

**The impact of socioeconomic status on the link between osteoarthritis and the onset of
common comorbidities**

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Abstract

Objectives

The temporal relationship between osteoarthritis and comorbidity is unclear and may vary with socioeconomic status. The aims of this study were to identify if osteoarthritis was associated with onset of common comorbidities, and if the association was moderated by deprivation.

Methods

Prospective cohort study combining questionnaire and medical record data (n=3910). Associations between osteoarthritis and onset of comorbidity at three year follow-up were examined using regression models. Interaction terms and stratified analysis were used to examine moderation.

Results

Osteoarthritis was associated with onset of all comorbidities ($p < 0.05$). After adjusting for confounders, osteoarthritis was associated with onset of widespread pain (adjusted odds ratio 2.49; 95% confidence interval 1.96-3.17) and insomnia (1.58; 1.14-1.19). Interactions between osteoarthritis and change in income and onset cognitive impairment ($p = 0.047$; onset was higher when income became inadequate), and between osteoarthritis and education and onset widespread pain ($p = 0.012$; onset was higher in those with high levels of education) were significant.

Conclusion

Consulters for osteoarthritis were more likely to develop physical and psychological comorbidities than those without osteoarthritis. The moderation analyses indicate that mechanisms to comorbidity differ by socio-economic strata and a need for different approaches to prevent comorbidity for consulters with OA from different levels of deprivation.

INTRODUCTION

Osteoarthritis is the most common joint condition in adults and is the fastest increasing major health condition globally [1]. It is a common reason for health care consultation, and is associated with the presence of comorbidity, particularly from age fifty onwards, although the temporal nature of this association is unclear [2]. Establishing if osteoarthritis predicts common comorbidities that present to health care would indicate a need to further explore if osteoarthritis has a causative role and if people with osteoarthritis should be a target group for preventative strategies.

In addition, osteoarthritis and its impact is often associated with low socioeconomic status [3,4]. Low educational attainment, low income, and area level deprivation are associated with increased consultation to healthcare, including the need for arthroplasty [5-7]. Socioeconomic status tends to be included as a covariate or confounder in studies, however the mechanism to poor outcomes will differ depending on the socioeconomic conditions that people experience [8,9]. Interventions to promote health and prevent comorbidity may need to differ for different socioeconomic groups. Based on a representative cohort of primary care consulters, the aims of this study were to determine if osteoarthritis predicted the onset of morbidities that commonly present in patients and if this link differed by levels of socioeconomic deprivation.

METHODS

Study population

The North Staffordshire Osteoarthritis project (NorStOP) is a population-based prospective cohort study. The sampling frame comprised individuals aged 53 years and over who were registered to receive care from one of six general practices in North Staffordshire, United

Kingdom (UK), gave written consent for medical record review and were mailed a baseline questionnaire, in 2005, which collected data on health, sociodemographic factors. In the UK, general practice registers offer a convenient sampling frame for population based studies; an estimated 98% of UK residents are registered. Reminders were sent to non-responders two and four weeks after the initial mailing. The North Staffordshire Local Research Ethics Committee approved this study; all participants gave written consent to participate.

Analyses included those who responded to baseline (2005) and three year follow-up (2008) questionnaires and had complete data for outcomes and confounders. Of 6696 potential participants, 4392 (65.6%) responded at three year follow-up. A further 482 had missing data leaving 3910 for the analysis. Compared to those subjects that did not respond or have complete data (n=2786), included participants were on average significantly younger, have higher education and less comorbidity (all $p < 0.001$) but were no more likely to consult for osteoarthritis ($p = 0.241$) or be female ($p = 0.237$).

Identification of osteoarthritis

A combination of medical record and questionnaire data were used to identify clinically significant osteoarthritis [10]. General practitioners in the study used the Read system to code the reasons for clinical encounters in primary care consultations [11]. Morbidity data (i.e. symptoms and diseases) in this system are grouped under 19 main Read chapters. Data collected at the second hierarchical level or above was used to identify diagnostic groups. Individuals were defined as having osteoarthritis if they had consulted general practice for osteoarthritis between 2000 and 2005 based on Read codes (N05.. category) for primary care consultations and indicated moderate to severe pain interference on daily life in the Medical Outcomes Short Form 36 [12] at baseline.

Outcomes

The onset of seven morbidities included in the analyses were highlighted in preliminary work with patients with osteoarthritis as a concern and a common reason for further consultation to primary and secondary care. Two (stress and neurosis) were identified using medical records and the same approach described above for osteoarthritis and five (anxiety, depression, cognitive impairment, widespread pain, insomnia) were identified by self-report via questionnaires (Table 2; detail in Online Appendix 1), with three year onset of each morbidity defined as moving from absence of the outcome at baseline to presence at three year follow-up.

Socioeconomic status

Individual level socioeconomic status was reported by questionnaire. Educational attainment (finished education on leaving school; gone onto full-time education including college or university) was included as a proxy measure of lifetime status. Income was measured by comparing perceived adequacy of income at follow-up to baseline to give categories of no deprivation (remain adequate (referent category), new adequate) and two categories of deprivation (new inadequate, remain inadequate).

Area-level deprivation was assessed using the Index of Multiple Deprivation 2004 for England (based on postcode and ranked using tertiles (least, mid, most deprived) [13].

Statistical analysis

The frequency of the onset of each comorbidity was calculated, overall and stratified by osteoarthritis at baseline. Univariate logistic regression models were constructed to examine if osteoarthritis was associated with the onset of each comorbidity. Multivariate models were then constructed for each comorbidity that included all other morbidities and putative confounders (age, gender, socioeconomic status and comorbidity). To determine whether

any associations were moderated by socioeconomic status, interaction terms between each socioeconomic factor and osteoarthritis (e.g. osteoarthritis*education) were examined in the multivariate analysis for each comorbidity. Where there was a significant interaction (i.e. $p < 0.05$), a categorical interaction variable (e.g. no osteoarthritis/further education, no osteoarthritis/no further education, osteoarthritis/further education, osteoarthritis/no further education) was examined in a fully adjusted model. Analyses were conducted with STATA 14.0 (StataCorp 2015, College Station, TX, StataCorp LP).

RESULTS

Sample characteristics (n=3910)

Mean age was 66 (SD 8.4) and 55% were female (Table 1). 942 (24%) participants had clinically significant osteoarthritis. Osteoarthritis was associated with lower education (11% cf 17% without osteoarthritis who went onto higher education)) and lower income (remained inadequate income between baseline and follow-up; 42% versus 25%). Of those living in the most deprived areas 24% had osteoarthritis and 19% did not.

Association with new comorbidity

Adults with osteoarthritis were more likely to experience the onset of all seven comorbidities than those that did not have osteoarthritis (Table2). The most common comorbidity was widespread pain, with 38.5% of those with osteoarthritis developing widespread pain three years later; those with osteoarthritis were more than three times as likely to develop widespread pain than those without osteoarthritis (odds ratio 3.3; 95% confidence interval 2.7, 4.1). In fully adjusted models osteoarthritis was associated with widespread pain (adjusted odds ratio 2.5; 95% confidence interval 2.0, 3.2) and insomnia

(1.5; 1.1, 2.1); for depression, anxiety, cognitive impairment, stress and neurosis the association attenuated to insignificance with adjustment for socio-demographic factors and comorbidity. The associations between the socio-economic factors and the onset of each comorbidity are presented in Online Appendix 2.

Interaction between osteoarthritis and socioeconomic status

There were two significant interactions (both were non-multiplicative); (i) between osteoarthritis and income and the onset of cognitive impairment ($p=0.047$) and (ii) between osteoarthritis and education and the onset of widespread pain ($p=0.012$). In both instances, the frequency of onset was greater for those with osteoarthritis compared to those that did not (Figure 1 & Online Appendix 3). 30% of those with osteoarthritis and had an income that remained adequate across the three years experienced the onset of cognitive impairment compared to 38% of those with osteoarthritis who income remained inadequate (indicating higher deprivation). In contrast, 50% of those with osteoarthritis and had gone onto further education (indicating lower deprivation) experienced the onset of widespread pain compared to 37% who had osteoarthritis and a school education only.

DISCUSSION

Consulters for osteoarthritis were more likely to develop new comorbidities that commonly present to healthcare than those that had not consulted for osteoarthritis. Whilst socioeconomic factors and other comorbidities explained some of these associations, osteoarthritis consulters represent a target group that may benefit from proactive strategies to prevent further morbidity. Osteoarthritis and baseline morbidity were higher in lower socioeconomic groups and further exploration across the life-course will help to establish

the role of socioeconomic status on the natural history of osteoarthritis and its impact. Despite no significant multiplicative interactions, the results highlight that higher and lower levels of deprivation provide an added contribution to the development of comorbidity. Perhaps with expectations, and in line with previous studies that include socioeconomic status as a covariate, higher individual deprivation was linked with cognitive impairment [14,15]. However previous reviews indicate that the relationship between pain and socioeconomic status is not straightforward and few studies have looked at the development of widespread pain in those with OA and how this differs by socio-economic status [16]. The higher frequency of onset of widespread pain in those with higher education suggests that once osteoarthritis is experienced and diagnosed, those with higher levels of education are more sensitive to reporting additional symptoms and are more likely to seek healthcare.

For clinical practice and health improvement, these results indicate that the mechanisms to onset vary by deprivation level and warrant different interventions. For research these results indicate the need to consider socioeconomic status as a moderator rather than a covariate. The sample is representative of primary care consulters with physician diagnosed osteoarthritis, relevant to primary care practices. Data on most variables was by self-report, but validated instruments were used to measure anxiety, depression and pain interference. Attrition and missing data indicates there may be some bias due to differences in age, socioeconomic and health status between those who dropped out and those included, but this is likely to be minimal, as the differences between the participants and non-participants on key variables were not large [17].

Acknowledgements

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Table 1. Sample characteristics at baseline (n=3910)

		Total sample (n=3910) No. (%)	OA (n=942) No. (%)		Non-OA (n= 2968) No. (%)		P value
Age*		66 (8.4)	67.8	(8.5)	65.4	(8.3)	<0.001
Sex	Male	1759 (45.0)	347	36.8	1412	47.6	<0.001
	Female	2151(55.0)	595	63.2	1556	52.4	
Income	Stayed adequate	1925(49.2)	316	33.6	1609	54.2	<0.001
	Stayed inadequate	1140(29.2)	394	41.8	746	25.1	
	New inadequate	444(11.4)	110	11.7	334	11.3	
	New adequate	401(10.3)	122	13.0	279	9.4	
Area level deprivation	20% least deprived	801 (20.5)	175	18.6	626	21.1	0.004
	Middle 60%	2334(59.7)	546	58	1788	60.3	
	20% most deprived	774(19.8)	221	23.5	553	18.6	
Further education	No	3262 (83.4)	825	87.6	2437	82.1	<0.001
	Yes	596 (15.2)	105	11.2	491	16.5	
	Unknown	52 (1.3)	12	1.3	40	1.4	
BMI	Normal weight	1230(31.5)	197	20.9	1033	34.8	<0.001
	Underweight	101(2.6)	17	1.8	84	2.8	
	Overweight	1689(43.2)	402	42.7	1287	43.4	
	Obese	816(20.9)	307	32.6	509	17.2	
	Unknown	74(1.9)	19	2.0	55	1.9	
Number of health conditions	0	2436 (62.3)	472	50.1	1964	66.2	<0.001
	1	1076 (27.5)	315	33.4	761	25.6	
	2	327 (8.4)	134	14.2	193	6.5	
	3	71 (1.8)	21	2.2	50	1.7	
Number of health impairments	0-1	2320 (59.3)	323	34.3	1997	67.3	<0.001
	≥ 2	1590 (40.7)	619	65.7	971	32.7	
Depression	Non-case	3274 (83.7)	639	67.8	2635	88.8	<0.001
	Poss/prob case	636 (16.3)	303	32.8	333	11.2	
Anxiety	Non-case	2700 (69.1)	492	52.2	2208	74.4	<0.001
	Poss/prob case	1210(30.9)	450	47.8	760	25.6	
Cognitive impairment	No	2126 (54.4)	340	36.1	1786	60.2	

	Yes	1784 (45.6)	602	63.9	1182	39.8	<0.001
Quality of sleep	Refreshed	3287 (84.1)	661	70.2	2626	88.5	
	Unrefreshed	623(15.9)	281	29.8	342	11.5	<0.001
Stress	No	3278 (83.8)	791	84.01	2487	83.8	0.898
	Yes	632 (16.2)	151	16.0	481	16.2	
Neurosis	No	3138 (80.3)	687	72.9	2451	82.6	<0.001
	Yes	772 (19.7)	255	27.0	517	17.4	

All values are N (%) except * which is mean and standard deviation.

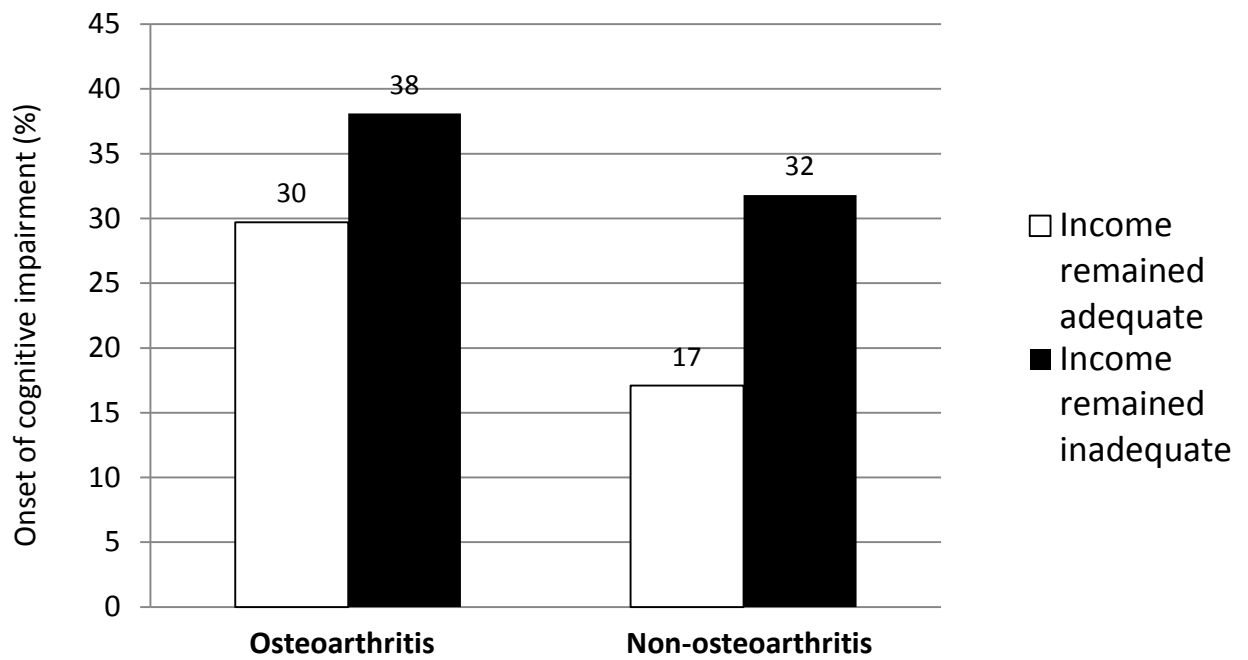
Table 2: Association between osteoarthritis and the onset of comorbidity; odds ratios with 95% confidence intervals

Onset of	Definition	Overall No. (%)	Osteoarthritis No. (%)	No Osteoarthritis No. (%)	Univariate analysis		Multivariate model	
					OR ⁺	95% CI	Adj OR [#]	95% CI
Depression*	Free	2948 (83.7)	529 (82.8)	2419 (91.8)	1		1	
	Onset	326 (16.3)	110 (17.2)	216 (8.2)	2.3	1.8, 3.0	1.3	0.99, 1.8
Anxiety*	Free	2343 (86.8)	393 (79.9)	1950 (88.3)	1		1	
	Onset	357 (13.2)	99 (20.1)	258 (11.7)	1.9	1.5, 2.5	1.3	0.95, 1.7
Cognitive impairment*	Free	1616 (76.0)	218 (64.1)	1398 (78.3)	1	1.6, 2.6	1	
	Onset	510 (24.0)	122 (35.9)	388 (21.7)	2.0		1.2	0.9, 1.6)
Widespread pain*	Free	2289 (80.3)	303 (61.5)	1986 (84.2)	1		1	
	Onset	563 (19.7)	190 (38.5)	373 (15.8)	3.3	2.7, 4.1	2.5	2.0, 3.2
Insomnia*	Free	2837 (92.7)	537 (92.7)	2300 (94.3)	1		1	
	Onset	222 (7.3)	83 (13.4)	139 (5.7)	2.6	1.0, 3.4	1.5	1.1, 2.1
Neurosis*	Free	2990 (95.3)	633 (92.1)	2357 (96.2)	1		1	
	Onset	148 (4.7)	54 (7.9)	94 (3.8)	2.1	1.5, 3.0	1.3	0.9, 2.0
Stress*	Free	3053 (93.1)	720 (91.0)	2333 (93.8)	1		1	
	Onset	225 (6.9)	71 (9.0)	154 (6.2)	1.5	1.1, 2.0	1.4	0.97, 1.9

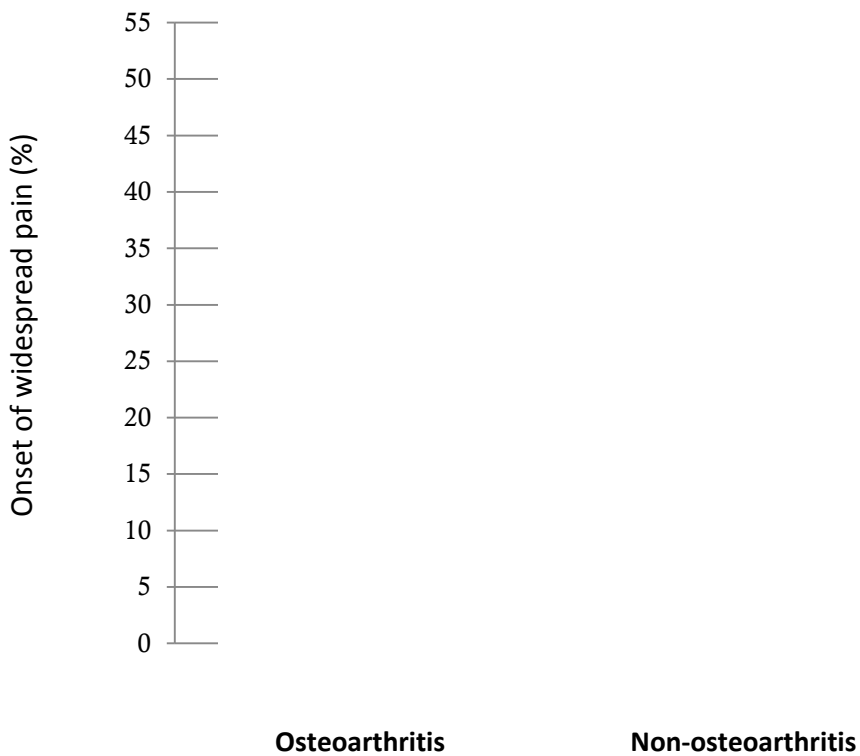
*Adjusted for putative confounders, measured at baseline: demographic factors (age, gender), lifestyle (smoking status (current, previous, never), alcohol use (daily, weekly, monthly, annually, never)) and comorbidity (Body Mass Index from self-reported height and weight categorised into standard BMI groups (i) normal weight (BMI 20-24.9kgm⁻²), (ii) underweight (BMI <20kgm⁻²), (iii) overweight (BMI 25 – 29.9 kgm⁻²) and (iv) obesity (BMI ≥30kgm⁻²); Number of health conditions was a simple count of the presence of four self-reported health conditions common in older adults (chest problems, heart problems, diabetes and raised blood pressure) and eight impairments (falls, memory difficulties, cough with spit, breathless when walking, dizziness, weakness in arms/legs, deafness, problems with eyesight). From these single items, counts of health conditions (0-3), impairments (0-9); the other morbidities (depression, anxiety, cognitive impairment, widespread pain, insomnia, stress, neurosis) measured at baseline.

Figure 1: Onset of comorbidity stratified by osteoarthritis and deprivation

A: Onset of cognitive impairment stratified by osteoarthritis and income adequacy



B: Onset of widespread pain stratified by osteoarthritis and education



Appendix 1: Measurement of comorbidities

Depression and anxiety were measured using the Hospital Anxiety and Depression Scale (HADS). Raw scores were categorised as free (0-7; absent) or possible/probable cases (8-21; present); onset was movement from free to a possible/probable case [Zigmond AS, Snaith RP. The hospital anxiety and depression scale, *Acta Psychiatr Scand* 1983;67:361-70.]. Cognitive impairment was measured using the Cognitive and Alertness behaviour subscale of the Functional Limitations Profile. Raw scores were categorised to no impairment (score of 0; absent) and cognitive impairment (score >0; present); onset was defined as movement from absent at baseline to present at three years [Bergner M, Bobbitt RA, Carter WB, et al. The sickness impact profile: the development and final revision of a health status measure, *Med Care* 1981;19:787-805.]. Widespread pain was identified using pain manikins; each participant was asked to shade where they had pain on a two-view (front and back) blank body manikin the location of their pain. At each time point participant's reports of pain were categorized to widespread pain (American College of Rheumatology definition [Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. *Arthritis Rheum* 1990; Feb;33(2):160-72.] or no widespread pain; onset was defined as no widespread pain at baseline and widespread pain at three year follow-up. Sleep quality was measured using a single item on non-restorative sleep from the Jenkins Sleep Questionnaire [Jenkins CD, Stanton BA, Niemcryk SJ, Rose RM. A scale for the estimation of sleep problems in clinical research. *J Clin Epidemiol* 1988;41(4):313-21]. Onset of insomnia was defined as moving from feeling tired and worn out on none or some nights (absence) at baseline to most nights at follow-up (presence). The onset of stress and neurosis were identified using medical records; onset for both was defined as no consultation for the morbidity between 2000 and 2005 and one or more consultations for the morbidity between 2005 and 2008.

Appendix 2: Association between education, income, area deprivation and the onset of new comorbidities

	Onset of Depression				Onset of Anxiety				Onset of Cognitive impairment			
	OR	95%CI	Adj.OR	95%CI	OR	95%CI	Adj.OR	95%CI	OR	95%CI	Adj.OR	95%CI
Education												
Further education	1		1		1		1		1		1	
No further education	1.6	1.1,2.2	1.1	0.7,1.6	1.3	0.9,1.8	1.1	0.8,1.5	1.4	1.1,1.9	1.2	0.8,1.4
Education unknown	1.9	0.7,5.2	1.2	0.4,3.3	1.2	0.4, 3.7	1.0	0.3,3.2	1.1	0.4,3.0	0.8	0.3,2.2
Income												
Stayed adequate	1		1		1		1		1		1	
Stayed inadequate	2.0	1.6,2.7	1.4	1.0,1.8	1.8	1.4,2.3	1.4	1.0,1.8	2.2	1.7,2.8	1.8	1.3,2.3
New inadequate	1.5	1.0,2.2	1.2	0.8,1.7	1.4	0.9,2.0	1.1	0.8,1.7	1.3	0.9,1.9	1.2	0.8,1.7
New adequate	1.6	1.1,2.3	1.2	0.8,1.8	1.6	1.1,2.3	1.3	0.9,1.9	2.2	1.6,3.0	2.0	1.5,2.8
Area level deprivation												
20% least deprivation	1		1		1		1		1		1	
Middle 60%	1.5	1.1,2.0	1.4	0.97,1.9	1.1	0.8,1.4	1.0	0.8,1.4	1.2	0.9,1.6	1.2	0.9,1.6
20% most deprivation	1.9	1.3,2.7	1.3	0.9,1.9	1.4	0.99,2.0	1.2	0.8,1.7	1.6	1.1,2.1	1.3	0.9,1.8

	Onset of sleep				Onset of widespread pain				Onset of Neurosis				Onset of stress			
	OR	95%CI	Adj. OR	95%CI	OR	95%CI	Adj. OR	95%CI	OR	95%CI	Adj. OR	95%CI	OR	95%CI	Adj. OR	95%CI
Education																
Further education	1		1		1		1		1		1		1		1	
No further education	0.9	0.6,1.3	0.8	0.5,1.2	1.2	0.9,1.5	1.0	0.7,1.3	1.1	0.7,1.8	1.1	0.6,1.8	1.0	0.7,1.5	0.9	0.6,1.4
Education unknown	1.1	0.3,3.6	0.7	0.2,2.7	0.7	0.3,1.8	0.7	0.3,1.7	2.3	0.8,7.2	2.2	0.7,7.5	1.0	0.3,3.2	0.9	0.3,3.1
Income																
Stayed adequate	1		1		1		1		1		1		1		1	
Stayed inadequate	3.0	2.2,4,1	1.9	1.4,2.7	1.9	1.5,2.3	1.3	1.0,1.6	1.4	0.99,2.1	0.8	0.5,1.2	1.1	0.8,1.5	0.9	0.6,1.2
New inadequate	1.1	0.7,1.9	0.8	0.5,1.5	1.3	.97,1.8	1.0	0.8,1.4	0.9	0.5,1.7	0.6	0.3,1.2	1.0	0.7,1.6	0.9	0.6,1.5
New adequate	1.5	0.9,2.5	1.3	0.8,2.1	1.4	1.0,1.9	1.1	0.8,1.6	1.1	0.6, 1.9	0.9	0.5,1.7	1.7	1.1,2.6	1.6	1.0,2.4
Area level deprivation																
20% least deprivation	1		1		1		1		1		1		1		1	
Middle 60%	1.2	0.8,1.8	1.1	0.7,1.6	1.1	0.9,1.4	1.0	0.8,1.3	1.6	0.99,2.7	1.6	0.9,2.7	2.2	1.4,3.5	2.2	1.4,3.5
20% most deprivation	1.6	1.0,2.4	1.1	0.7,1.7	1.7	1.2,2.2	1.3	0.9,1.7	2.2	1.3,3.8	1.7	0.9,3.1	6.0	3.6,9.7	6.0	3.6,10.0

Appendix 3: Association between stratified variables and onset of new comorbidity

Association between osteoarthritis/income and the onset of cognitive impairment					
	Total sample (n=2126)	New onset		Adj. OR (95% CI)	
	No.	No.	(%)		
Osteoarthritis & income					
No osteoarthritis, income stayed adequate	1069	183	17.1	1	
No osteoarthritis, income stayed inadequate	362	115	31.8	2.03	1.52, 2.70
No osteoarthritis, income became inadequate	183	37	20.2	1.10	0.73, 1.65
No osteoarthritis, income became adequate	172	53	30.8	2.06	1.42, 2.99
Osteoarthritis, income stayed adequate	138	41	29.7	1.51	0.99, 2.30
Osteoarthritis, income stayed inadequate	126	48	38.1	1.67	1.07, 2.59
Osteoarthritis, income became inadequate	30	13	43.3	2.23	1.01, 4.91
Osteoarthritis, income became adequate	46	20	43.5	2.94	1.57, 5.50

Association between osteoarthritis/education and the onset of widespread pain					
	Total sample (n=2852)	New onset		Adj. OR (95% CI)	
	No.	No.	(%)		
Osteoarthritis & education					
No osteoarthritis, further education	399	53	13.3	1	
No osteoarthritis, school education only	1923	315	16.4	1.27	0.91, 1.77
Osteoarthritis, further education	38	29	50.0	5.22	2.81, 9.71
Osteoarthritis, school education only	428	160	37.4	2.87	1.95, 4.22
No Osteoarthritis, education unknown	37	5	13.5	1.01	0.37, 2.81
Osteoarthritis, education unknown	7	1	14.3	0.83	0.09, 7.68

