An assessment of the relative influence of pain coping, negative thoughts about pain and pain acceptance on health-related quality of life among people with hemophilia

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Abstract

Many people with hemophilia are affected by chronic arthritic joint pain as well as acute bleeding pain. In this cross-sectional study, 209 men with hemophilia A or B completed the Hemophilia Pain Coping Questionnaire (HPCQ), the Chronic Pain Acceptance Questionnaire (CPAQ), and the RAND 36-item Health Survey (SF-36), a measure of health-related quality of life. Multiple regression was used to test the influence of active pain coping, passive adherence coping, and negative thoughts about pain (HPCQ scales), and activity engagement and pain willingness (CPAQ scales), on physical and mental components of quality of life (SF-36 PCS and MCS scales), taking account of age, hemophilia severity, use of clotting factor, and pain intensity. Pain intensity was the main influence on physical quality of life and negative thoughts was the main influence on mental quality of life. Activity engagement and pain willingness had small but significant influences on physical and mental quality of life. Pain willingness also moderated and partly mediated the influence of pain intensity on physical quality of life, and activity engagement and pain willingness mediated the influence of negative thoughts on mental quality of life. Negative thoughts moderated and partly mediated the influence of pain intensity on mental quality of life. There was no evidence that active pain coping influenced quality of life. The findings suggest that quality of life in hemophilia could potentially be improved by interventions to increase pain acceptance and reduce negative thoughts about pain, especially among those with less severe pain.

Key Words: Hemophilia, Pain coping, Pain acceptance, Joint pain, Negative thoughts, Quality of life.

1. Introduction

Hemophilia ca n cause arthritic pain when joints are damaged by repeated joint bleeds, as well as causing acute pain during joint bleeds [6]. Clotting factor concentrates can minimise the impact of spontaneous bleeds, but many patients, especially those aged over 40, are affected by arthritic joint damage caused before factor concentrates were available.

In hemophilia, age and indicators of illness severity typically explain only small proportions of the variance in the physical component of health-related quality of life, as measured by the SF-36, and are not usually associated with the mental component [11, 28, 29, 38, 39, 42], so further variance could be explained by factors such as pain coping and acceptance, which have been extensively studied in chronic pain conditions but not those where pain is an important but secondary feature. In hemophilia, there is limited evidence about pain coping [7, 36] and none to our knowledge about acceptance.

Pain coping usually refers to purposeful efforts, including both active and passive strategies, to manage pain or reduce its impact, irrespective of whether those efforts are successful [16, 17, 44]. Pain coping inventories sometimes also include negative thoughts about pain, such as fear, anger and catastrophizing [12, 33], which probably reflect emotional distress associated with pain rather than efforts at coping [13, 43, 44].

Pain coping is sometimes characterised as efforts to overcome pain by controlling, reducing, or avoiding it [21], whereas pain acceptance involves 'willingness to experience continued pain without needing to reduce, avoid or otherwise change it' [20, p. 93] and 'disengagement from struggling with pain' [21, p. 198]. The rationale for acceptance is that when pain is chronic, attempts to control or avoid it can be counter-productive, and better adjustment can be achieved by directing efforts towards more achievable goals [19].

Among studies that compared the relative influence of those factors in chronic pain conditions, two showed that acceptance-related factors were more closely associated with improved functioning [22, 25], one found that changes in acceptance and catastrophizing both influenced treatment outcome [47], and another showed that acceptance influenced functional status whereas coping influenced emotional distress [9]. We therefore wished to assess the relative influence of coping, negative thoughts and acceptance as predictors of quality of life in hemophilia.

Coping, negative thoughts and acceptance could also mediate and/or moderate the effects of pain. A mediator 'accounts for the relationship' and a moderator 'affects the direction and/or strength of the relationship' between predictor and outcome [4, pp. 1174, 1176]. Negative thoughts mediated the effects of pain intensity on depression and interference with daily life in sickle cell disease [3], and low acceptance partly mediated the effects of catastrophizing on physical and psychological functioning in chronic pain [46]. Acceptance moderated the effect of pain severity in chronic pain, such that 'expected increases in negative affect during pain exacerbations were buffered by higher levels of pain acceptance' [18, p. 291]. We therefore wished to assess the mediation of pain intensity by negative thoughts, the mediation of negative thoughts by acceptance, and the moderation of pain intensity by pain coping, negative thoughts and acceptance.

2. Methods

2.1. Participants

Recruitment to the study was through the membership and registration list of the Haemophilia Society UK. The procedure for recruitment and data collection preserved the anonymity of participants. The Haemophilia Society retained all information about the identity and contact details of participants, and mailings using the Society membership and registration list were undertaken by the Society. For data management, participants were identified only by a number assigned specifically for the study.

The inclusion criteria were having hemophilia A or B, being aged over 18 years, and Society membership or registration with good mailing status. The exclusion criteria were medical conditions that complicate pain coping (such as Alzheimer's disease) or having previously indicated unwillingness to participate in research.

Individuals meeting the study criteria were sent an invitation to participate, along with a questionnaire booklet and return envelope. A reminder invitation with a 6-item questionnaire about reasons for non-participation was sent to those who did not return a completed questionnaire within four weeks. Of 568 individuals who met the inclusion criteria, 209 (37%) returned completed questionnaires. All the individuals in the sample were male. Mean age was 49.5 years (SD 12.8 years). There were 165 (78.9%) with hemophilia A, 39 (18.7%) with hemophilia B, and 5 (2.4%) where hemophilia type was not known. There were 46 (22%) with mild hemophilia, 24 (11.5%) with moderate hemophilia, 132 (63.2%) with severe hemophilia, and 7 (3.3) where severity was not known.

Information about reasons for non-participation was provided by 85 individuals (24% of non-participants). The most common reason given was having a mild form of hemophilia or experiencing little or no bleeding and/or pain (71 individuals, or 84% of those giving reasons). There were 21 individuals (25% of those giving reasons) who indicated they did not wish to take part in research, 14 (17%) who indicated they did not have time to complete the questionnaire, and 5 (6%) who indicated they were 'too old' (some individuals indicated more than one reason).

Group-level comparisons between participants and non-participants were possible for age and type and severity of hemophilia. Participants were more likely than non-participants to have severe rather than mild or moderate hemophilia ($\chi^2_{(1)} = 18.5$, $p < .001$), but there were no significant differences in age ($F_{(1,526)} = 0.75$, $p = 0.39$) or hemophilia type A vs. B ($\chi^2_{(1)} = 0.10$, $p = 0.75$).

Comparisons between the sample and the national UK population of adults with hemophilia, using summary data from returns made by UK Haemophilia Centres (John Morris, personal communication), showed that the proportions of hemophilia types A and B were similar in both sets of data, but the sample had higher proportions with severe hemophilia and people aged over 40.

2.2. Measures

2.2.1. Joint pain

Participants rated the frequency and intensity of arthritic joint pain. Pain frequency was rated on a 5-point scale where 1 = never, 2 = rarely, 3 = once a week, 4 = more than once a week, and 5 = daily. Pain intensity in the last month was rated on a 10cm visual analogue scale labelled 'no pain' to 'worst pain possible'.

2.2.2. Use of clotting factor

This was measured using two items ('I treat myself with factor VIII or IX when I feel a bleed' and 'No matter where I am I treat myself with the correct amount of factor'), both scored from 0 ('never do that') to 6 ('always do that'). Both items were taken from the long version of the hemophilia-adapted pain coping strategies questionnaire [5] but are not included in the pain coping measure used in the present study. A single score was computed as the mean of the two items.

2.2.3. Pain coping and negative thoughts about pain

The Hemophilia Pain Coping Questionnaire (HPCQ) is a 27-item measure of pain coping and negative thoughts about pain in hemophilia [8]. Respondents rate each item on a seven-point scale, with each item scored from 0 ('never do that') to 6 ('always do that'). Scores are computed for three scales: 'active coping', 'negative thoughts' and 'passive adherence'. The active coping scale is made up of 10 items about diverting attention from pain, ignoring pain sensations, reinterpreting pain sensations, increasing behavioural activity when in pain, and coping self-statements. Higher scores indicate greater use of active pain coping strategies. The negative thoughts scale is made up of nine items about catastrophizing, anger, fear and seeking isolation when in pain. Higher scores indicate greater negative and emotional thinking about pain. The passive adherence scale is made up of six items about resting, using painkillers and using ice when in pain. Higher scores indicate greater use of passive pain coping strategies. Scale scores are obtained by summing across items and dividing by the number of items. Internal reliabilities were 0.86 for negative thoughts, 0.80 for active coping and 0.76 for passive adherence. Six-month test-retest reliabilities were 0.73 for negative thoughts, 0.70 for active coping and 0.64 for passive adherence. Validity was demonstrated by differential relationships with other measures of responses to pain [8].

2.2.4. Pain acceptance

The Chronic Pain Acceptance Questionnaire (CPAQ) is a 34-item self-report measure of the extent to which individuals are able to desist from attempts to avoid or reduce their chronic pain. Each item is scored on a six-point scale, from 'never true' (0) to 'almost always true' (5). Subscale scores are obtained by summing scores across items. The revised scoring method was used, in which 20 items give scores for two subscales [23]. The activity engagement subscale comprises 11 items about engaging in activities when in pain, and the pain willingness subscale comprises nine items about recognising that avoidance and control are often unworkable methods of adapting to chronic pain. Higher scores indicate higher levels of acceptance. The two subscales had internal reliabilities of 0.82 and 0.78, and their validity was supported by significant relationships with other measures of patient functioning [23].

2.2.5. Health-related quality of life

The RAND 36 (SF-36) is a 36-item questionnaire that gives eight subscale scores: physical functioning (10 items), role limitations due to physical health problems (4 items), role limitations due to emotional problems (3 items), energy/fatigue (4 items), emotional well-being (5 items), social functioning (2 items), pain (2 items), and general health (5 items). For each subscale, higher scores indicate greater quality of life [14, 15]. Scores for physical and mental component summary scales (PCS and MCS) are computed by standardizing each subscale score, computing two aggregate component scores, and then transforming the component scores to T scores with means of 50 and SDs of 10 [48]. In each case, higher scores indicate greater health-related quality of life. This is one of the most widely used measures of health-related quality of life, with well-established reliability and validity [26, 27]. A two-factor structure (PCS and MCS), internal consistency, and discriminant validity were supported in general population samples [31, 40], and the reliability, validity and responsiveness of the PCS and MCS scales were supported in painful conditions like rheumatoid arthritis [35]. The SF-36 was recommended for use in chronic pain samples [2] and is a frequently used measure in hemophilia [10], with good internal consistency and good discrimination between patients with differing hemophilia severity [41].

2.3. Data Analysis

The statistical analysis was carried out using SPSS 14.0 for windows. Where a small number of items were missing for a scale, scale scores were computed based on estimated (mean) values in place of missing items. The SF-36 scoring recommendation is to compute scale scores using estimated values where at least half of the items per scale are non-missing [49]. We adopted that upper limit for missing values substitution. In fact, however, there were just 82 missing values substitutions out of 17,138 data points, and just 70 scale scores with missing value substitutions out of 2,926 scale scores (14 scales x 209 participants), of which 62 (89%) involved just one estimated item and 6 (8.6%) just two estimated items per scale.

Pearson correlations among variables were computed, and two multiple linear regression analyses were conducted, with SF-36 physical and mental component summary scales as the dependent variables. For the regression analyses all the predictor variables were converted to Z scores with means of zero and standard deviations of 1.0. Interaction terms were computed as products of pairs of scores. Predictor variables were added to the regression models in successive blocks. First, factors that have previously been associated with quality of life in hemophilia (age, hemophilia severity, use of clotting factor, and pain intensity) were added, using the forced entry method so that those variables were retained and controlled for in subsequent blocks. Then the measures of pain coping, negative thoughts and pain acceptance were added, using the stepwise method. For the analysis with the mental component summary scale (MCS) as the dependent variable, negative thoughts and pain acceptance variables were added in separate blocks to test the mediation of negative thoughts by pain acceptance. Finally interaction terms were added, using the stepwise method.

The influence of coping, negative thoughts and acceptance was assessed by testing the increases in variance accounted for (ΔR^2) when those variables were added to the regression models.

The mediation of pain intensity by negative thoughts was assessed by examining the change in beta weight for pain intensity when negative thoughts were added to the model. If the beta weight was reduced, the indirect effect of pain intensity via negative thoughts was tested with a Sobel test [37], using the SPSS macro provided by Preacher and Hayes [30]. The mediation of negative thoughts by acceptance variables was tested in the same way; if the beta weight for negative thoughts was reduced when acceptance variables were added, Sobel tests of the indirect effects were conducted.

The moderation of pain intensity by coping, negative thoughts and acceptance was assessed by testing interaction effects. Significant interactions were explored using simple slopes analyses [1], in which regression equations for pain intensity were conducted at the mean and one standard deviation above and below the mean of the moderating variable in each case.

3. Results

There were 164 participants (78%) who reported arthritic joint pain at least once a week, and 119 (57%) who reported it every day. Descriptive statistics are given in table 1.

For pain coping and negative thoughts, scores can be compared with a previous sample of 68 people with severe hemophilia (mean age 41 years), where a longer version of the HPCQ was used, with scale scores computed in a comparable way, giving means of 2.2 (SD 0.90) for active coping, 2.7 (SD 1.10) for negative thoughts and 2.4 (SD 1.10) for passive adherence [7]. Compared with those data, the present sample scored slightly higher for active coping, lower for negative thoughts, and higher for passive adherence. When Pain Coping Strategies Questionnaire (CSQ) subscales were compared

between patients with hemophilia and previous samples with sickle cell disease and chronic low back pain, the score profiles were similar across conditions, except that hemophilia patients scored lower than the other groups for praying and hoping [5] (.

For pain acceptance, comparisons with chronic pain patients are of interest because these are the first data to our knowledge on pain acceptance in hemophilia. In a sample of 235 men and women referred to a UK interdisciplinary pain management programme with histories of prolonged chronic pain, most commonly low back pain, mean scores were 29.3 (SD 12.0) for activity engagement and 17.4 (SD 9.7) for pain willingness [23]. In the present sample, scores were substantially higher than those, suggesting greater acceptance of pain in hemophilia.

Table 1. Descriptive statistics for study variables

	Items	Mean	SD	Range	Alpha
Use of clotting factor	2	3.75	2.22	0.0-6.0	.85
Pain intensity	1	5.04	3.05	0-10	-
HPCQ					
Active pain coping	10	2.44	1.12	0.0-6.0	.81
Negative thoughts about pain	9	2.02	1.37	0.0-5.9	.86
Passive adherence pain coping	6	3.40	1.40	0.0-6.0	.76
CPAQ					
Activity engagement	11	39.8	11.0	10-65	.81
Pain willingness	9	25.2	9.3	3-51	.75
RAND-36					
Physical functioning	10	44.1	31.3	0-100	.95
Role limitations physical	4	31.8	40.0	0-100	.89
Role limitations emotional	3	57.5	44.6	0-100	.89
Energy/fatigue	4	43.6	20.0	0-100	.79
Emotional well-being	5	66.1	18.3	16-100	.82
Social functioning	2	57.5	27.4	0-100	.89
Pain	2	47.5	26.5	0-100	.90
General health	5	41.8	23.7	5-100	.83
Physical component summary (PCS)	8	32.2	12.6	8-66	.89
Mental component summary (MCS)	8	46.8	11.4	15-69	.89

For health-related quality of life, PCS scores were lower than MCS scores, consistent with previous research. In one previous sample of 65 patients with severe hemophilia (mean age 37.6 years), mean scores were 31.9 (SD 14.8) for PCS and 52.5 (SD 11.1) for MCS [29]. In a more varied sample of 164 patients with hereditary coagulation disorders (mean age 42 years), mean scores were 44.0 (SD 12.2) for PCS and 52.2 (SD 8.4) for MCS [39]. Lower scores, indicating poorer quality of life, are sometimes reported among chronic pain patients; among 273 chronic pain patients at an interdisciplinary pain programme, mean scores were 28.5 (SD 6.4) for PCS and 36.5 (SD 11.6) for MCS [2].

Correlations among variables are shown in table 2. Age was negatively correlated with severity, use of clotting factor and the physical component of quality of life (PCS). Severity, use of clotting factor and pain intensity were positively inter-correlated. Activity engagement was positively correlated with active coping, and both activity engagement and pain willingness were negatively correlated with negative thoughts and passive adherence. The physical component of quality of life (PCS) was negatively correlated with age, severity, use of clotting factor, pain intensity and passive adherence, and positively correlated with activity engagement and pain willingness. The mental component (MCS) was negatively correlated with negative thoughts, and positively correlated with activity engagement and pain willingness.

Table 2. Pearson correlations among predictor variables

1. Age	1.0									
2. Hemophilia severity[1]	-.28**	1.0								
3. Use of clotting factor	-.27**	.63**	1.0							
4. Pain intensity	.03	.35**	.16*	1.0						
5. Active coping	.002	-.05	-.01	-.10	1.0					
6. Negative thoughts	-.08	-.07	-.06	.19*	.07	1.0				
7. Passive adherence	.001	-.01	.04	.16*	-.04	.37**	1.0			
8. Activity engagement	.05	-.09	-.16*	-.37**	.34**	-.38**	-.29**	1.0		
9. Pain willingness	-.14	-.06	-.03	-.38**	.06	-.49**	-.26**	.41**	1.0	
10. Physical component summary (PCS)	-.22*	-.35**	-.20*	-.68**	.09	-.12	-.18*	.31**	.41**	1.0
11. Mental component summary (MCS)	-.03	.09	.03	-.14	-.04	-.57**	-.13	.37**	.42**	.01
	1	2	3	4	5	6	7	8	9	10

1. Coded mild/moderate = 1, severe = 2.

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

Table 3 shows the results of the regression analysis of physical component scores (PCS). In block 1, age and pain intensity were significant negative predictors, with greater age and more intense pain associated with lower PCS scores, and block 1 variables accounted for a substantial proportion of the variance in PCS scores. Hemophilia severity was not a significant predictor in block 1 (Beta = -.143, p = .056), but was significant in blocks 2 and 3, with greater severity associated with lower PCS scores.

Table 3. Standardized regression coefficients (beta weights), proportions of variance accounted for (R^2), and changes in R^2 (ΔR^2) from hierarchical linear regression analyses with PCS scores as the dependent variable.

	Block 1	Block 2	Block 3
Age	-.31***	-.29***	-.28***
Hemophilia severity	-.14	-.16*	-.16*
Use of clotting factor	-.13	-.12	-.11
Pain intensity	-.57***	-.51***	-.52***
Pain willingness		.16**	.14*
Pain intensity x pain willingness			-.14**
R^2	.505	.528	.547
ΔR^2	.505***	.023**	.019**

* $p < .05$; ** $p < .01$; *** $p < .001$

In block 2, pain willingness was the only significant additional predictor, with greater pain willingness associated with higher PCS scores, and pain willingness increased the variance in PCS scores accounted for by a small but significant amount, Although not specifically predicted, the beta weight for pain intensity fell from -.57 to -.51 when pain willingness was added to the model, and there was significant mediation of pain intensity by pain willingness (Sobel = -0.88, 95% CIs -1.53 to -0.23, p = .0084).

In block 3 the interaction of pain intensity and pain willingness was significant and increased the variance in PCS scores accounted for by a small but significant amount. The interaction is shown in fig 1. Pain willingness moderated (reduced) the impact of pain intensity, which was significant at each level of pain willingness, but reduced as pain willingness increased (low pain willingness B (unstandardized coefficient) = -9.29, $p < .001$; moderate pain willingness B = -7.36, $p < .001$); high pain willingness B = -5.43, $p < .001$).

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Fig 1. Effects of interaction between pain intensity and pain willingness on physical component summary (PCS) scores

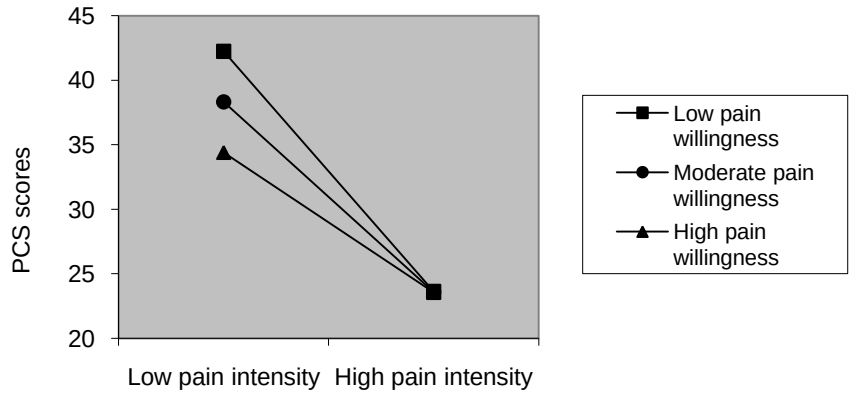


Table 4 shows the results of the regression analysis of mental component scores (MCS). In block 1, hemophilia severity and pain intensity, but not age, were significant predictors of MCS scores, but accounted for much less variance than in block 1 of the analysis of PCS scores, and the influence of severity was positive, indicating greater severity associated with higher MCS scores. In subsequent blocks, however, the effect of severity was non-significant.

Table 4. Standardized regression coefficients (beta weights), proportions of variance accounted for (R^2), and changes in R^2 (ΔR^2) from hierarchical linear regression analyses with MCS scores as the dependent variable.

	Block 1	Block 2	Block 3	Block 4
Age	.02	-.05	-.01	.02
Hemophilia severity	.24*	.12	.09	.09
Use of clotting factor	-.08	-.08	-.03	.00
Pain intensity	-.19*	-.05	.04	.03
Negative thoughts		-.54***	-.41***	-.42***
Pain willingness			.17*	.16*
Activity engagement			.15*	.15*
Pain intensity x negative thoughts				.14*
R^2	.052	.318	.358	.377
ΔR^2	.052	.267***	.040*	.019*

* $p < .05$; ** $p < .01$; *** $p < .001$

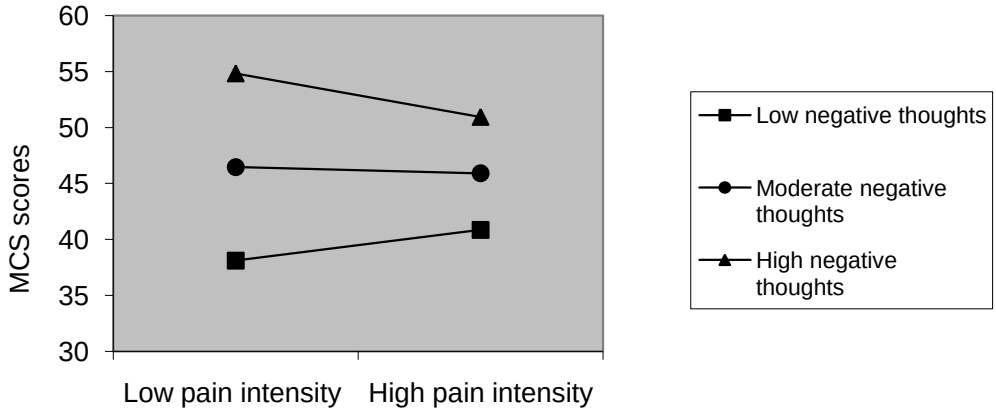
In block 2, negative thoughts was a very significant predictor, with greater negative thoughts associated with lower MCS scores, and negative thoughts increased the variance in MCS scores accounted for by a substantial amount. The beta weight for pain intensity fell from -.19 to -.05 when negative thoughts was added to the model, and there was significant mediation of pain intensity by

negative thoughts (Sobel = -1.29, 95% CIs -2.29 to -0.29, *p* = .0117). Although not specifically predicted, the beta weight for hemophilia severity also fell from .24 to .16 when negative thoughts was added, but there was no significant mediation of severity by negative thoughts (Sobel = 0.56, 95% CIs -0.39 to 1.50, *p* = .25).

In block 3, activity engagement and pain willingness were significant predictors, and increased the variance in MCS scores accounted for by a small but significant amount. The beta weight for negative thoughts fell from -.54 to -.41 when activity engagement and pain willingness were added to the model, and there was significant mediation of negative thoughts by activity engagement (Sobel = -0.74, 95% CIs -1.38 to -0.11, *p* = .022) and pain willingness (Sobel = -0.97, 95% CIs -1.78 to -0.16, *p* = .019).

In block 4 the interaction of pain intensity and negative thoughts was significant and increased the variance in MCS scores accounted for by a small but significant amount. The interaction is shown in fig 2. Negative thoughts moderated (increased) the impact of pain intensity, which was greater at higher levels of negative thoughts, although the effect of pain intensity was not significant for any single level of negative thoughts (low negative thoughts B = 1.38, p = .18; moderate negative thoughts B = -0.29, p = .71; high negative thoughts (B = -1.95, p = .062).

Fig 2. Effects of interaction between pain intensity and negative thoughts on mental component summary (MCS) scores



4. Discussion

The findings extend what we know about pain acceptance, by showing its association with health-related quality of life in a condition where pain is secondary to other symptoms, and extend our understanding of hemophilia, by showing that pain acceptance and negative thoughts about pain were associated with health-related quality of life.

Pain acceptance variables increased the variance in physical and mental quality of life accounted for by age, severity and pain intensity, and moderated and partly mediated the influence of pain intensity on physical quality of life. Pain acceptance also partly mediated the influence of negative thoughts on mental quality of life. Negative thoughts were the strongest associate of the mental component of quality of life, and moderated and partly mediated the influence of pain intensity on mental quality of life.

These findings are from a cross-sectional survey, so causal relationships cannot be assumed. For example, the interpretation that pain acceptance influenced health-related quality of life is consistent with acceptance theory, but the influence could also have been in the other direction. Longitudinal data or evaluations of interventions would be needed to establish the direction of causation more conclusively.

The response rate was similar to comparable postal questionnaire studies, and there were no differences between participants and non-participants in age or hemophilia type, although participants were more likely to have severe hemophilia. Compared with the national UK adult hemophilia population, the sample had higher proportions of people with severe hemophilia and people aged over 40. Hemophilia-related joint pain affects older people and those with severe hemophilia more than others, so the sample is more representative of those affected by joint pain than the general population of people with hemophilia. The descriptive data indicate that the sample had similar quality of life to previous hemophilia samples, but had less impaired quality of life and greater acceptance of pain than previous chronic pain samples.

The mediation of pain intensity by pain willingness suggests that pain intensity affects physical quality of life at least partly because it reduces pain willingness (the degree to which people have experiences of pain without trying to avoid or control them). The moderation of pain intensity by pain willingness showed that pain willingness reduced the impact of pain intensity on physical quality of life, but seemed to have more impact when pain was less intense (fig 1). This seems paradoxical, but in hemophilia more intense joint pain is associated with more severe illness, and when pain and illness are most severe there may be less scope for acceptance to influence physical quality of life. Alternatively, factors other than pain acceptance may be more important in hemophilia when pain is more intense.

It is also possible that the impact of pain acceptance in hemophilia could be extended by training or interventions to promote acceptance, for acceptance-based interventions have been effective in chronic pain conditions [24, 45]. However, it is important to be cautious about recommending this approach in hemophilia. Even in chronic pain conditions, advocates of acceptance-based approaches have noted that acceptance will not be relevant or important for some patients [21], and in hemophilia there is a clear physiological basis for pain and important steps that people can take to avoid and minimise the ultimate cause of pain, which is often not the case in chronic pain conditions. Any intervention for pain in hemophilia should take account of the need to recognise and treat bleeding episodes when they occur, for these are the ultimate cause of arthritic joint pain and the immediate cause of acute bleeding pain.

The mediation of pain intensity by negative thoughts suggests that pain intensity affects mental quality of life at least partly because it increases negative thoughts about pain, and the mediation of negative thoughts by activity engagement and pain willingness suggests that negative thoughts affect mental quality of life at least partly because they reduce pain acceptance.

The moderation of pain intensity by negative thoughts showed that negative thoughts increased the impact of pain intensity on mental quality of life, but seemed to have more impact when pain was less intense (fig 2). Together with the moderation of pain intensity by pain willingness (fig 1), this would seem to suggest there is greater scope for factors such as acceptance and negative thoughts to influence quality of life when hemophilia-related pain is less intense. Again, however, it is possible that factors other than negative thoughts could influence mental quality of life among individuals with more intense pain caused by hemophilia, or that interventions to reduce negative thoughts could enhance the impact of lower negative thoughts.

Negative thoughts about pain emerged as a very important factor in mental quality of life, being a strong predictor in its own right, and also moderating and partly mediating the effect of pain intensity. Perhaps this is not surprising considering that factors such as catastrophizing have been characterised by some as pain-related emotional distress [43, 44]. Interventions to improve psychological adjustment in hemophilia could therefore focus on reducing negative thoughts about pain, and from the effects observed here would be expected to be moderately effective, especially among those with less intense pain. It has been speculated that 'enhanced acceptance of pain may be the means to reduce the frequency, unpleasantness, or impact of catastrophic thoughts about pain.' [21, p. 202]. Negative thoughts were negatively correlated with both activity engagement and pain willingness in the present sample, and the effect of negative thoughts was partly mediated by both activity engagement and pain willingness, so it is possible that acceptance-based training or intervention in hemophilia could be a way to reduce negative thoughts about pain.

In the present sample there were no significant effects of active pain coping. However, it is possible that important aspects of coping are not tapped by the pain coping measure employed here, for the HPCQ is based on the Coping Strategies Questionnaire [33], and there are measures that include other aspects of pain coping [17, 32]. It may also be that active coping per se may not be important or relevant in hemophilia. Indeed, in the chronic pain literature, it has been suggested that active attempts to cope with pain may be less important or effective than has often been assumed [21].

Previous research suggested that quality of life in hemophilia could be improved by extending prophylactic and on-demand treatment with clotting factor concentrates [10, 34], but the present findings suggest it could also potentially be improved by interventions to promote greater acceptance of pain and reduce negative thoughts about pain. Further research on the impact of pain in hemophilia could include investigations of condition-specific aspects of joint pain, taking into account the steps affected people must take to avoid and treat the bleeding episodes that are the cause of joint pain. Longitudinal studies of pain coping, negative thoughts, acceptance, and quality of life in hemophilia would also be informative about how one factor influences others, as would evaluations of interventions designed to improve adjustment to pain and quality of life.

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