Is Chronic Widespread Pain a Predictor of All-Cause Morbidity? A 3 Year Prospective Population Based Study in Family Practice

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ABSTRACT. ***Objective.*** To investigate whether chronic widespread pain predicts illness seen in general practice in a 3 year followup period.

Methods. A postal questionnaire was conducted in an adult family practice population sample of 3968, and there were 2606 responders (66%). From the 2296 responders who consented to their record review, we identified 184 subjects with chronic widespread pain and assessed their outcome based on the first recorded morbidity within each of 15 categories during a 3 year followup period of computerized family practice records. Psychological distress at baseline was also measured using the Hospital Anxiety and Depression scale.

Results. Of the survey responders, 2089 subjects (91%) completed the full 3 year followup period. Out of the 15 main morbidity categories examined, 11 were associated with pain status at baseline. The strongest associations between chronic widespread pain at baseline and subsequent morbidity, adjusted for age, sex, and social deprivation, were for musculoskeletal (MSK) disorders (rate ratio 4.36; 95% confidence interval 3.2–5.9), accidents (2.46; 95% CI 1.2–5.1), mental health disorders (2.24; 95% CI 1.5–3.3), dermatological disorders (2.16; 95% CI 1.6–2.9), and infections (1.96; 95% CI 1.3–2.9). Controlling for psychological distress reduced the strength of associations between chronic widespread pain and future morbidity, but 9 of the 11 were still statistically significant. In the 3 year followup period, an estimated 7.7% of all non-MSK and 12.6% of all MSK morbidity consultations were related to chronic widespread pain as reported at baseline.

Conclusion. People who report chronic widespread pain subsequently consult more frequently about non-MSK and MSK problems than people with no pain, and this is not explained by psychological distress. The overall impact on healthcare use is substantial. Our study provides more evidence for overlap and links between morbidities that may be part of a larger pathological or somatization syndrome. (J Rheumatol 2005;32:1341–8)

Key Indexing Terms:
PAIN MORBIDITY PROSPECTIVE STUDIES FAMILY PRACTICE

Chronic widespread pain is a commonly reported symptom in the general population, with a one-month prevalence of around 10%[1], and followup studies suggest that it is a persisting condition[2,3]. It is the cardinal symptom of fibromyalgia syndrome, although only a minority of sufferers will have a high tender point count in addition to widespread pain[4]. In the American College of Rheumatology criteria for fibromyalgia, chronic widespread pain is defined for classification purposes as axial pain and pain in any part of contralateral body quadrants that has persisted for at least 3 months[5]. In the rheumatology literature, chronic widespread pain and regional pain syndromes have been considered as specific musculoskeletal (MSK) disorders. However, a cross sectional population study[6] described an association between chronic widespread pain and other symptoms, which suggested they may be part of a "complex syndrome" of overlapping functional or medically unexplained symptoms[7]. Possible explanations of such overlap include the close relationship between chronic widespread pain and psychological distress[8], the occurrence of which together results in persistence of the pain symptom[9,10] or underlying physiological mechanisms such as abnormal responses to stress[7]. Prospective studies have examined the link between chronic widespread pain and subsequent self-reported morbidity, healthcare use, and certified causes of mortality[6,11]. However, there has been no prospective study investigating the hypothesis of a link between chronic widespread pain and all-cause morbidity. We have prospectively examined whether chronic widespread pain, ascertained by self-report in a population sample, predicts subsequent morbidity as measured by family practice consultations over a 3 year period in the surveyed population.

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MATERIALS AND METHODS

The design was a prospective population based study. There were 2 phases: Phase 1 was a postal survey of an adult general population sample registered with one group family practice; Phase 2 followed up the family practice records of survey responders for a 3 year period.

Study setting and sample. The study took place in a semi-urban group practice of 4 general (family) practitioners in the region of North Staffordshire, United Kingdom. As more than 95% of the British population is registered with a family practitioner, the practice register forms an effective sampling frame of a local population, regardless of actual use of healthcare. A 50% random sample of adults aged 18 to 75 years (n = 3968) registered with the study general practice were mailed the survey in August 1996. The study practice had complete computerized records of all patient contacts since 1990 and is a recording practice for the Royal College of General Practitioners (UK), which collects family practice data for a national morbidity database. The project had Local Research Ethics Committee approval.

Phase 1: Establishing the study cohort. The postal survey included front and back body drawings on which subjects were asked to shade the location of any pain they had experienced in the previous month and which had lasted for more than one day. Duration of the most troublesome pain was recorded as the number of days in pain during the previous 12 months. This pain manikin has been validated as a measure of pain for the purposes of research[12,13]. A major potential confounder of the link between chronic widespread pain and subsequent consultation is psychological distress, because it is known to be a strong predictor of healthcare use and because it has been linked to widespread pain. So the questionnaire also included the Hospital Anxiety and Depression (HAD) scale[14] to assess self-reported psychological status, a tool that has been validated for use in the general population. There were 2606 (66%) responders to our questionnaire survey, of whom 2348 gave consent to record review. After excluding those with missing data, the baseline cohort consisted of 2296 subjects who had full questionnaire data and had consented to record review. An initial record review was also completed that covered the period 12 months before the survey. The medical record review was used to classify survey responders at baseline according to whether they had or had not consulted for a particular morbidity in the year before the survey.

Phase 2: Followup. This was based on record review for the 36 months after the survey (August 1996 to August 1999). All clinical morbidity was identified from computerized diagnostic coding used by the family practitioners and based on the Read Code classification[15,16], a standard coding system within the National Health Service in the UK. This classification system groups specific clinical conditions into 19 main diagnostic chapters, e.g., Chapter E (Mental disorders) or Chapter N (Musculoskeletal disorders), and provides an additional set of categories that reflect the features of problems seen in family practice, for example Chapter R (Symptoms and signs), Chapter S (Injuries relating to trauma, e.g., minor injuries and fractures), Chapter T (Accidents relating to miscellaneous causes, e.g., falls, transport accidents, medical procedures), and Chapter Z (Unspecified problems). The Read classification has a hierarchical structure in which each of the 19 Read chapters is divided into 4 further subgroupings, and there are over 100,000 morbidity codes that could have been used by the family practitioner in consultations. While we had the consultation detail on individual morbidity, because of sample size issues, we grouped all the individual morbidity codes that had been used by the family practitioners into 15 main chapter groupings.

Information downloaded from practice records also included residential postal codes. These postal codes were used to determine social deprivation status based on the Townsend score[17]. This score uses data from the national UK census on housing quality, car ownership, and number of persons in the household, to produce a composite score of relative deprivation. All clinical records were anonymized for the purposes of the study.

Study definitions: "exposures." The American College of Rheumatology definition of chronic widespread pain is axial pain and pain in any part of 2 contralateral body quadrants that has persisted for at least 3 months, so the baseline cohort was classified into 4 groups: (1) no pain; (2) pain of less than 3 months' duration — nonchronic pain (NCP); (3) non-widespread pain of more than 3 months' duration — chronic regional pain (CRP); and (4) widespread pain of more than 3 months' duration — chronic widespread pain (CWP). The HAD scale was defined into 3 categories of psychological distress using thresholds suggested in previous studies[18,19]: (1) non-case (score 0 to 7), (2) borderline case (score 8 to 10), and (3) definite case (score 11 or greater).

Study definitions: "outcomes." Nineteen diagnostic chapters were potential morbidity outcomes, but 4 were excluded because of small numbers. The outcomes were defined in 2 ways. The first was a morbidity count, based on how many of the 15 morbidity outcomes occurred at least once in each individual's record in the 3 year followup period, categorized into (1) "average" morbidity count — consultation for 2 morbidities or less, or (2) "higher" morbidity count — consultation for 3 or more morbidities. The second definition examined each of the 15 chapters separately. Using consultation data for the 12 months prior to the survey, any individuals who had consulted within a particular chapter in that period were excluded from the analyses of that morbidity in the followup period. The first event of that morbidity in the followup period was identified in all individuals with no such prior event and this was identified as the "incident" outcome.

Statistical analysis. Descriptive statistics on the cohort groups are given by age, sex, and Townsend deprivation score, and chi-square tests were used to assess associations between cohort groups and sociodemographic characteristics.

The association of pain status for the whole study cohort and psychological distress at baseline with morbidity count in the followup period was assessed using unconditional logistic regression. Odds ratios were adjusted first for age, sex, and deprivation, and then for age, sex, deprivation, baseline pain status, and psychological distress. "Incident" rate was defined as the number of subjects with a "first" recorded morbidity category per 1000 person-years at risk, calculated as time from baseline to the "first" event in the followup period, for the subcohort of individuals without that consultation category in the year before survey. Multivariate analyses using Cox regression were used to compare morbidity outcomes in the 3 year followup period in each pain group with the no-pain group. Rate ratios were adjusted for (1) age, sex, and deprivation, and (2) age, sex, deprivation, and psychological distress. Chi-square tests were also used to assess biases in nonresponse to the survey and in dropout during the 3 year followup period. Statistical significance is defined as $p < 0.05$, all hypothesis testing was 2-tailed, and analyses were performed using Stata version 7.0.

The influence of chronic widespread pain on future family practice workload was assessed using 2 broad categories for the consultation outcomes: any MSK (Read Chapter N only) and any non-MSK consultation (all other 14 Read chapters). Population attributable fractions (PAF)[20] were calculated for the individual pain groups compared to the no-pain group using odds ratios adjusted for age, sex, and deprivation score only. With the pain exposure status based on 3 levels, the formula used to calculate PAF was: $PAF_k = p_k' (\theta_k - 1)/\theta_k$, where level k is one of the 3 pain groups (no-pain group is reference category), p_k' is the fraction of the total cases attributable to exposure at level k, and θ_k is the level-specific adjusted odds ratio.

RESULTS

Characteristics of the study cohort. Of the total 2296 subjects at baseline, 812 (35.4%) had no pain, 705 (30.7%) had nonchronic pain, 595 (25.9%) had chronic regional pain, and 184 (8.0%) had chronic widespread pain (Table 1). There were no sex or deprivation differences between the pain groups. However, the proportion who reported chronic widespread pain was higher in the oldest age group, 61–75 years (13.0%), compared with the youngest age group,

Table 1. Characteristics of the baseline cohort groups. Figures in brackets are percentage of each respective risk factor category.

Risk Factors	Category	No Pain (n = 812), n (%)	NCP (n = 705), n (%)	CRP (n = 595), n (%)	CWP (n = 184), n (%)	Totals, n (%)	p†
Sex	Male	367 (34.3)	335 (31.3)	284 (26.5)	84 (7.9)	1070 (46.6)	0.740
	Female	445 (36.3)	370 (30.2)	311 (25.4)	100 (8.1)	1226 (53.4)	
Age, yrs	18–30	177 (45.0)	138 (35.1)	64 (16.3)	14 (3.6)	393 (17.1)	< 0.001
	31–40	175 (42.0)	153 (36.8)	76 (18.3)	12 (2.9)	416 (18.1)	
	41–50	152 (31.0)	170 (34.7)	138 (28.2)	30 (6.1)	490 (21.3)	
	51–60	125 (28.8)	115 (26.4)	140 (32.2)	55 (12.6)	435 (18.9)	
	61–75	183 (32.5)	129 (23.0)	177 (31.5)	73 (13.0)	562 (24.5)	
Deprivation score*	–2.72 to –0.62 (affluent)	222 (36.1)	191 (31.1)	159 (25.8)	43 (7.0)	615 (26.8)	0.938
	–0.61 to 0.09	194 (35.8)	167 (30.8)	133 (24.5)	48 (8.9)	542 (23.6)	
	0.10 to 0.60	197 (36.0)	160 (29.2)	145 (26.4)	46 (8.4)	548 (23.9)	
	0.61 to 2.24 (deprived)	189 (33.3)	179 (31.5)	154 (27.1)	46 (8.1)	568 (24.7)	
HAD score	Non-case	620 (42.6)	429 (29.5)	326 (22.4)	80 (5.5)	1455 (63.4)	< 0.001
	Borderline	121 (26.2)	150 (32.5)	140 (30.4)	50 (10.9)	461 (20.1)	
	Definite	71 (18.7)	126 (33.1)	129 (34.0)	54 (14.2)	380 (16.6)	

*Less than the total of 2296 because of 23 missing values. † Chi-square tests. NCP: nonchronic pain, CRP: chronic regional pain, CWP: chronic widespread pain, HAD: Hospital Anxiety and Depression scale.

18–30 years (3.6%), and in those with definite psychological distress (14.2%) compared with no psychological distress (5.5%). There was complete 3 year record review followup for 2089 (91%) subjects.

Study risk factors and subsequent morbidity counts. Table 2 shows the effect of pain and psychological distress on subsequent morbidity count. Chronic widespread pain was significantly associated with a higher morbidity count compared to the no-pain group, having adjusted for age, sex, and deprivation (odds ratio 5.55; 95% confidence interval 3.6–8.6); and definite cases of psychological distress were more likely to have a higher morbidity count compared to non-cases (2.42; 95% CI 1.9–3.2). The final column (Table 2) shows the effect of psychological distress on the association between chronic widespread pain and subsequent morbidity count. Psychological distress confounds this association, resulting in reduction of the strength of association between chronic widespread pain and subsequent higher morbidity count (4.68; 95% CI 3.0–7.3).

Pain and subsequent morbidity

Chronic widespread pain and morbidity. The highest consulting rates in the chronic widespread pain group were for MSK disorders (rate per 1000 person-years = 568; 95% CI 438–736), symptoms and signs (245; 95% CI 190–315), dermatological disorders (203; 95% CI 93–130), respiratory disorders (182; 95% CI 135–244), neurological and sense organ disorders (176; 95% CI 136–228), and mental health disorders (103; 95% CI 75–140). There were 11 statistically significant associations between chronic widespread pain and morbidity, having adjusted for age, sex, and deprivation (Tables 3A, 3B, 3C). Future morbidity was also linked to

Table 2. Association between study risk factors measured at baseline and subsequent morbidity count in the 3 year followup period for all 2296 subjects in the cohort.

Group	Category	Total No. of Consultations	No. with Low (2 or less) Morbidity Count (%)	No. with High (3 or more) Morbidity Count (%)	Adjusted OR* (95% CI)	Adjusted OR** (95% CI)
Baseline pain status	No pain, n = 812	11,328	417 (51.3)	395 (48.7)	1.0†	1.0†
	NCP, n = 705	9,704	259 (36.7)	446 (63.3)	1.89 (1.5–2.3)	1.76 (1.4–2.2)
	CRP, n = 595	9,674	174 (29.2)	421 (70.8)	2.48 (2.0–3.1)	2.22 (1.8–2.8)
	CWP, n = 184	3,566	27 (14.7)	157 (85.3)	5.55 (3.6–8.6)	4.68 (3.0–7.3)
HAD Score	Non-case, n = 1455	19,428	646 (44.4)	809 (55.6)	1.0†	1.0†
	Borderline, n = 461	7,445	140 (30.4)	321 (69.6)	1.68 (1.3–2.1)	1.47 (1.2–1.9)
	Definite, n = 380	7,399	91 (24.0)	289 (76.0)	2.42 (1.9–3.2)	1.94 (1.5–2.5)

* Odds ratio adjusted for age, sex and deprivation. ** Odds ratio adjusted for age, sex, deprivation, baseline pain status, and Hospital Anxiety and Depression scale score. † Reference category. NCP: nonchronic pain, CRP: chronic regional pain, CWP: chronic widespread pain.

Table 3A. Incident followup morbidity rates in relation to baseline status in subjects without that morbidity consultation in the 12 months before survey.

Incident Cohort Groups	Morbidity	No. (%)	Incidence Rate per 1000 Person-Years (95% CI)	Adjusted Rate Ratio (1)*	Adjusted Rate Ratio (2)*
No pain, n = 715	Musculoskeletal	203 (28.4)	116.2 (101.3–133.4)	1.0†	1.0†
NCP, n = 544	disorders	230 (42.3)	200.9 (176.6–228.7)	**1.75** (1.5–2.1)	**1.72** (1.4–2.1)
CRP, n = 359		187 (52.1)	261.9 (227.0–302.3)	**2.10** (1.7–2.6)	**2.04** (1.7–2.5)
CWP, n = 74		57 (77.0)	567.8 (438.0–736.2)	**4.36** (3.2–5.9)	**4.11** (3.0–5.7)
No pain, n = 807	Accidents	21 (2.6)	9.1 (6.0–14.0)	1.0†	1.0†
NCP, n = 699		20 (2.9)	10.1 (6.5–15.7)	1.16 (0.6–2.2)	1.03 (0.6–1.9)
CRP, n = 585		30 (5.1)	18.4 (12.9–26.4)	**2.00** (1.1–3.5)	1.68 (0.9–3.0)
CWP, n = 181		12 (6.6)	24.3 (13.8–42.7)	**2.46** (1.2–5.1)	1.88 (0.9–4.0)
No pain, n = 760	Mental health	98 (12.9)	47.5 (39.0–57.9)	1.0†	1.0†
NCP, n = 642	disorders	96 (15.0)	56.6 (46.3–69.1)	1.20 (0.9–1.6)	1.03 (0.8–1.4)
CRP, n = 535		102 (19.1)	75.1 (61.8–91.2)	**1.62** (1.2–2.2)	1.32 (0.99–1.8)
CWP, n = 156		39 (25.0)	102.5 (74.9–140.3)	**2.24** (1.5–3.3)	**1.67** (1.1–2.5)
No pain, n = 712	Dermatological	175 (24.6)	99.2 (85.6–115.1)	1.0†	1.0†
NCP, n = 612	disorders	156 (25.5)	103.0 (88.1–120.5)	1.04 (0.8–1.3)	0.98 (0.8–1.2)
CRP, n = 493		133 (27.0)	110.0 (92.8–130.4)	1.12 (0.9–1.4)	1.05 (0.8–1.3)
CWP, n = 150		65 (43.3)	203.3 (159.4–259.2)	**2.16** (1.6–2.9)	**1.95** (1.5–2.6)
No pain, n = 771	Infections	105 (13.6)	51.1 (42.2–61.9)	1.0†	1.0†
NCP, n = 646		118 (18.3)	70.4 (58.8–84.3)	**1.41** (1.1–1.8)	**1.33** (1.0–1.7)
CRP, n = 551		92 (16.7)	63.7 (51.9–78.1)	**1.40** (1.1–1.9)	1.31 (0.98–1.8)
CWP, n = 168		35 (20.8)	83.4 (59.9–116.1)	**1.96** (1.3–2.9)	**1.75** (1.2–2.6)

* Rate ratios adjusted for: (1) age, sex, and deprivation, and (2) for age, sex, deprivation, and HAD score. † Reference category. Bold type indicates significance at 95% level. NCP: nonchronic pain, CRP: chronic regional pain, CWP: chronic widespread pain.

Table 3B. Incident followup morbidity rates in relation to baseline status in subjects without that morbidity consultation in the 12 months before survey.

Incident Cohort Groups	Morbidity	No. (%)	Incidence Rate per 1000 Person-Years (95% CI)	Adjusted Rate Ratio (1)*	Adjusted Rate Ratio (2)*
No pain, n = 716	Genitourinary	138 (19.3)	74.3 (62.9–97.8)	1.0†	1.0†
NCP, n = 604	disorders	147 (24.3)	98.8 (84.0–116.1)	**1.40** (1.1–1.8)	**1.34** (1.1–1.7)
CRP, n = 517		107 (20.7)	83.0 (68.7–100.3)	**1.29** (1.0–1.7)	1.22 (0.9–1.6)
CWP, n = 160		46 (28.8)	120.7 (90.4–161.1)	**1.87** (1.3–2.6)	**1.70** (1.2–2.4)
No pain, n = 776	Endocrine	42 (5.4)	19.3 (14.3–26.2)	1.0†	1.0†
NCP, n = 675	disorders	38 (5.6)	20.3 (14.8–27.9)	1.13 (0.7–1.8)	1.11 (0.7–1.7)
CRP, n = 555		46 (8.3)	30.2 (22.6–40.3)	1.33 (0.9–2.0)	1.29 (0.8–2.0)
CWP, n = 168		21 (12.5)	47.2 (30.8–72.4)	**1.86** (1.1–3.2)	**1.79** (1.0–3.1)
No pain, n = 697	Symptoms	205 (29.4)	121.3 (105.7–139.0)	1.0†	1.0†
NCP, n = 551	and signs	201 (36.5)	160.7 (140.0–184.6)	**1.34** (1.1–1.6)	**1.24** (1.0–1.5)
CRP, n = 466		189 (40.6)	184.8 (160.3–213.2)	**1.44** (1.2–1.8)	**1.32** (1.1–1.6)
CWP, n = 119		60 (50.4)	244.5 (189.9–314.9)	**1.86** (1.4–2.5)	**1.60** (1.2–2.2)
No pain, n = 714	Neurological and	153 (21.4)	84.6 (72.2–99.1)	1.0†	1.0†
NCP, n = 625	sense organ disorders	187 (29.9)	125.8 (109.0–145.2)	**1.52** (1.2–1.9)	**1.50** (1.2–1.9)
CRP, n = 504		147 (29.2)	123.3 (104.9–144.9)	**1.39** (1.1–1.8)	**1.37** (1.1–1.7)
CWP, n = 144		57 (39.6)	175.6 (135.5–227.7)	**1.79** (1.3–2.4)	**1.74** (1.3–2.4)
No pain, n = 763	Cardiovascular	99 (13.0)	48.0 (39.4–58.4)	1.0†	1.0†
NCP, n = 649	disorders	73 (11.2)	41.5 (33.0–52.2)	0.93 (0.7–1.3)	0.90 (0.7–1.2)
CRP, n = 517		84 (16.2)	61.3 (49.5–75.9)	1.06 (0.8–1.4)	1.00 (0.8–1.4)
CWP, n = 153		43 (28.1)	116.8 (86.6–157.5)	**1.75** (1.2–2.5)	**1.65** (1.1–2.4)
No pain, n = 756	Gastrointestinal	103 (13.6)	51.2 (42.2–62.1)	1.0†	1.0†
NCP, n = 638	disorders	119 (18.7)	73.1 (61.1–87.5)	**1.47** (1.1–1.9)	**1.37** (1.1–1.8)
CRP, n = 521		117 (22.5)	90.4 (75.4–108.4)	**1.68** (1.3–2.2)	**1.57** (1.2–2.1)
CWP, n = 153		35 (22.9)	91.7 (65.9–127.8)	**1.61** (1.1–2.4)	1.40 (0.9–2.1)

* Rate ratios adjusted for: (1) age, sex, and deprivation, and (2) for age, sex, deprivation, and HAD score. † Reference category. Bold type indicates significance at 95% level. NCP: nonchronic pain, CRP: chronic regional pain, CWP: chronic widespread pain.

Table 3C. Incident followup morbidity rates in relation to baseline status in subjects without that morbidity consultation in the 12 months before survey.

Incident Cohort Groups	Morbidity	No. (%)	Incidence Rate per 1000 Person-Years (95% CI)	Adjusted Rate Ratio (1)*	Adjusted Rate Ratio (2)*
No pain, n = 804	Unspecified	31 (3.9)	13.7 (9.6–19.5)	1.0†	1.0†
NCP, n = 692		31 (4.5)	16.0 (11.2–22.7)	1.72 (0.7–1.9)	1.10 (0.7–1.8)
CRP, n = 579		34 (5.9)	21.2 (15.1–29.6)	1.45 (0.9–2.4)	1.33 (0.8–2.2)
CWP, n = 180		13 (7.2)	26.7 (15.5–46.0)	1.73 (0.9–3.3)	1.49 (0.8–2.9)
No pain, n = 781	Neoplasms	49 (6.3)	22.6 (17.1–29.8)	1.0†	1.0†
NCP, n = 689		60 (8.7)	31.9 (24.7–41.0)	1.42 (0.97–2.1)	1.40 (0.96–2.1)
CRP, n = 571		49 (8.6)	31.3 (23.6–41.4)	1.35 (0.9–2.0)	1.33 (0.9–2.0)
CWP, n = 174		19 (10.9)	40.8 (26.0–63.9)	1.70 (0.99–2.9)	1.66 (0.95–2.9)
No pain, n = 620	Respiratory	209 (33.7)	152.5 (133.2–174.7)	1.0†	1.0†
NCP, n = 519	disorders	207 (39.9)	185.4 (161.7–212.4)	**1.23** (1.0–1.5)	1.19 (0.98–1.5)
CRP, n = 430		191 (44.4)	212.6 (184.5–245.0)	**1.39** (1.1–1.7)	**1.35** (1.1–1.7)
CWP, n = 114		44 (38.6)	181.9 (135.3–244.4)	1.22 (0.9–1.7)	1.17 (0.8–1.6)
No pain, n = 768	Injury	155 (20.2)	79.1 (67.6–92.6)	1.0†	1.0†
NCP, n = 648		177 (27.3)	111.2 (95.9–128.8)	**1.37** (1.1–1.7)	**1.32** (1.1–1.7)
CRP, n = 536		140 (26.1)	107.5 (91.1–126.8)	**1.41** (1.1–1.8)	**1.33** (1.1–1.7)
CWP, n = 172		38 (22.1)	88.7 (64.5–121.8)	1.18 (0.8–1.7)	1.08 (0.8–1.6)

* Rate ratios adjusted for (1) age, sex, and deprivation, and (2) age, sex, deprivation, and HAD score. † Reference category. Bold type indicates significance at 95% level. NCP: nonchronic pain, CRP: chronic regional pain, CWP: chronic widespread pain.

nonchronic and chronic regional pain, but these associations were weaker than for chronic widespread pain. The strongest associations between chronic widespread pain and subsequent morbidity were for MSK disorders (rate ratio 4.36; 95% CI 3.2–5.9), accidents (2.46; 95% CI 1.2–5.1), mental health disorders (2.24; 95% CI 1.5–3.3), dermatological disorders (2.16; 95% CI 1.6–2.9), and infections (1.96; 95% CI 1.3–2.9) (Table 3A). Four outcomes did not show an association with chronic widespread pain: unspecified disorders, neoplasms, respiratory disorders, and injury (Table 3C).

Effect of psychological distress. Adjusting for self-reported psychological distress, in addition to age, sex, and deprivation, resulted in reduction of the strength of all associations between the pain groups and subsequent morbidity. However, most (9 of the 11) chronic widespread pain associations with subsequent morbidity remained significant (Tables 3A, 3B, 3C).

The confounding effect of psychological distress on the association between chronic widespread pain and morbidity outcome was estimated by comparing rate ratios adjusted for age, sex, and deprivation with the same rate ratios adjusted additionally for psychological distress. Confounding effect of psychological distress was greatest for accidents (2.46 vs 1.88), mental health disorders (2.24 vs 1.67), and MSK disorders (4.36 vs 4.11) (Table 3A), and least for neurological and sense organ disorders (1.79 vs 1.74), endocrine disorders (1.86 vs 1.79), and cardiovascular disorders (1.75 vs 1.65) (Table 3B).

Estimating impact on family practice consultations. Out of the total cohort, 2050 subjects had consulted for at least one non-MSK disorder and 1108 subjects had consulted at least once for a MSK disorder in the 3 year followup period. Of these, 180 (8.8%) and 155 (14.0%), respectively, were in the chronic widespread pain group (Table 4). The chronic widespread pain group was more likely than the no-pain group to have consulted for non-MSK disorders (adjusted OR 8.31, 95% CI 3.0–23.0) and MSK disorders (adjusted 9.84; 95% CI 6.4–15.1), having adjusted for age, sex, and deprivation. Therefore, in the general population, an estimated 7.7% of all non-MSK and 12.6% of all MSK consultations are related to chronic widespread pain.

Survey nonresponse and dropout in the followup period. The study cohort of 2296 was drawn from the sample of 2606 survey responders, but there were 1362 (34.3%) subjects who had not responded to the baseline survey. Responders were more likely to be older (chi-square tests $p < 0.001$), female ($p < 0.001$), and relatively affluent ($p < 0.05$) compared to nonresponders.

The number of subjects who were lost to followup over the 3 year study period was 210 (9.1% of sample). The mean time of followup for these dropouts was 1.6 years (SD 0.84 yrs). The principal reason for dropout was mostly relocation from the study practice (n = 160), and the remainder (n = 50) was due to deaths in the 3 year followup period. Of the no-pain group ("unexposed"), 8.9% were lost over the 3 year period compared with 9.1% of the chronic widespread pain group lost to followup.

DISCUSSION

Chronic widespread pain predicted higher subsequent consultation rates in 11 out of the 15 categories of family prac-

Table 4. Influence of baseline pain status on subsequent non-MSK and MSK morbidity in family practice using the total of 2296 subjects.

Cohort Groups	Morbidity	No. with Morbidity	Fraction of Total Cases	Adjusted OR* (95% CI)	PAF (%)
No pain, n = 812	Non-MSK disorders	685	0.334	1.0†	NA
NCP, n = 705		637	0.311	1.76 (1.3–2.4)	13.4
CRP, n = 595		548	0.267	2.17 (1.5–3.1)	14.4
CWP, n = 184		180	0.088	8.31 (3.0–23.0)	7.7
No pain, n = 812	MSK disorders	253	0.229	1.0†	NA
NCP, n = 705		335	0.302	2.04 (1.7–2.5)	15.4
CRP, n = 595		365	0.329	3.18 (2.5–4.0)	22.6
CWP, n = 184		155	0.140	9.84 (6.4–15.1)	12.6

* Odds ratios adjusted for age, sex, and deprivation score. † Reference category. PAF: population attributable fraction, NCP: nonchronic pain, CRP: chronic regional pain, CWP: chronic widespread pain, NA: not applicable.

tice morbidity, and these associations were independent of age, sex, and social deprivation. The strongest associations were with musculoskeletal disorders, accidents, mental health, and dermatological disorders. These results suggest a broad picture of elevated morbidity in subjects with chronic widespread pain in a 3 year followup period. The chronic widespread pain cohort was compared with controls drawn from the same population base, and for each morbidity category a separate analysis was constructed that excluded at baseline those cohort members who had consulted for that morbidity in the year prior to the baseline survey. This strengthens the assumption that chronic widespread pain at baseline was studied for its potential causal association with the onset of the subsequent episode of morbidity. The associations observed suggested a dose-response relationship — weakest in the nonchronic pain group, moderate in the chronic regional pain group, and strongest in the chronic widespread pain group.

We examined separately the confounding effect of psychological distress on these associations. Self-reported psychological distress contributed to the associations between chronic widespread pain and subsequent morbidity, particularly those for accidents and mental health disorders, but did not explain them entirely. The association of chronic widespread pain with MSK disorders and mental health disorders suggests a causal coherence, in terms of the strength of association, plausibility, and consistency, based on previous studies[8,21]. While causal inference is possible for some of the morbidity outcomes, the caveat in the assessment of multiple outcomes is that some may have occurred by chance, and that for some morbidity outcomes based on consultations, the pain "exposure" at baseline may not in fact have been measured before their development.

Hypothesizing possible mechanisms of the study associations. Different explanations can be offered for the study findings. First, it is possible that chronic widespread pain in itself triggers a propensity to seek healthcare more frequently for a range of symptoms. Such heightened symptom awareness and illness behavior, whatever their cause, seem to be features of patients with chronic widespread pain[6]. Psychological distress is one predictor of this propensity, as reflected in the higher morbidity count in the 3 year followup period, and this has been confirmed in other studies[22,23]. However, the weaker but persisting associations after adjusting for psychological distress suggest that propensity to consult is unlikely to be the full explanation for these associations. Second, it is possible that frequent presentation provides the opportunity for family practitioners to detect or record more health problems (for example, cardiovascular disease or undifferentiated symptoms). Third, chronic widespread pain may be a part or consequence of the subjective health and personal experiences of the patients. In a qualitative exploration of the symptom of pain from the perspective of the patient, the wider meaning of pain encompassed not only bodily function, but also underlying explanations such as injuries and psychological causes, and the consequences of pain for their everyday life[24]. Therefore these chronic widespread pain associations might represent an overall "marker" of possible somatic syndromes[25,26]. Fourth, there are plausible reasons for supposing some of these associations might be related to shared pathological mechanisms or the influence one condition might have on increasing vulnerability to another. There is evidence that a range of symptoms and clinical conditions is more likely to be reported by such patients in specialist settings[27], and certain associations of pain are well reported, for example with depression[8] and gastrointestinal disorders[28]. There is some evidence that also supports the associations with genitourinary disorders[29], neurological disorders[30], cardiovascular disorders[31], and accidents[32]. The underlying mechanisms for these associations are a matter for developing debate, but potential pathogenic mechanisms based on neuroendocrine dysfunction in polysymptomatic syndromes have been proposed[32].

Chronic widespread pain was related to an estimated 7.7% of all non-MSK and 12.6% of MSK consultations, which suggests a substantial impact on consultation morbidity. Each of the morbidity categorizations used in this study included self-limiting, acute, and chronic disorders, and further examination would be required to disentangle the dis-

orders that are functional or that are objectively disease based. However, whatever the underlying explanations, an important fact remains: there are high levels of morbidity associated with chronic widespread pain that patients consult for, and which are likely to have an impact on their overall health status and use of healthcare.

Morbidity based on family practice consultations. Diagnosis in family practice has to take account of the undifferentiated and vague way in which symptoms often present. The morbidities were identified by broad terms used by family practitioners in everyday clinical contact. These labels possess face validity for family practice, but may differ from a diagnosis based on criteria such as blood tests for diabetes or radiographs for osteoarthritis. For the purposes of the study, we assumed that the broad terms represent symptoms presented to the family practitioner that are suggestive of a disease in one of the body systems. Although some of the labels such as "symptoms and signs" and "unspecified" are not defined clearly, it is also quite plausible that they might represent earlier stages of disease before the diagnosis is applied. While previous studies have validated the use of this type of data in family practice[33-36], morbidity based on consultations may be subject to misclassification errors. However, this issue is countered by the fact that misclassification in routine clinical data collection is likely to be random, thus underestimating any actual associations. It is also possible that there has been selectivity in what people might choose to present to their family practitioners, but our population sample was unselected by any healthcare or membership of particular groups, suggesting that the findings of this study would be internally valid.

Survey sampling and losses to followup. There were sociodemographic differences between the study cohort and nonresponders, and this may limit interpretation of the study in terms of overall generalizability. However, the losses to followup were small. For bias to result there would have to be differential dropout related to exposure and outcome. Since the major reason for dropout was relocation to a different family practice, it is difficult to envisage a link for dropout to be related to exposure measurement of pain by questionnaire and outcome measurement of morbidity by family practice records.

Implications for clinical practice. This study provides the first evidence of a link between chronic widespread pain and all-cause morbidity. While the precise role of this symptom in the development of the morbidity process is unknown, chronic widespread pain may have the potential as a useful symptom check for family practitioners in identifying a group of patients with complex clinical needs. The likely high impact on healthcare resources also suggests that subjects with such pain symptoms represent a target group for research into the mechanisms and prevention of a range of linked morbidities.

Our study has shown that people who report chronic widespread pain subsequently consult more frequently for nonmusculoskeletal as well as musculoskeletal problems than people with no pain, and this is independent of age, sex, or social deprivation. Psychological distress is a coexisting factor that influences, but does not account for, these relationships. The overall influence on healthcare use is substantial. Our study provides more evidence for overlap and links between morbidities that may be part of a larger pathological or somatization syndrome. The usefulness of pain as a marker of vulnerability to future morbidities or to future propensity to consult about symptoms, and the potential for reducing future morbidity with more effective management of chronic widespread pain, needs further investigation.

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