportions of variance accounted for (R^2), adjusted R^2, changes in R^2 (ΔR^2), and Beta weights from hierarchical multiple linear regression with painkiller dependence as the dependent variable.

Block and predictor variable[1]	R^2	Adj. R^2	ΔR^2	Entry Beta[2]	Final Beta[2]
1. Demographic/clinical factors	0.05	0.05	0.05*		
Gender				-0.21*	-0.12
2. Pain and painkiller use	0.31	0.29	0.26**		
Pain intensity				0.18*	0.05
Prescription painkiller use				0.49**	0.21*
3. Psychological factors	0.47	0.44	0.16**		
SOAPP score				0.33**	0.31**
Pain acceptance				-0.29**	-0.29*
4. Interaction effects	0.57	0.53	0.10**		
Pain frequency x alexithymia				0.220*	0.28**
Pain frequency x anxiety				-0.20*	-0.20*
Pain intensity x pain acceptance				-0.17*	-0.19*

Notes to table 3:

* $p <= .05$; ** $p <= .001$

1. Variables were added to the model using the stepwise method in each block. The criteria for entry and removal were $p < 0.05$ and $p > 0.10$ respectively. Only predictor variables that were entered are shown in the table.
2. Standardized regression coefficient

Fig. 1. The influence of pain frequency and alexithymia on painkiller dependence

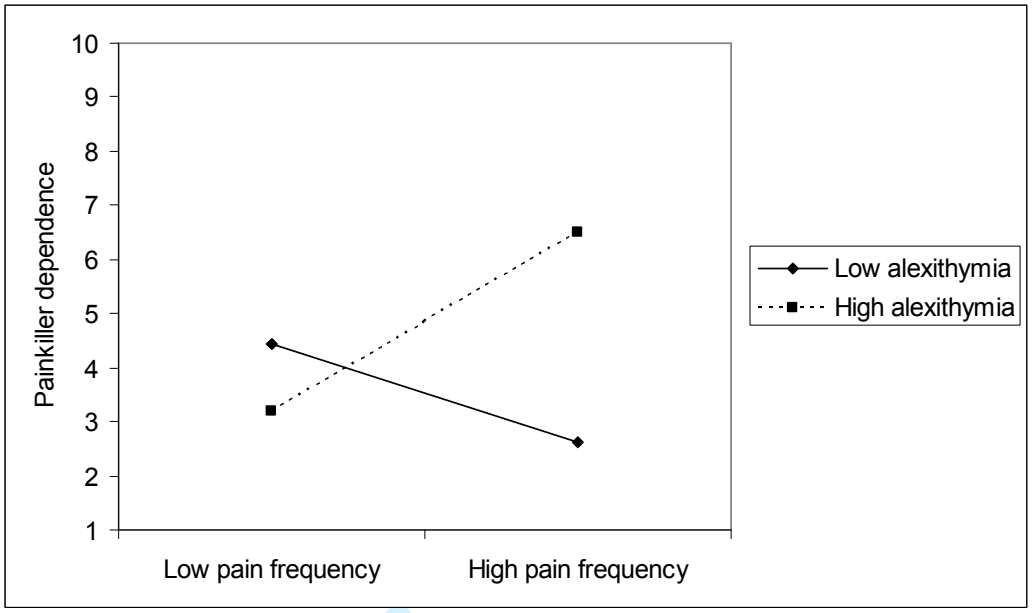

Fig. 2. Effects of pain frequency and anxiety on painkiller dependence

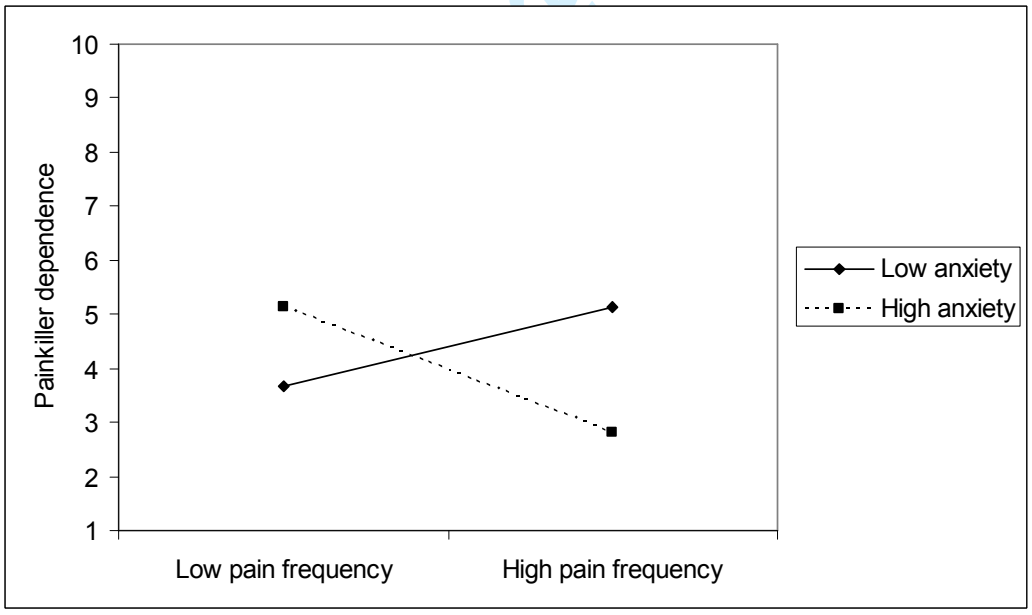

Fig. 3. Effects of pain intensity and pain acceptance on painkiller dependence

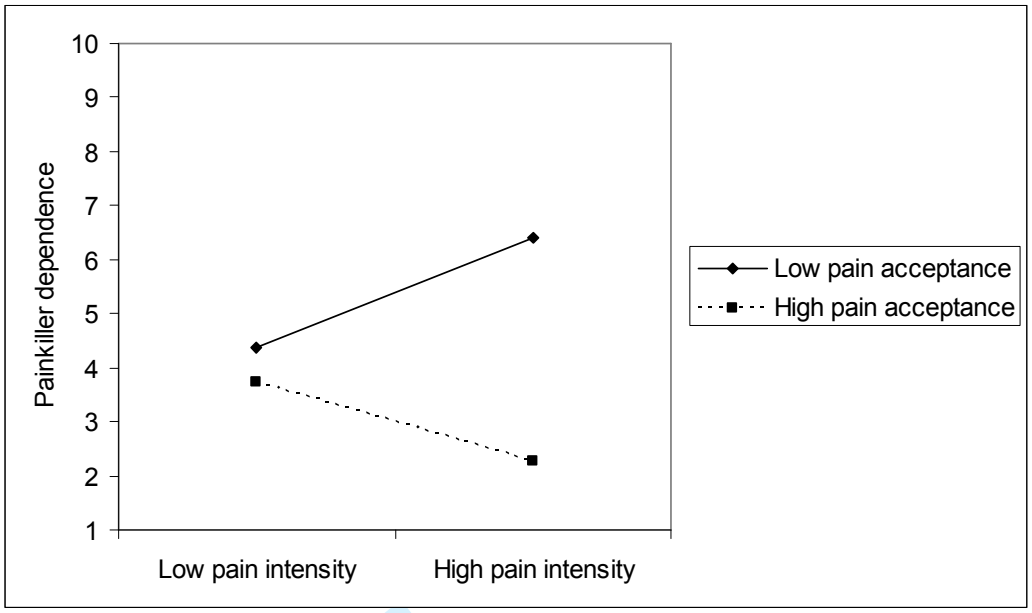

Fig. 4. A preliminary model of influences on painkiller dependence