ORIGINAL ARTICLE

Self-reported pain severity is associated with a history of coronary heart disease

S. Parsons[1], J. McBeth[1], G.J. Macfarlane[2], P.C Hannaford[3], D.P.M Symmons[1,4]

1 Arthritis Research UK Centre for Epidemiology, Manchester Academic Health Science Centre, University of Manchester, UK

2 Aberdeen Pain Research Collaboration (Epidemiology Group), Institute of Applied Health Sciences, University of Aberdeen, UK

3 Aberdeen Pain Research Collaboration (Primary Care Group), Institute of Applied Health Sciences, University of Aberdeen, UK

4 NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester University Hospitals NHS Foundation Trust and the University of Manchester partnership, UK

Correspondence
Deborah P.M. Symmons
E-mail: Deborah.symmons@manchester.ac.uk

Conflicts of interest
None declared.

Abstract

Background: Previous studies have found an association between chronic pain and cardiovascular (CV) mortality.

Objective: To explore the relationship between the severity of pain and non-fatal CV disease.

Methods: A total of 45,994 adults randomly selected from general practice registers in Manchester and Aberdeen were posted a survey, which included a Chronic Pain Grade questionnaire, pain manikin and questions about lifestyle and medical history. A single component measuring pain severity was extracted using factor analysis. Logistic regression was used to test for an association between quintiles of pain severity and a history of CV disease, adjusting for confounders.

Results: Of the 15,288 responders, 61% ($n = 9357$) reported pain for ≥ 1 day in the past month. Compared with the first (lowest) pain severity quintile, the fully adjusted odds ratio for heart attack in the second severity quintile was 1.25 (95% confidence interval 0.68, 2.30); third quintile: 1.65 (0.93, 2.94); fourth quintile: 1.76 (1.00, 3.11) and fifth (highest) quintile 2.47 (1.43, 4.28). Corresponding figures for angina (excluding heart attack) were: 1.79 (0.93, 3.45), 1.91 (1.00, 3.62), 1.03 (0.50, 2.11) and 3.17 (1.71, 5.85).

Conclusion: A history of CV disease is reported more often in those with severe pain than would be expected by chance, even when adjusting for shared risk factors.

1. Introduction

Chronic pain is common in the general population (Smith et al., 2001; Gerdle et al., 2004; Raftery et al., 2011) and represents a substantial economic burden, through loss of productivity (Smith et al., 2001; Raftery et al., 2011), as well as a burden on the individual, through decreased quality of life and psychological distress (Becker et al., 1997; Fishbain et al., 1997; Breivik et al., 2006). This burden is higher among those with more severe pain (Becker et al., 1976; Blyth et al., 2004), which can be described in

terms of the intensity of pain, the disability associated with pain and the number of pain sites. In surveys of the general population, around 19% of adults report chronic pain of moderate to severe intensity (Breivik et al., 2006), 25% report disabling pain (Palmer et al., 2005) and 11% report that their pain is widespread (Bergman et al., 2002).

Although it is often difficult to find a physical cause for chronic pain, intense, disabling and widespread pain are associated with poor health outcomes and may have an association with cardiovascular (CV) disease. Previous studies have found that chronic

What's already known about this topic?

- There is some evidence that chronic pain is associated with cardiovascular mortality. Few studies have examined the relationship between chronic pain severity and cardiovascular disease.

What does this study add?

- Severe pain and a history of coronary heart disease co-occur more often than would be expected solely due to shared risk factors.

widespread pain (CWP) is associated with a higher risk of mortality from CV conditions (Andersson, 2009; McBeth et al., 2009). However, few studies have examined whether the severity of pain is associated with CV disease. In a community-based cohort linkage study of 5858 people in Scotland, Torrance et al found that 10-year mortality from circulatory disorders was more strongly associated with severe pain than mild pain (Torrance et al., 2010). However, this result was not adjusted for CV risk factors such as body mass index (BMI) and smoking. A Swedish study of 2278 people from the general population found that CWP was more strongly associated with subsequent periods of inpatient hospital care for coronary heart disease (CHD) than chronic regional pain (Lindgren and Bergman, 2010).

One possible explanation is that individuals with pain that is more intense, disabling or widespread may have a worse CV risk profile than those with less severe pain. Pain intensity and disability levels have been found to be associated with greater fat mass (Urquhart et al., 2011), obesity (Goodson et al., 2010), dyslipidaemia (Goodson et al., 2010) and smoking (Goodson et al., 2010). Individuals with higher levels of pain intensity and disability scores have significantly worse median scores in all domains of the short form-36 (SF-36), including those that measure ability to undertake physical activity or simple physical tasks, compared with those who have lower levels of intensity and disability (Penny et al., 1999). The number of pain sites is also associated with decreased functioning in terms of physical fitness, daily and social activities (Kamaleri et al., 2008b) as well as psychological distress (Kamaleri et al., 2008a). Additionally, individuals who smoke, have a higher BMI and/or have lower levels of physical activity report a higher number of pain sites (Kamaleri et al., 2008a). A higher prevalence of CV risk factors among those with intense, disabling or widespread pain may lead to an increased risk of CV disease among these individuals.

The aim of this study was to investigate whether pain severity was associated with CV disease and to determine if this relationship was independent of age, gender, lifestyle factors and co-morbidities.

2. Methods

2.1 Survey methods

Data were collected as part of the Managing Unexplained Symptoms In primary Care: Involving traditional and Accessible New approaches (MUSICIAN) clinical trial (Macfarlane et al., 2012) baseline survey that sought to identify eligible trial subjects. A postal questionnaire was sent to a random sample ($n = 45994$) of individuals aged 25 years or over, identified from the general practice lists of eight practices in the Aberdeen and Manchester regions. A letter from the practice was included with the questionnaire. Individuals who did not reply to the initial mailing were sent a reminder letter and questionnaire approximately 2 weeks later.

2.2 Study questionnaire and data manipulation

The baseline questionnaire collected information about the date of birth, gender and current employment status. Individuals were categorized as 'employed/student' if they indicated that they were working full-time, part-time or were a student; 'unemployed' if they were 'unable to work because of illness or disability', 'unemployed and looking for work' or 'at home and not looking for paid employment'; or 'retired'. Self-reported height (m) and weight (kg) were used to calculate BMI [weight (kg) divided by height (m²)]. Weight was categorized using World Health Organization (WHO) definitions (World Health Organization, 2000). Underweight was defined as BMI <18.5 kg/m², recommended weight as BMI ≥18.5 kg/m² & <25 kg/m², overweight as BMI ≥25 kg/m² & <30 kg/m² and obesity as ≥30 kg/m². Exercise level was determined through the question 'how many times a week do you usually do 30 min of moderate physical activity or walking that increases your heart rate or makes you breathe harder than normal?; answer options: 'none', '1–2 times/week', '3–4 times/week' and '5 or more times/week'. Respondents were asked if they had ever smoked cigarettes regularly for longer than a month and if they had smoked regularly over the past month. Responses to these two questions were used to categorize individuals into: current smoker – smoked ≥1 cigarettes for a period of ≥1 month and smoked over the past month; ex-smoker – smoked ≥1 cigarettes for a period of ≥1 month but had not smoked over the past month; never smoker – had not smoked in the past or over the last month. Subjects were asked if they had ever drunk alcohol at least once per week for ≥1 month and the average number of units they drank per week. Alcohol intake then was classified as drinks alcohol/does not drink alcohol, with the number of units of alcohol drunk by drinkers categorized into: '0–10', '11–20' and '≥21'. Another question asked whether an indi-

vidual's general health was 'excellent', 'very good', 'good', 'fair' or 'poor', with responses aggregated for analysis into: 'excellent/very good', 'good/fair' and 'poor'.

2.3 Cardiovascular status

The presence of various health conditions was ascertained using the question 'have you ever been told by a doctor that you have any of the following diseases: '. The list of conditions provided included 'osteoarthritis', 'rheumatoid arthritis', 'diabetes', 'high blood pressure', 'angina', 'heart attack', 'stroke' and 'depression.' From the responses, we identified those with a history of CHD (heart attack, with or without angina, and angina alone, which we have termed 'isolated' angina). The design of the MUSICIAN survey and trial did not include examination of medical records or a clinical examination at which self-reported CV disease (or height, weight, etc) could be confirmed.

2.4 Pain assessments

Respondents were asked 'Thinking back over the past month, have you had any aches or pains that lasted 1 day or longer?' If they said 'yes', they were asked to shade on a blank body manikin the areas of the body where they had pain and to complete the Chronic Pain Grade questionnaire (Von et al., 1992). The pain manikin was scored by hand using a transparent scoring template, which was split into 35 pain sites. The Chronic Pain Grade questionnaire has seven scales (ranging from 1 to 10) on which participants rate different aspects of their pain. Three of the scales relate to pain intensity, three to pain-related disability and one to the chronicity of pain (the number of days on which pain has kept the respondent from their usual activities). All of the scales relate to pain in the past 6 months, apart from the first, which asks about intense pain at the present time.

From the responses to the seven scales, pain intensity score and disability points can then be calculated. This is described in detail in Von et al. (1992) and Smith et al. (1997). In brief, the pain intensity score was calculated as the mean of the three scales which relate to pain intensity. The disability score was calculated as the mean of the three scales which relate to disability caused by pain. Both of these scores were multiplied by 100, to give a 1–100 scale of pain intensity and disability. Disability points were then calculated using the disability score and the chronicity of pain score (the number of days on which pain has kept the respondent from their usual activities). To do this, disability score was first recoded as 0–29 = 0, 30–49 = 1, 50–69 = 2 and ≥70 = 3. The chronicity of pain score was recoded as 0–6 days = 0, 7–14 days = 1, 15–30 days = 2 and ≥31 days = 3. The recoded disability score and pain chronicity scale were then added together to create a disability point score, which ranged from 0 to 6.

2.5 Statistical analysis

The data were analysed using STATA version 11 (Stata Corporation, College Station, Texas, USA). Prevalence rates,

Table 1 Varimax rotated component loadings for the three pain scales.

Pain measure	Factor loading
Intensity score	0.67
Disability points	0.64
Pain sites	0.52
Eigenvalue	1.12

stratified by age and sex, were calculated for self-reported heart attack and 'isolated' angina. The denominator used in the prevalence calculations was all those who responded to the question relating to that condition. The denominator used to calculate the prevalence of self-reported pain intensity, disability and pain sites was the number of people who answered the question relating to 'aches or pains' for ≥1 day in the last month.

A factor analysis with varimax rotation was conducted using the three separate pain measures: pain intensity, disability points and number of pain sites. A single factor was extracted that accounted for all of the variance (Table 1). The factor loadings indicate that all three measures were correlated with the factor. As the three measures are all dimensions of pain severity, it is argued that the factor is a latent variable measuring the severity of pain. The factor was categorized into quintiles, with the lowest quintile equating to the least severe pain and the highest to the most severe pain.

Logistic regression was used to test for an association of pain severity with self-reported heart attack and 'isolated' angina, each as the dependent variable. Models were first run adjusted for age and gender, with potential confounders then introduced in a stepwise fashion. The second model was adjusted for age, sex and lifestyle factors (smoking, alcohol intake, physical activity) and the final model adjusted for age, sex, lifestyle factors and co-morbidities (high blood pressure, BMI, diabetes and depression).

Results are presented as odds ratios (OR) with 95% confidence intervals (CI). For all models, the area under the receiver operating characteristic curve (AUC) was calculated to ascertain how well the model predicted a self-reported history of heart attack or 'isolated' angina. The regression models only used individuals with complete records for each variable used in the analysis (number shown in the results of each model).

2.6 Ethical approval

The study was approved by the Cheshire Research Ethics Committee (REC ref: 07/Q1506/61).

3. Results

3.1 Population characteristics

Of the 45,994 questionnaires sent, 15,288 (response rate = 33%) eligible individuals returned a completed

Table 2 Characteristics of respondents (*n* = 15288).

Characteristics	
Age, mean (SD) years	56 (16)
Female, *n* (%)	8687 (57)
BMI	
Obese, *n* (%) (BMI ≥ 30 kg/m²)	2569 (17)
Overweight, *n* (%) (BMI ≥ 25 & < 30 kg/m²)	5512 (37)
Recommended weight, *n* (%) (BMI ≥18.5 & <25 kg/m²)	6541 (44)
Underweight, *n* (%) (BMI <18.5 kg/m²)	232 (2)
Physical activity	
None, *n* (%)	2909 (19)
1–2 times per week, *n* (%)	5395 (36)
3–4 times per week, *n* (%)	3623 (24)
≥5 times per week, *n* (%)	3113 (21)
Smoking status	
Current smoker, *n* (%)	1765 (12)
Ex-smoker, *n* (%)	4512 (30)
Never smoked, *n* (%)	8706 (58)
Alcohol consumption	
Drinks alcohol, *n* (%)	10,677 (71)
Units per week:	
0–10, *n* (%)	7956 (69)
11–20, *n* (%)	2281 (20)
≥21, *n* (%)	1289 (11)
Self-rated health	
Excellent/very good, *n* (%)	7270 (48)
Good/fair, *n* (%)	7501 (49)
Poor, *n* (%)	422 (3)
Employment status	
Employed/student, *n* (%)	8324 (56)
Retired, *n* (%)	4961 (33)
Unemployed, *n* (%)	1555 (10)

BMI, body mass index; SD, standard deviation.

questionnaire. Eight thousand eighty-one (54%) were obese or overweight at the time of the survey and 6277 (42%) were current or ex-smokers (Table 2). Three thousand one hundred thirteen (21%) met the recommended exercise levels set by WHO of exercising moderately for 30 min ≥5 times per week (World Health Organization, 2010). Over a third (4961) had retired and 8324 (56%) were employed or a student.

3.2 Prevalence of self-reported pain and a history of cardiovascular conditions among respondents

The prevalence of self-reported heart attack and angina increased with age in both men and women and was slightly higher in those reporting pain on ≥1 day over the past month. Of those aged ≥65, 16% of men and 10% of women reported a heart attack. The percentage reporting heart attack was slightly higher, at 17% and 11% for men and women, respectively, among those reporting ≥1 day of pain over the past month (Table 3). Two hundred sixty-five (47%) of those reporting a past history of heart attack also reported a history of angina, and 223 (34%) of those reporting a history of angina also reported a history of heart attack. 'Isolated' angina had similar frequency in men (11%) and women (11%) aged 65 and over. The frequency of 'isolated' angina was the same in men with ≥1 day of pain over the past month but somewhat higher in women with pain (13%).

Nine thousand three hundred fifty-seven (61%) of 15,253 respondents reported having aches or pains

Table 3 Prevalence of self-reported cardiovascular conditions that an individual has 'ever' been told by a doctor they have, among all respondents and those reporting pain for ≥1 day during last month, by age and gender.

	Frequency (%)					
	All respondents (*n* = 15,288)			Those reporting pain ≥1 day over past month (*n* = 9357)		
Condition	25–44	45–64	≥65	25–44	45–64	≥65
Heart attack[a]						
Male	4 (0)	78 (3)	280 (16)	1 (0)	56 (4)	178 (17)
Female	4 (0)	30 (1)	174 (10)	2 (0)	22 (1)	120 (11)
Total	8 (0)	108 (2)	454 (13)	3 (0)	78 (2)	298 (14)
Angina[b]						
Male	2 (0)	104 (4)	345 (19)	1 (0)	80 (5)	221 (21)
Female	5 (0)	49 (2)	296 (16)	5 (0)	41 (2)	225 (19)
Total	7 (0)	153 (3)	641 (17)	6 (0)	121 (4)	446 (20)
'Isolated' angina[c]						
Male	2 (0)	75 (3)	204 (11)	1 (0)	55 (4)	126 (11)
Female	5 (0)	36 (1)	214 (11)	5 (0)	30 (2)	163 (13)
Total	7 (0)	111 (2)	418 (11)	6 (0)	85 (2)	289 (12)

[a]Includes individuals who reported ever having angina.
[b]Includes individuals who reported ever having a heart attack.
[c]Excludes individuals who reported ever having a heart attack.

Table 4 Prevalence of self-reported levels of intensity score, disability points and number of pain sites in the last 6 months.

Pain measure	Frequency (column %)											
	All respondents (*n* = 15,288)						Those reporting pain ≥1 day over past month (*n* = 9357)					
	Male			Female			Male			Female		
	25–44	45–64	≥65	25–44	45–64	≥65	25–44	45–64	≥65	25–44	45–64	≥65
Intensity score												
0–20	103 (8)	203 (7)	137 (6)	116 (5)	167 (5)	129 (5)	100 (13)	192 (11)	123 (9)	115 (8)	163 (7)	108 (6)
21–40	279 (21)	604 (21)	410 (17)	388 (16)	608 (17)	397 (14)	278 (36)	593 (33)	395 (28)	377 (28)	599 (26)	378 (22)
41–60	247 (18)	567 (20)	436 (18)	484 (20)	773 (22)	544 (20)	245 (32)	556 (31)	421 (30)	479 (35)	755 (33)	521 (30)
61–80	105 (8)	305 (11)	277 (12)	287 (12)	524 (15)	425 (15)	102 (13)	295 (17)	267 (19)	286 (21)	517 (23)	407 (23)
81–100	31 (2)	120 (4)	139 (6)	79 (3)	211 (6)	243 (9)	30 (4)	118 (7)	133 (10)	75 (5)	205 (9)	238 (14)
Disability points												
0	496 (36)	1091 (38)	689 (29)	813 (34)	1261 (35)	736 (27)	490 (64)	1060 (59)	663 (48)	795 (58)	1229 (54)	696 (40)
1	121 (9)	262 (9)	149 (6)	173 (7)	297 (8)	196 (7)	121 (16)	258 (14)	143 (10)	171 (13)	291 (13)	188 (11)
2	56 (4)	130 (5)	114 (5)	125 (5)	213 (6)	150 (5)	54 (7)	126 (7)	111 (8)	123 (9)	211 (9)	144 (8)
3	27 (2)	86 (3)	81 (3)	92 (4)	141 (4)	111 (4)	26 (3)	84 (5)	76 (5)	91 (7)	136 (6)	106 (6)
4	18 (1)	59 (2)	50 (2)	44 (2)	86 (2)	92 (3)	18 (2)	57 (3)	47 (3)	43 (3)	86 (4)	88 (5)
5	15 (1)	46 (2)	58 (2)	45 (2)	69 (2)	99 (4)	14 (2)	45 (3)	57 (4)	45 (3)	69 (3)	95 (5)
6	31 (2)	103 (4)	79 (3)	67 (3)	158 (4)	154 (6)	31 (4)	99 (6)	75 (5)	65 (5)	154 (7)	152 (9)
Pain sites												
0–5	377 (28)	937 (33)	764 (32)	593 (25)	1,022 (29)	907 (33)	362 (47)	885 (50)	675 (48)	570 (42)	973 (42)	767 (44)
6–10	277 (20)	620 (22)	523 (22)	531 (22)	811 (23)	602 (22)	277 (36)	606 (34)	506 (36)	525 (38)	798 (35)	580 (33)
11–15	95 (7)	209 (7)	157 (7)	190 (8)	342 (10)	252 (9)	93 (12)	206 (12)	150 (11)	188 (14)	337 (15)	249 (14)
16–20	20 (1)	60 (2)	44 (2)	44 (2)	108 (3)	112 (4)	20 (3)	59 (3)	43 (3)	43 (3)	106 (5)	110 (6)
21–25	10 (1)	21 (1)	17 (1)	24 (1)	47 (1)	28 (1)	10 (1)	21 (1)	17 (1)	24 (2)	47 (2)	26 (1)
26–30	7 (1)	3 (0)	2 (0)	7 (0)	24 (1)	18 (1)	7 (1)	2 (0)	2 (0)	7 (1)	24 (1)	17 (1)
30–35	2 (0)	3 (0)	2 (0)	7 (0)	6 (0)	5 (0)	2 (0)	3 (0)	2 (0)	7 (1)	6 (0)	5 (0)

that lasted for ≥1 day over the past month. Pain intensity and pain-related disability both tended to be higher among women and to increase with age (Table 4). For example, 28% of men and 36% of women aged 25–44 had a pain intensity score >40, compared with 37% of men and 45% of women aged ≥65 years. Six percent of men and 11% of women aged 25–44 had ≥3 disability points compared with 10% of men and 17% of women aged ≥65 years. The number of pain sites, however, did not seem to vary substantially by age, although they were somewhat higher in women. Thirty-one percent of men and 34% of women aged 25–44 had ≥6 pain sites. Thirty-three percent of men and 38% of women aged ≥65 years had ≥6 pain sites.

3.3 Association between self-reported pain severity in the last 6 months and a history of heart attack or 'isolated' angina

The fourth and fifth pain severity quintiles were significantly associated with a past history of heart attack, even after adjustment for age, sex and lifestyle factors [Table 5: fourth quintile OR 2.51 (95% CI 1.60, 3.92); fifth quintile OR 3.43 (95% CI 2.22, 5.30]. The asso-

ciation of heart attack with the fourth severity quintile was attenuated after adjustment for co-morbidities. When age, gender, lifestyle factors and co-morbidities were held constant, the odds of heart attack were, on average, 2.47 (95% CI 1.43, 4.28) times higher among those in the high pain severity quintile compared with those in the lowest quintile. A self-reported history of diabetes [OR 1.97; 95% CI (1.23, 3.16)] and high blood pressure [OR 2.42; 95% CI (1.73, 3.39)] were strongly associated with CV disease, even when adjusting for age, gender, lifestyle factors and pain severity. The final model was very effective at predicting a past history of heart attack, with an AUC of 0.89.

In the age and sex adjusted model, pain severity was associated with a history of 'isolated' angina [Table 5: third quintile OR 2.01; 95% CI (1.30, 3.09); fourth quintile OR 1.58; 95% CI (1.01, 2.47); fifth quintile OR 3.57; 95% CI (2.40, 5.32)]. After adjustment for lifestyle factors and co-morbidities, only the association with moderately severe pain (third quintile) and the most severe pain remained significant (fifth quintile). The association of angina with the most severe pain quintile was of a similar magnitude to the association with heart attack. Those in the most severe pain quintile had, on average, 3.17 (95% CI 1.71,

Table 5 Association between self-reported pain severity quintile and a history of heart attack or 'isolated' angina.

	OR (95% CI)					
	Model number					
	Heart attack			'Isolated' angina		
	I (n = 6921)	II (n = 6754)	III (n = 6433)	I (n = 7101)	II (n = 6927)	III (n = 6470)
Pain severity						
1 (lowest)	Ref					
2	1.35 (0.85, 2.16)	1.43 (0.88, 2.33)	1.25 (0.68, 2.30)	1.35 (0.85, 2.15)	1.41 (0.86, 2.31)	1.79 (0.93, 3.45)
3	1.50 (0.95, 2.38)	1.58 (0.98, 2.55)	1.65 (0.93, 2.94)	2.01 (1.30, 3.09)**	2.03 (1.28, 3.22)**	1.91 (1.00, 3.62)*
4	2.59 (1.70, 3.96)***	2.51 (1.60, 3.92)***	1.76 (1.00, 3.11)	1.58 (1.01, 2.47)*	1.61 (1.00, 2.59)	1.03 (0.50, 2.11)
5	3.87 (2.58, 5.80)***	3.43 (2.22, 5.30)***	2.47 (1.43, 4.28)**	3.57 (2.40, 5.32)***	3.50 (2.27, 5.39)***	3.17 (1.71, 5.85)***
Age	1.09 (1.08, 1.11)***	1.09 (1.08, 1.10)***	1.09 (1.07, 1.10)***	1.08 (1.07, 1.09)***	1.08 (1.07, 1.09)***	1.07 (1.05, 1.08)***
Female	0.41 (0.32, 0.53)***	0.40 (0.30, 0.53)***	0.39 (0.27, 0.56)***	0.72 (0.56, 0.92)**	0.65 (0.50, 0.84)**	0.46 (0.32, 0.67)***
Lifestyle factors						
Ex-smoker		1.63 (1.24, 2.15)***	1.58 (1.12, 2.24)*		1.22 (0.93, 1.61)	0.86 (0.59, 1.26)
Current smoker		1.52 (0.99, 2.35)	1.89 (1.10, 3.24)*		1.78 (1.20, 2.65)**	1.21 (0.69, 2.15)
Drink alcohol regularly		0.75 (0.56, 1.00)*	0.79 (0.55, 1.14)		0.60 (0.46, 0.79)***	0.61 (0.42, 0.89)*
Physical activity:						
1–2 times per week		0.66 (0.48, 0.92)*	0.81 (0.53, 1.22)		1.07 (0.77, 1.47)	1.22 (0.78, 1.92)
3–4 times per week		0.59 (0.40, 0.86)**	0.59 (0.36, 0.98)*		1.00 (0.69, 1.45)	1.16 (0.69, 1.94)
≥5 times per week		0.86 (0.59, 1.25)	1.20 (0.75, 1.92)		0.97 (0.65, 1.44)	1.08 (0.62, 1.89)
Co-morbidities						
BMI			1.02 (0.98, 1.05)			1.03 (0.99, 1.06)
Diabetes			1.97 (1.23, 3.16)**			1.61 (0.97, 2.69)
High blood pressure			2.42 (1.73, 3.39)***			2.70 (1.87, 3.90)***
Depression			1.61 (1.09, 2.39)*			2.27 (1.53, 3.36)***
AUC	0.86	0.87	0.89	0.83	0.84	0.85

AUC, area under the receiver operating characteristic curve; BMI, body mass index; CI, confidence interval; OR, odds ratio; I, age and sex adjusted; II, adjusted for age, sex, smoking, alcohol consumption, physical activity; III, adjusted for age, sex, smoking, alcohol consumption, physical activity, BMI, diabetes, high blood pressure, depression.

*$p < 0.05$.
**$p < 0.01$.
***$p < 0.001$.

5.85) times higher odds of a history of 'isolated' angina than those in the least severe quintile, when all other factors were held constant. Similarly, a self-reported history of high blood pressure was strongly associated with 'isolated' angina in the final model (OR 2.70; 95% CI 1.87, 3.90). The odds of reporting angina were also 2.27 (95% CI 1.53, 3.36) times higher, on average, among those reporting a history of depression than those not reporting it in the fully adjusted model. The final AUC value of 0.85 indicated that the variables included in the model were accurate predictors of a history of angina.

Thus, in summary, there was a significant association between pain severity and a history of heart attack and 'isolated' angina. The association was partly explained by co-morbidities and lifestyle factors at lower pain severities. The same relationship was found with separate components of pain severity: intensity score, disability points and number of pain sites (data not shown).

4. Discussion

The major finding of this study was an association between self-reported severity of pain, defined as a composite measure of intensity, disability and number of pain sites, and a self-reported past history of CHD. These relationships were independent of age, gender, co-morbidities and lifestyle factors measured in this study.

Few previous studies have reported on the association of self-reported CHD with different levels of pain severity. One study examined patient-reported pain severity and disability caused by back pain among elderly women reporting a history of CV disease (defined as one or more of stroke, myocardial infarction or heart attack, angina, rheumatic heart disease or any other heart problems) (Vogt et al., 1997). The odds ratios reported were comparable to those found for severe pain in the present study. There was a non-significant association between a history of CV disease and mild/moderate back pain (OR 1.3; 95% CI 1.0, 1.6) and a significant association with severe pain (OR 2.6; 95% CI 1.7, 4.0). Severe impairment was also more strongly associated (OR 1.6; 95% CI 1.4, 2.3) with a history of CV disease than mild/moderate impairment (OR 3.6; 95% CI 2.0, 6.5). Two studies have also focused on how widespread pain is, i.e. the number of pain sites. Widespread pain was more strongly associated with subsequent CV disease (cerebrovascular and ischaemic heart conditions) than regional pain in a study of 2278 Swedish hospital patients (OR 1.6; 95% CI 1.0, 2.4) and CWP (OR 1.9;

95% CI 1.2, 3.1) (Lindgren and Bergman, 2010). A further study examined the number of fibromyalgia tender points among individuals who had undergone coronary angiography and found individuals with coronary pathology had a significantly higher number of tender points than those with no pathology or healthy controls who had not undergone the procedure (Ablin et al., 2009).

The main limitation of this study is its cross-sectional design. Therefore, the direction of the associations found is unknown. One possible explanation for the association between pain severity and non-fatal heart attack or 'isolated' angina is that those with pain tend to have an adverse CV risk profile (Andersson et al., 1998; Kamaleri et al., 2008b; Viikari-Juntura et al., 2008; Goodson et al., 2010; Urquhart et al., 2011). Adjusting for the CV risk factors included in this study reduced some of the odds ratios found, but many associations were independent of the factors measured in this study. Adding the CV risk factors into the age and gender adjusted models (which tended to predict a past history of CV disease with an accuracy of 83–86%) led to only modest improvements in the model's explanatory capacity. The association between pain severity and CV disease, however, may still be the result of residual confounding. For example, we did not measure lipid levels, medication, e.g. non-steroidal anti-inflammatory drugs, or psychological factors other than depression. Chronic pain is associated with a range of psychological factors, including distress and anxiety (Linton, 1976; McWilliams et al., 2003). In addition, there is evidence for significant associations between pain intensity and pain-related disability, and the 'emotional', 'social functional' and 'mental health' domains of SF-36 (Smith et al., 1997). Psychological distress is known to be associated with CV disease (Rugulies, 2002; Stansfeld et al., 2002); therefore, it is possible it could confound the pain severity and CV disease relationship.

An alternative explanation for the results found is that severe pain is a symptom of subjects' CHD. Individuals who have had angina or heart attack may be substantially disabled by their condition (Lavey and Winkle, 1979; Pinsky et al., 1990) and angina may be the origin of intense and disabling pain. For some individuals, angina may be part of a wider chronic pain syndrome. There is evidence that, compared with healthy controls, pain perception is altered in those who have chest pain but a normal coronary angiogram. One study found that the central nervous system of these individuals responds abnormally to nociceptive input, in the form of electrical stimulation

of the oesophagus and sternal skin (Frobert et al., 1996). These patients also have significantly more pain in the neck, thoracic spine and pain that radiates into the arms than age-matched healthy controls (Frobert et al., 1999).

A further limitation of this study was the self-reported nature of the outcome and confounders. Only a small proportion of the respondents were eligible and agreed to participate in the subsequent MUSICIAN trial (Macfarlane et al., 2012). Agreement between self-report and medical record data has been shown to be moderate to good for heart attack (Bush et al., 1989; Rosamond et al., 1995; Haapanen et al., 1997; Okura et al., 2004) and angina (Bush et al., 1989; Haapanen et al., 1997; Lampe et al., 1999). A further limitation was the low response rate, which has been previously discussed (Macfarlane et al., 2012). Finally, this study could not assess causality. For example, we considered adjusting for 'self reported health' since high pain intensity and pain-related disability are associated with reports of poor health. However, although the correlation between pain intensity and 'fair or poor' rated health was moderate (0.4), the relationship between a history of heart attack and poor self-reported health was even stronger. (44.8% of people reporting a heart attack vs. 12.2% of those not reporting a heart attack rated their health as 'fair or poor'). A prospective study is needed to investigate the direction of the associations between pain, self-rated health and CV disease.

Strengths of this study were its large sample size, with data on a range of potential confounding factors. Pain intensity and disability were assessed using validated questionnaires (Smith et al., 1997) and, as the experience of pain is subjective, self-report may be the best method of assessing pain levels. The pain manikin is regularly used to assess pain in population surveys and pain location indicated on a manikin has a good correlation with direct questions assessing pain at individual locations (Muller et al., 2008). There is also support for using a count of pain sites as a measure of how widespread pain is, as it allows the extent of pain to be considered as a continuum rather than an artificial set of cut offs (Kamaleri et al., 2008a).

The results of this study provide more evidence to support the hypothesis of an association between pain, in particular intense, disabling and widespread pain, and CHD. It has also not previously been demonstrated that this relationship is independent of the CV risk factors measured in this study. Intense, disabling or widespread pain could be an important marker for patients at risk of CV disease. Clinicians should be mindful that those consulting with severe pain may

have a history of CHD. This study has also demonstrated that the prevalence of moderate intensity pain is high among individuals with a history of CHD and that, in some in individuals, this pain may be widespread or limiting. Therefore, good pain management is likely to be important in those who have a known history of CHD.

Acknowledgments

Author contributions

S.P. was involved in conducting statistical analysis, interpreting the data and producing the first draft of the manuscript. J.McB, G.J.M., P.C.H. and D.P.M.S. were involved in the conception and design of the study. J.McB and G.J.M. were involved in the acquisition of data. J.McB and D.P.M.S. were involved in the interpretation of data and writing the manuscript. All authors contributed to the preparation of the manuscript and read and approved the final version.

References

Ablin, J.N., Beilinson, N., Aloush, V., Elkayam, O., Finkelstein, A. (2009). Association between fibromyalgia and coronary heart disease and coronary catheterization. *Clin Cardiol* 32, E7–E11.

Andersson, H., Ejlertsson, G., Leden, I. (1998). Widespread musculoskeletal chronic pain associated with smoking. An epidemiological study in a general rural population. *Scand J Rehabil Med* 30, 185–191.

Andersson, H.I. (2009). Increased mortality among individuals with chronic widespread pain relates to lifestyle factors: A prospective population-based study. *Disabil Rehabil* 31, 1980–1987.

Becker, A., Held, H., Redaelli, M., Strauch, K., Chenot, J.F., Leonhardt, C., Keller, S., Baum, E., Pfingsten, M., Hildebrandt, J., Basler, H.D., Kochen, M.M., Donner-Banzhoff, N. (1976). Low back pain in primary care: Costs of care and prediction of future health care utilization. *Spine (Phila Pa 1976)* 35, 1714–1720.

Becker, N., Bondegaard, T.A., Olsen, A.K., Sjogren, P., Bech, P., Eriksen, J. (1997). Pain epidemiology and health related quality of life in chronic non-malignant pain patients referred to a Danish multidisciplinary pain center. *Pain* 73, 393–400.

Bergman, S., Herrstrom, P., Jacobsson, L.T., Petersson, I.F. (2002). Chronic widespread pain: A three year followup of pain distribution and risk factors. *J Rheumatol* 29, 818–825.

Blyth, F.M., March, L.M., Brnabic, A.J., Cousins, M.J. (2004). Chronic pain and frequent use of health care. *Pain* 111, 51–58.

Breivik, H., Collett, B., Ventafridda, V., Cohen, R., Gallacher, D. (2006). Survey of chronic pain in Europe: Prevalence, impact on daily life, and treatment. *Eur J Pain* 10, 287–333.

Bush, T.L., Miller, S.R., Golden, A.L., Hale, W.E. (1989). Self-report and medical record report agreement of selected medical conditions in the elderly. *Am J Public Health* 79, 1554–1556.

Fishbain, D.A., Cutler, R., Rosomoff, H.L., Rosomoff, R.S. (1997). Chronic pain-associated depression: Antecedent or consequence of chronic pain? A review. *Clin J Pain* 13, 116–137.

Frobert, O., Fossgreen, J., Sondergaard-Petersen, J., Hede, J., Bagger, J.P. (1999). Musculo-skeletal pathology in patients with angina pectoris and normal coronary angiograms. *J Intern Med* 245, 237–246.

Frobert, O., Rendt-Nielsen, L., Bak, P., Funch-Jensen, P., Peder, B.J. (1996). Pain perception and brain evoked potentials in patients with angina despite normal coronary angiograms. *Heart* 75, 436–441.

Gerdle, B., Bjork, J., Henriksson, C., Bengtsson, A. (2004). Prevalence of current and chronic pain and their influences upon work and healthcare-seeking: A population study. *J Rheumatol* 31, 1399–1406.

Goodson, J.N., Smith, S.B., Goebel, A. (2010). Cardiovascular risk factors are increased in people reporting chronic pain symptoms. *Rheumatology (Oxford)* 49 (Suppl. 1), i32.

Haapanen, N., Miilunpalo, S., Pasanen, M., Oja, P., Vuori, I. (1997). Agreement between questionnaire data and medical records of chronic diseases in middle-aged and elderly Finnish men and women. *Am J Epidemiol* 145, 762–769.

Kamaleri, Y., Natvig, B., Ihlebaek, C.M., Benth, J.S., Bruusgaard, D. (2008a). Number of pain sites is associated with demographic, lifestyle, and health-related factors in the general population. *Eur J Pain* 12, 742–748.

Kamaleri, Y., Natvig, B., Ihlebaek, C.M., Bruusgaard, D. (2008b). Localized or widespread musculoskeletal pain: Does it matter? *Pain* 138, 41–46.

Lampe, F.C., Walker, M., Lennon, L.T., Whincup, P.H., Ebrahim, S. (1999). Validity of a self-reported history of doctor-diagnosed angina. *J Clin Epidemiol* 52, 73–81.

Lavey, E.B., Winkle, R.A. (1979). Continuing disability of patients with chest pain and normal coronary arteriograms. *J Chronic Dis* 32, 191–196.

Lindgren, H., Bergman, S. (2010). Chronic musculoskeletal pain predicted hospitalisation due to serious medical conditions in a 10 year follow up study. *BMC Musculoskelet Disord* 11, 127.

Linton, S.J. (1976). A review of psychological risk factors in back and neck pain. *Spine (Phila Pa 1976)* 25, 1148–1156.

Macfarlane, G.J., Beasley, M., Jones, E.A., Prescott, G.J., Docking, R., Keeley, P., McBeth, J., Jones, G.T. (2012). The prevalence and management of low back pain across adulthood: Results from a population-based cross-sectional study (the MUSICIAN study). *Pain* 153, 27–32.

McBeth, J., Symmons, D.P., Silman, A.J., Allison, T., Webb, R., Brammah, T., Macfarlane, G.J. (2009). Musculoskeletal pain is associated with a long-term increased risk of cancer and cardiovascular-related mortality. *Rheumatology* 48, 74–77.

McWilliams, L.A., Cox, B.J., Enns, M.W. (2003). Mood and anxiety disorders associated with chronic pain: An examination in a nationally representative sample. *Pain* 106, 127–133.

Muller, U., Tanzler, K., Burger, A., Staub, L., Tamcan, O., Roeder, C. (2008). A pain assessment scale for population-based studies: Development and validation of the pain module of the Standard Evaluation Questionnaire. *Pain* 136, 62–74.

Okura, Y., Urban, L.H., Mahoney, D.W., Jacobsen, S.J., Rodeheffer, R.J. (2004). Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension, myocardial infarction and stroke but not for heart failure. *J Clin Epidemiol* 57, 1096–1103.

Palmer, K.T., Calnan, M., Wainwright, D., Poole, J., O'Neill, C., Winterbottom, A., Watkins, C., Coggon, D. (2005). Disabling musculoskeletal pain and its relation to somatization: A community-based postal survey. *Occup Med (Lond)* 55, 612–617.

Penny, K.I., Purves, A.M., Smith, B.H., Chambers, W.A., Smith, W.C. (1999). Relationship between the chronic pain grade and measures of physical, social and psychological well-being. *Pain* 79, 275–279.

Pinsky, J.L., Jette, A.M., Branch, L.G., Kannel, W.B., Feinleib, M. (1990). The framingham disability study: Relationship of various coronary heart disease manifestations to disability in older persons living in the community. *Am J Public Health* 80, 1363–1367.

Raftery, M.N., Sarma, K., Murphy, A.W., De la, H.D., Normand, C., McGuire, B.E. (2011). Chronic pain in the Republic of Ireland – community prevalence, psychosocial profile and predictors of pain-related disability: Results from the Prevalence, Impact and Cost of Chronic Pain (PRIME) study, part 1. *Pain* 152, 1096–1103.

Rosamond, W.D., Sprafka, J.M., McGovern, P.G., Nelson, M., Luepker, R.V. (1995). Validation of self-reported history of acute myocardial infarction: Experience of the Minnesota Heart Survey Registry. *Epidemiology* 6, 67–69.

Rugulies, R. (2002). Depression as a predictor for coronary heart disease. a review and meta-analysis. *Am J Prev Med* 23, 51–61.

Smith, B.H., Elliott, A.M., Chambers, W.A., Smith, W.C., Hannaford, P.C., Penny, K. (2001). The impact of chronic pain in the community. *Fam Pract* 18, 292–299.

Smith, B.H., Penny, K.I., Purves, A.M., Munro, C., Wilson, B., Grimshaw, J., Chambers, W.A., Smith, W.C. (1997). The Chronic Pain Grade questionnaire: Validation and reliability in postal research. *Pain* 71, 141–147.

Stansfeld, S.A., Fuhrer, R., Shipley, M.J., Marmot, M.G. (2002). Psychological distress as a risk factor for coronary heart disease in the Whitehall II Study. *Int J Epidemiol* 31, 248–255.

Torrance, N., Elliott, A.M., Lee, A.J., Smith, B.H. (2010). Severe chronic pain is associated with increased 10 year mortality. A cohort record linkage study. *Eur J Pain* 14, 380–386.

Urquhart, D.M., Berry, P., Wluka, A.E., Strauss, B.J., Wang, Y., Proietto, J., Jones, G., Dixon, J.B., Cicuttini, F.M. (2011). Increased fat mass is associated with high levels of low back pain intensity and disability. *Spine (Phila Pa 1976)* 36, 1320–1325.

Viikari-Juntura, E., Shiri, R., Solovieva, S., Karppinen, J., Leino-Arjas, P., Varonen, H., Kalso, E., Ukkola, O. (2008). Risk factors of atherosclerosis and shoulder pain – is there an association? A systematic review. *Eur J Pain* 12, 412–426.

Vogt, M.T., Nevitt, M.C., Cauley, J.A. (1997). Back problems and atherosclerosis. The study of osteoporotic fractures. *Spine (Phila Pa 1976)* 22, 2741–2747.

Von, K.M., Ormel, J., Keefe, F.J., Dworkin, S.F. (1992). Grading the severity of chronic pain. *Pain* 50, 133–149.

World Health Organization (2000). Obesity: Preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser* 894 (i–xii), 1–253.

World Health Organization. Global recommendations on physical activity for health. (2010).