EXTENDED REPORT

Musculoskeletal pain is more generalised among people from ethnic minorities than among white people in Greater Manchester

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Ann Rheum Dis 2002;61:151–156

Objective: To assess the prevalence of musculoskeletal symptoms among the major ethnic minority populations of Greater Manchester.

Method: The study group was a community sample of 2117 adults from the Indian, Pakistani, Bangladeshi, and African Caribbean communities. Questionnaires administered by post and by an interviewer were used to assess the presence of any musculoskeletal pain, pain in specific joints, and the level of physical function. Ethnicity was self assigned. The results were compared with those from a recent study in the local white population using the same methodology.

Results: Overall response rate was 75% among the south Asian (Indian, Pakistani, and Bangladeshi) community and 47% among the African Caribbean community. The profile of musculoskeletal pain among the ethnic minority groups differed from that in the white population. Although musculoskeletal symptoms were slightly more prevalent among people from ethnic minority groups than among the white population, pain in multiple sites was considerably more common among ethnic minorities.

Conclusions: The finding that musculoskeletal pain is more widespread among ethnic minority communities in the UK has not previously been reported. This may reflect social, cultural, and psychological differences. The cause of the differences in the profile of pain and the health needs that follow need further investigation.

usculoskeletal disorders are a major cause of pain in the UK¹ and throughout the world.² The annual cost in the UK of back pain alone has been estimated to be several billion pounds.3 The prevalence and characteristics of musculoskeletal pain in different ethnic groups may vary because of genetic,⁴ environmental,⁵ or cultural⁶ differences in addition to the known influences of age,⁷ sex,⁷ socioeconomic status,⁷ and body mass index.⁸ There is good evidence of variation in musculoskeletal disease epidemiology among ethnic groups outside the UK,^{9 10} and there is evidence of variation in the epidemiology of other diseases within the UK.11 12 In addition, higher rates of general practice attendance are found among ethnic minorities.13 Some research in the UK investigating a variety of conditions has suggested that there are variations in musculoskeletal disease according to ethnicity.14 The profile of pain appears to differ between south Asian and white populations within the UK,15 and the prevalence of musculoskeletal symptoms is higher among Pakistanis living in the UK than among those who live in Pakistan.¹⁶ However, there has been little research specifically directed towards musculoskeletal epidemiology among ethnic minorities within the UK. We aimed at studying the musculoskeletal health needs of the largest ethnic minority communities in Greater Manchester and this paper presents the findings of the prevalence of musculoskeletal symptoms.

We had previously studied the musculoskeletal health needs of the general population of Tameside, Greater Manchester.⁷ That recent study was a postal questionnaire survey of a population sample from three Tameside practices, not including the practices in this study, and the study group was almost entirely white. An age and sex stratified sample of 6000 adults was mailed and the response rate was 78.5%. No interviews were undertaken. The questionnaire used was almost identical to the one used in this study.

METHODS Setting

The study was set in three general practices in Greater Manchester and focused on the four ethnic minority communities with the largest populations (table 1). Practices 1 and 2 were in Tameside, to the east of Manchester, where many people who would describe themselves as south Asian (Indian, Pakistani, or Bangladeshi) were believed to be registered. Practice 3 was in central Manchester where we expected a high proportion of registered patients who would describe themselves as African Caribbean. Tameside and Glossop and Central Manchester local research ethics committees granted ethical approval.

Sample size

We stratified the study group by sex and the following age groups: 16-44; 45-64; 65-74; 75+. We aimed at obtaining as complete a picture as possible of the ethnic minority population of the three practices, which we hoped would subsequently be generalisable. If we had managed to study 750 people from each age-sex band and each ethnic group, we would have enabled a prevalence of 5% to be detected with a precision of 1% and with 80% power. However the size and age structure of the ethnic minority populations prevented us from achieving this. The chosen practices had relatively large proportions of people registered from ethnic minorities compared with their neighbouring practices, but numbers of people from ethnic minority communities were still too small to achieve the required sample size, especially among the older age groups. We still aimed at obtaining a full picture of the ethnic minority population of the practices, but the sample

Abbreviations: mHAQ, modified Health Assessment Questionnaire

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Accepted 23 July 2001

Age group	<16	16-44	45–64	65–74	75+	Total
White	475861	980959	512431	216218	165770	2351239
Black Caribbean	3655	7716	4444	1047	233	17095
Black - African	1629	2820	625	142	24	5240
Black - Other	5049	3737	333	65	18	9202
Indian	9802	14334	4613	710	282	29741
Pakistani	21896	21110	5650	552	162	49370
Bangladeshi	5785	3919	1603	115	23	11445
Chinese	2098	4827	1118	206	74	8323
Other	7425	8482	1447	316	116	17786
Total	533200	1047904	532264	219371	166702	2499441

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size was considerably reduced. The study group was still stratified into the four age groups and all age groups were studied. Numbers in the older age groups were small, but all people believed to be from ethnic minority communities in these age groups were mailed.

Subject selection

In practices 1 and 2 we identified all people aged 16 or over whose name suggested south Asian ethnicity; this method has been used before.¹⁷ Because of the age structure of the population, we excluded 50% of those aged under 45 by using computer generated random numbers. In practice 3 the practice staff identified people who might classify themselves as African Caribbean and we included all of those aged 16 or over. Lists of subjects were checked to exclude those who had recently died and general practitioners were asked to identify people unsuitable for the study.

Questionnaire

We mailed the study group a questionnaire in English which included questions about the presence of musculoskeletal pain in the past month lasting more than one week; the sites of any musculoskeletal pain; the presence of pain in most joints; physical function measured by the modified Health Assessment Questionnaire (mHAQ)¹⁸; access to health care; demography including ethnicity according to the 1991 census categories (table 1). The mHAQ comprises eight questions and the overall scores range from 0 (no disability) to 3 (severe disability). Categories for self definition of ethnicity were chosen to enable comparison with previous studies and with routinely collected data. A personally addressed covering letter from the subject's general practitioner endorsing the study and encouraging participation was sent with the questionnaire. A reply paid envelope was included. People who did not respond were sent a reminder and then a repeat questionnaire.

Practice	Age/sex group	Number mailed	Mail response	Number remaining fo interview/ telephone	or Interview/ telephone response	Declined to participate	Moved away/died	No contact or information	Response rate excluding moved away/died (%)
Practice 1	Men 16-44	209	65	144	55	16	40	33	71
	Men 45–64	146	45	101	39	14	22	26	68
	Men 65–74	36	9	27	9	3	7	8	62
	Men 75+	17	6	11	4	3	4	0	77
	Women 16-44	207	75	132	75	9	18	30	79
	Women 45-64	111	40	71	42	10	4	15	77
	Women 65-74	25	8	17	9	4	2	2	74
	Women 75+	15	2	13	7	0	2	4	69
	Total	766	250	516	240	59	99	118	73
Practice 2	Men 16-44	187	50	137	71	9	23	34	74
	Men 45–64	51	16	35	21	5	5	4	80
	Men 65–74	18	3	15	7	2	4	2	71
	Men 75+	7	0	7	1	1	3	2	25
	Women 16-44	150	37	113	73	7	13	20	80
	Women 45-64	71	16	55	35	3	6	11	78
	Women 65–74	10	3	7	3	1	3	0	86
	Women 75+	7	2	5	4	0	1	0	100
	Total	501	127	374	215	28	58	73	77
Practice 3	Men 16-44	226	42	184	14	18	22	130	27
	Men 45–64	90	40	50	9	4	9	28	60
	Men 65–74	57	25	32	4	7	3	18	54
	Men 75+	19	9	10	2	1	1	6	61
	Women 16-44	309	114	195	25	21	17	132	48
	Women 45-64	96	52	44	8	7	4	25	65
	Women 65-74	40	23	17	1	3	1	12	62
	Women 75+	13	7	6	0	0	0	6	54
	Total	850	312	538	63	61	57	357	47

Table 3	Self defined ethnicity of all respondents.
Results ar	e given as No (%)

Ethnicity	Practice 1	Practice 2	Practice 3
White	5 (1)	8 (2)	23 (6)
African Caribbean	0 (0)	0 (0)	252 (71)
Black African	1 (0)	0 (0)	21 (6)
Black British	0 (0)	0 (0)	38 (11)
Black European	0 (0)	0 (0)	1 (0)
Indian	251 (51)	3 (1)	0 (0)
Pakistani	155 (32)	2 (1)	0 (0)
Bangladeshi	64 (13)	315 (93)	0 (0)
Bangladeshi/Indian	0 (0)	2 (1)	0 (0)
Other	13 (3)	8 (2)	21 (6)
Total	489	338	356

 Table 4
 Numbers of respondents in each age and sex group and median age by ethnicity used for analysis

	Age				
Ethnicity and sex	16–44	45–64	65–74	75+	Median
White men*	405	558	597	554	66
African Caribbean					
men	40	38	25	9	60
Indian men	60	46	11	8	46
Pakistani men	41	29	4	1	43
Bangladeshi men	130	41	11	1	31
White women*	507	620	612	538	65
African Caribbean					
women	105	47	21	6	44
Indian women	57	50	15	7	46
Pakistani women	60	19	1	2	33
Bangladeshi women	129	58	3	6	29

*The figures for the white population were taken from a recent study⁷ by the same research group using the same methodology which took a stratified random sample from general practice lists.

Postal response rates among south Asian populations may not be high,¹⁷ although interviewers can achieve high response rates.¹⁴ We combined the low cost coverage of postal surveys with the high response rates of interviews. Thus, in Tameside those who did not respond to the second questionnaire were visited by an interviewer who administered orally a standardised validated translation of the questionnaire in the subject's preferred language. Translations of the English questionnaire were made in Gujarati, Urdu, Punjabi, Bangla, and Sylheti. Each language had a standardised translation, which was back-translated to assure validity. We did not ascertain the proportion of the study group who had not responded initially because of language or literacy problems, but levels of knowledge of English and literacy are relatively low among the elderly and among women in some ethnic minority communities.19 20 We compared the two administration methods by interviewing 55 people who had previously responded by post. The results supported the decision to analyse postal and interview responses together. In practice 3, the study group all spoke English and no community interviewers were available. Therefore a sample of people who had not responded to the postal questionnaire were telephoned, where possible, but no visits were made. Response rates were calculated based on the study group less those who had died or moved away and included in the denominator those who could not be traced. The case notes of a sample of people who had not responded to postal, interview or telephone questionnaires were selected by stratified random sampling from each practice. We noted the numbers of consultations and referrals, presence of comorbidity, and drugs used. These results were compared with the survey data provided by the responders.

Methods of analysis

Data were analysed by Microsoft Access and SPSS. Ethnicity was assigned according to the questionnaire response. The category of African Caribbean was created by combining Black-Caribbean and Black-Other with people describing themselves as Black British or Black European. Physical disability was defined as an mHAQ>0. Body mass index was calculated by the formula weight (kg)/height (m)². The Townsend score²¹ by census enumeration district was used to assign a measure of social deprivation to subjects based on their area of residence. This was based on quintiles of the population of Greater Manchester. Confidence intervals for prevalence were calculated using a formula for proportions. Logistic regression was carried out using the dependent variables of age, sex, body mass index, ethnicity, and social deprivation. The results from the different ethnic groups were compared with those from the local white population from the recent study in Tameside, which used similar methodology and which was undertaken by the same research team.⁷

RESULTS

The sample size was 2117 (table 2) and 689 (33%) mailed questionnaires were returned by post; 148 people declined to participate. After interviews in practices 1 and 2 and telephoning in practice 3, and once people who had died or moved away were removed from the denominator population, response rates were 73% in practice 1, 77% in practice 2, and 47% in practice 3. Table 3 shows the self defined ethnicities of respondents. Over 95% of practice 1 respondents described themselves as Indian, Pakistani, or Bangladeshi, while the vast majority of practice 2 respondents were Bangladeshi. African

Ethnicity and sex	Total respondents	Any musculoskeletal pain	Pain in most joints	mHAQ >0
White men*	405	36 (31 to 41)	1 (0 to 3)	17 (13 to 21)
African Caribbean men	40	53 (37 to 68)	10 (1 to 19)	32 (17 to 48)
Indian men	60	33 (21 to 45)	5 (0 to 11)	15 (6 to 24)
Pakistani men	41	46 (31 to 62)	17 (6 to 29)	31 (16 to 46)
Bangladeshi men	130	32 (24 to 40)	5 (2 to 9)	17 (11 to 24)
White women*	507	36 (32 to 40)	3 (1 to 4)	21 (18 to 25)
African Caribbean women	105	50 (41 to 60)	7 (2 to 11)	22 (14 to 30)
Indian women	57	32 (20 to 44)	4 (0 to 8)	18 (8 to 28)
Pakistani women	60	42 (29 to 54)	10 (2 to 18)	31 (19 to 42)
Bangladeshi women	129	29 (21 to 36)	7 (3 to 11)	16 (9 to 22)

	Total respondents	Any musculoskeletal pain	Pain in most joints	mHAQ >0
White men*	558	53 (49 to 58)	6 (4 to 8)	34 (29 to 38)
African Caribbean men	38	82 (69 to 94)	34 (19 to 49)	48 (28 to 68)
Indian men	46	63 (49 to 77)	33 (19 to 46)	51 (36 to 67)
Pakistani men	29	79 (65 to 94)	34 (17 to 52)	37 (19 to 55)
Bangladeshi men	41	83 (71 to 94)	37 (22 to 51)	80 (68 to 98)
White women*	620	55 (51 to 59)	8 (6 to 10)	34 (31 to 38)
African Caribbean women	47	70 (57 to 83)	30 (17 to 43)	33 (18 to 49)
Indian women	50	84 (74 to 94)	44 (30 to 58)	60 (46 to 74)
Pakistani women	19	89 (76 to 100)	37 (15 to 59)	56 (33 to 79)
Bangladeshi women	58	67 (55 to 79)	28 (16 to 39)	50 (37 to 63)

Table 6 Crude prevalences of pain and disability among respondents aged 45–64 by ethnicity. Results are shown as percentage (95% confidence intervals)

Caribbean, Black African, and Black British people constituted 87% of practice 3 respondents. Eighty seven per cent of respondents were aged under 65. The median age of respondents was lower for all ethnic groups than for the comparative white population, and the median age of men was higher than that of women, except among Indian subjects (table 4). It was not possible to determine response rates for individual ethnic minority groups, because the ethnicity of non-responders was not known. However, response rates in practices 1 and 2 reflect the South Asian community and practice 3 the African Caribbean community.

The primary care case notes of 93 questionnaire responders and 69 non-responders were examined. Comorbidity was present in 20 (22%) responders and 21 (30%) non-responders. Sixteen (17%) responders were prescribed drug treatment, compared with 19 (28%) non-responders. The median number of primary care consultations for musculoskeletal disease in the past year was the same for responders and non-responders in each practice. Past rheumatology referrals had taken place for two (2%) responders and three (4%) non-responders, past orthopaedic treatment for 21 (23%) responders and 12 (17%) non-responders, and past physiotherapy referrals for 11 (12%) responders and three (4%) non-responders.

Analysis of the results from the 55 people who completed both a mailed questionnaire and a face to face interview showed similar results for the two methods. Overall pain prevalence was the same by mail and by interview, although for 6/10 pain questions, more people reported pain in the postal questionnaire and for 6/8 disability questions more people reported disability at interview.

The results of the whole study were examined by age band and compared with results from the recent study of the white population using the same methodology.⁷ One hundred and two people reported musculoskeletal pain but not in one of the specified areas. Comparison of crude prevalence is only presented for people aged 16-64, because the sample sizes in the older age groups were small. However, those aged 65 or over are included in other analyses. The crude prevalence of musculoskeletal pain among people aged 16-44 ranged from 29% for Bangladeshi women to 53% for African Caribbean men, compared with 36% for the comparative white population (table 5). Among people aged 45-64, crude musculoskeletal pain prevalence was higher in all ethnic groups than in white subjects. Prevalence ranged from 63% among Indian men to 89% among Pakistani women, compared with 53% for white men and 55% for white women (table 6).

Pain in multiple areas was studied under two categories: (*a*) those people who agreed that they had had "pain in most joints" lasting more than one week in the past month; (*b*) the number of individual joint pain areas reported by the subject.

Sex/age group	Ethnic group	No joint pain areas	1 Joint pain area	2 Joint pain areas	≥3 Joint pain areas
Men 16-44	White*	65	19	8	7
	African Caribbean	48	26	19	6
	Indian	67	16	5	12
	Pakistani	54	17	10	20
	Bangladeshi	71	15	7	7
Men 45–64	White*	49	19	16	17
	African Caribbean	18	11	18	53
	Indian	37	11	9	54
	Pakistani	21	31	14	35
	Bangladeshi	22	12	15	51
Women 16-44	White*	65	14	12	9
	African Caribbean	50	17	16	17
	Indian	70	11	4	16
	Pakistani	60	12	15	13
	Bangladeshi	72	12	6	9
Women 45–64	White*	45	20	14	21
	African Caribbean	28	15	11	46
	Indian	18	16	14	52
	Pakistani	11	16	11	63
	Banaladeshi	36	16	21	28

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Table 8 Odds ratio of reporting any musculoskeletal pain, reporting pain in most joints and reporting mHAQ >0 compared with local white population from a recent study using the same methodology⁷ (95% confidence intervals) adjusted for age, sex, body mass index, and area of residence

Ethnic group	Odds ratio of any musculoskeletal pain	Odds ratio of reporting pair in most joints	Odds ratio of mHAQ >0
African Caribbean	1.3 (1.0 to 1.6)	2.2 (1.8 to 2.6)	0.9 (0.5 to 1.2)
Indian	1.2 (0.9 to 1.5)	4.3 (3.9 to 4.7)	1.4 (1.1 to 1.7)
Pakistani	1.7 (1.3 to 2.1)	5.1 (4.6 to 5.6)	1.7 (1.3 to 2.1)
Bangladeshi	1.1 (0.8 to 1.4)	3.4 (3.0 to 3.8)	1.5 (1.2 to 1.8)

 Table 9
 Odds ratio of reporting pain in one or more joint areas compared with

 local white population from a recent study using the same methodology⁷ (95% confidence intervals) adjusted for age, sex, body mass index, and area of residence

Ethnic group	Odds ratio of pain in one joint	Odds ratio of pain in two joints	Odds ratio of pain in three or more joints
African Caribbean	0.9 (0.5 to 1.3)	1.0 (0.6 to 1.4)	1.5 (1.2 to 1.8)
Indian	0.7 (0.3 to 1.1)	0.6 (0.1 to 1.1)	2.6 (2.2 to 2.9)
Pakistani	1.1 (0.6 to 1.5)	1.0 (0.6 to 1.5)	2.1 (1.6 to 2.5)
Bangladeshi	0.8 (0.5 to 1.2)	0.8 (0.4 to 1.2)	1.5 (1.1 to 1.8)

All ethnic groups had a considerably higher crude prevalence of "pain in most joints" than did the white population and this reached statistical significance in most cases (table 6). For example, white women aged 45–64 had a crude prevalence of 8% (95% CI 6 to 10%), compared with 37% (15 to 59%) for Pakistani women and 44% (30 to 58%) for Indian women. The proportion of people from ethnic minority communities reporting pain in three or more separate joint areas also tended to be greater than among white subjects (table 7). Twenty one per cent of white women aged 45–64 reported pain in three or more areas, compared with 46% of African Caribbeans, 52% of Indians, 63% of Pakistanis, and 28% of Bangladeshis.

Disability prevalence measured by an mHAQ>0 was not significantly different among ethnic minority groups aged 16–44, compared with the white population (table 5). Among those aged 45–64, disability prevalence tended to be higher among ethnic minority groups, but this only reached statistical significance for Indian men, Bangladeshi men, Indian women, and Bangladeshi women (table 6).

Logistic regression was used to compare the groups with the white population, controlling for age, sex, body mass index, and area of residence. The odds ratio for any musculoskeletal pain was only significantly raised among Pakistanis, although the odds ratio for an mHAQ>0 was significantly raised among Indians, Pakistanis, and Bangladeshis (table 8). The odds ratios for pain in specific joint areas tended to be slightly raised among ethnic minorities compared with white subjects. For example for back pain the odds ratios were African Caribbeans 1.2 (95% CI 0.8 to 1.5), Indians 1.6 (1.3 to 1.9), Pakistanis 1.5 (1.2 to 1.8), Bangladeshis 1.5 (1.2 to 1.8). For knee pain the odds ratios were African Caribbeans 1.2 (95% CI 0.8 to 1.5), Indians 2.0 (1.7 to 2.4), Pakistanis 1.7 (1.2 to 2.1), Bangladeshis 1.1 (0.8 to 1.5).

The adjusted odds ratios for "pain in most joints" were considerably higher than 1 for all groups comparing them with the white population and all were statistically significant. Figures ranged from 2.2 (95% CI 1.8 to 2.6) for African Caribbeans to 5.1 (4.6 to 5.6) for Pakistanis (table 8). This tendency for increased prevalence of pain in several areas is also reflected in the odds ratios for reporting pain in three or more separate areas. Odds ratios for pain in one or two areas were not significantly different from 1 among ethnic minority groups compared with the white population. However, the odds ratios for three or more areas were significantly greater than 1 among all four ethnic minority groups (table 9).

DISCUSSION

We have demonstrated differences in the prevalence of musculoskeletal symptoms among different ethnic minority groups in a population study that achieved a high response rate in the south Asian community. It is reasonable to equate this practice based study with the population, because the great majority of people from ethnic minority communities are known to be registered with primary care practices.¹⁹ Joint pain lasting for more than one week in the past month was slightly more prevalent among ethnic minorities. Pain reported in "most joints" and pain in three or more individual sites were markedly more prevalent among the ethnic minorities than in the white population. The small increase in prevalence in individual joint areas among ethnic minorities might be explained as being part of a picture of widespread pain rather than indicating differences in specific joints. Few studies of the prevalence of musculoskeletal symptoms among ethnic minority populations in the UK have been published. Comparison is possible with results from other countries, although methodology and case definitions differ and the focus of some studies has been radiological abnormality rather than symptoms. Bremner et al noted a similar prevalence of radiological osteoarthritis between a white British population and one from rural Jamaica, although they reported that symptoms and incapacity were lower among Jamaicans.9 Gibson et al found similar levels of joint disease in Pakistan and in white European populations.10 In the USA, levels of self reported arthritis have been found to vary little by ethnicity,²² and musculoskeletal disability was similar in African-American and white populations.²³ A telephone study of acute back pain in North Carolina, USA, found a slightly lower prevalence in non-white subjects.²⁴ Our results are compatible with these studies in that we have shown only small differences in overall pain prevalence between ethnic minority and white populations. As far as we know, our finding of markedly increased prevalence of "pain in most joints" has not previously been reported.

The difficulties associated with any study of this type mean that some caution must be expressed. Extrapolation outside the four ethnic groups studied is not possible. The response rate was far higher among south Asian subjects than among the African Caribbean community and, inevitably, the sample sizes in most age-sex groups were small, given the population age structure of ethnic minorities in the UK. There was good equivalence between interviews and questionnaires. Precise estimates of the effects of the administration method used and non-response were not possible, but there was no evidence of large systematic differences that might have altered prevalence estimates or odds ratios greatly. Also, case note analysis showed that responders and non-responders had a reasonably similar profile. We have used responders as the denominator population for prevalence estimates and so assumed that responders and non-responders had a similar prevalence of pain. We might have used the entire study group as the denominator, assuming that non-responders had no pain, but because pain prevalence between responders and non-responders appears similar, this would have underestimated the overall pain prevalence. However, it is still possible that there were some systematic differences between the different samples. Self reported pain is likely to have major cultural influences, but it is the symptoms that are presented in clinical consultations and differences in symptomatology which are worthy of note, even if the underlying objective morbidity is similar. Using the Townsend score to represent socioeconomic deprivation has limitations and other socioeconomic factors may contribute to the results. However, despite its limitations, this study presents important evidence of clinically significant differences among ethnic groups.

Further research examining other ethnic minority populations in other locations would be valuable. It would also be of great interest to look more closely at the relation between symptoms and objective measures of morbidity, and at the phenomenon of widespread musculoskeletal pain among people from ethnic minority communities. There are several possible explanations for the differences in pain reporting by different ethnic groups. These include pain thresholds and the experience of pain, the effect of change of culture and migration, and mental health issues. Widespread pain might, for example, be an indication of mental distress and, possibly, migration, rather than ethnicity, is a key factor. A review of published reports of these issues has recently been carried out with an emphasis on South Asian subjects.15 The authors of the review call for further work to investigate the extent and nature of musculoskeletal disease among ethnic minorities. Our study has made a contribution to a study of this issue, but further work is needed to assess specific healthcare needs, whether or not the actual needs are for musculoskeletal care, and then to deal with those needs.

ACKNOWLEDGMENTS

The authors acknowledge, in particular, the following: Dr Diane Lowcock for her training and data collection work; staff and patients of Gordon Street, Niramoy, and Park Surgery general practices; the Ashton Asian Health Development Project.

Manchester, Stockport, and West Pennine Health Authorities R&D Liaison Group funded this research through the NHS Executive North West Regional Office.

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TA had the original idea for the project, secured funding, gained ethical approval, and was the overall project leader. TA, DS, TB, AR, MR, and MU developed the methodology in the light of previous work and PH refined the methodology for the African Caribbean population. TA, TB, PH, and MU participated in data collection and analysis under the supervision of DS, AR, and MR. All authors contributed to the final version of the paper.

Work included in this paper is to be submitted to the University of Cambridge by TA for the degree of MD.

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