Arthritis Care & Research
Vol. 65, No. 6, June 2013, pp 910–919
DOI 10.1002/acr.21918

ORIGINAL ARTICLE

Reasons Why Multimorbidity Increases the Risk of Participation Restriction in Older Adults With Lower Extremity Osteoarthritis: A Prospective Cohort Study in Primary Care

ROSS WILKIE, MILISA BLAGOJEVIC-BUCKNALL, KELVIN P. JORDAN, ROSIE LACEY, AND JOHN McBETH

Objective. **To determine why multimorbidity causes participation restriction in adults ages ≥50 years who consult primary care with lower extremity osteoarthritis (OA).**

Methods. **This was a population-based prospective cohort study of 1,053 consulters for lower extremity OA who were free of participation restriction at baseline. Path analysis was used to test proposed mechanisms by examining for mediation of the association between multimorbidity at baseline, defined by self-report and consultation data separately, and incident participation restriction at 3 years by lower extremity pain severity, obesity, locomotor disability, and depression.**

Results. **Multimorbidity was associated with incident participation restriction (adjusted odds ratio [OR] 2.83, 95% confidence interval [95% CI] 2.03–3.94 for multimorbidity [self-report]; OR 1.59, 95% CI 1.15–2.21 for multimorbidity [consultation data]). The extent of mediation of the association of baseline multimorbidity, defined by self-report, and incident participation restriction was greater for severe lower extremity pain than obesity (standardized beta coefficients for indirect effect 0.032 [SE 0.015] and 0.020 [SE 0.019], respectively). The addition of depression and locomotor disability increased the amount of mediation (0.115 [SE 0.028]) and reduced the proportion explained by severe lower extremity pain (0.014 [SE 0.015]) and obesity (0.006 [SE 0.010]). Locomotor disability was the strongest mediator.**

Conclusion. **The additional impact on participation in social and domestic life that multimorbidity places on individuals with lower extremity OA appears to be mediated through further restriction of locomotor disability, as well as through depression. The results suggest that the effect of multimorbidity on the daily lives of people with lower extremity OA will be ameliorated by active management of depression and locomotor disability.**

INTRODUCTION

Social participation encompasses social function and social roles, such as being a worker, caregiver, or community member (1). Maintaining social participation in older people is associated with lower rates of morbidity and mortality (2,3). In the UK among adults ages ≥50 years, 1 in 20 consultations to a general practitioner are for lower extremity osteoarthritis (OA), i.e., OA in hip, knee, or foot, or a combination (4,5). Lower extremity OA increases the risk of restricted social participation, although the reasons why this occurs are not fully understood (6). Importantly, despite the presence of lower extremity OA, participation can be maintained (6). Identifying the mechanisms that increase the risk of restricted social participation in this group of patients, particularly those that are amenable to change, will inform future management and preventive strategies (7).

Certain factors have been consistently linked to restricted participation in persons with lower extremity OA, including lower extremity pain severity, obesity, locomotor disability, and depression, which all represent potential targets for intervention to improve participation in this large group of older people (6,8–10). However, another important factor is the frequent occurrence of multimorbidity in people with lower extremity OA, which

Supported by the Medical Research Council UK (grant G9900220) and the North Staffordshire Primary Care R&D Consortium.

Ross Wilkie, BSc, PhD, Milisa Blagojevic-Bucknall, BSc, PhD, Kelvin P. Jordan, BComm, MSc, PhD, Rosie Lacey, BSc, PhD, John McBeth, MSc, PhD: Arthritis Research UK Primary Care Centre, Keele University, Staffordshire, UK.

Address correspondence to Ross Wilkie, BSc, PhD, Arthritis Research UK Primary Care Centre, Primary Care Sciences, Keele University, Keele, Staffordshire, UK, ST5 5BG. E-mail: r.wilkie@keele.ac.uk.

Submitted for publication May 1, 2012; accepted in revised form November 16, 2012.

Significance & Innovations

- Epidemiologic studies have identified a number of factors that increase the risk of participation restriction in older adults with osteoarthritis (OA) and multimorbidity. However, it is unclear whether or not these risk factors are on the pathway, i.e., are causally related to participation restriction or are simply prognostic factors.
- Using the International Classification of Functioning framework, this novel study has tested whether these common risk factors mediate the link between multimorbidity and the onset of participation restriction among people with OA.
- Cumulatively the pathway variables explained a maximum of 12% of the outcome. Locomotor disability was the strongest mediator.
- The vast majority of the link between multimorbidity and the onset of participation restriction was explained by the direct effect.

is higher than expected compared with similar-aged persons who do not have OA (11,12). The presence of multimorbidity in this group is associated with poorer outcomes, including increased rates of participation restriction (8,12). One possibility is that the disease processes represented by concurrently occurring morbidities directly affect participation independent of the OA. However, it is also possible that multimorbidity acts to enhance the mechanisms by which lower extremity OA results in participation restriction. It is this latter hypothesis that we have set out to explore in this study.

The aim of this study was to test potential mechanisms of the impact of lower extremity OA and multimorbidity on incident participation restriction, among patients consulting in primary care, based on path analysis techniques. Specifically, the study tested the hypotheses that among patients with lower extremity OA, those with multimorbidity would have an increased risk of restricted social participation and that this increased risk would be mediated by pain severity, obesity, locomotor disability, and depression.

PATIENTS AND METHODS

Study design and participants. The study was a prospective cohort study nested within the North Staffordshire Osteoarthritis Project, a population-based longitudinal study of musculoskeletal health in the North Staffordshire area of England. Ethical approval was obtained from the North Staffordshire Local Research Ethics Committee. Details of cohort recruitment have been described previously in detail (13). In brief, all individuals ages ≥50 years (n = 19,818) and registered with 6 general practices were mailed a baseline questionnaire in 2002 that collected data on general health, sociodemographic factors, and pain. All participants were followed up 3 years later. At both time points, reminders were sent to nonresponders 2 and 4 weeks after the initial questionnaire. Participants in this analysis were those who consented to a review of their medical records, consulted a general practitioner regarding OA in the 18-month period prior to baseline (Read code starting N05) (14), and in the baseline questionnaire indicated hip, knee, or foot pain, but were free of participation restriction.

Mechanisms from multimorbidity to the onset of restricted participation. Two potential mechanisms that combine the conceptual approach of the International Classification of Functioning, Disability and Health (ICF) (1) and previous research (6,10,15–17) (Figure 1) were proposed for the action of multimorbidity on incident participation restriction in persons with lower extremity OA. The first mechanism concerns the role of severe lower extremity pain on the onset of restricted participation in persons with multimorbidity; pain is greater in

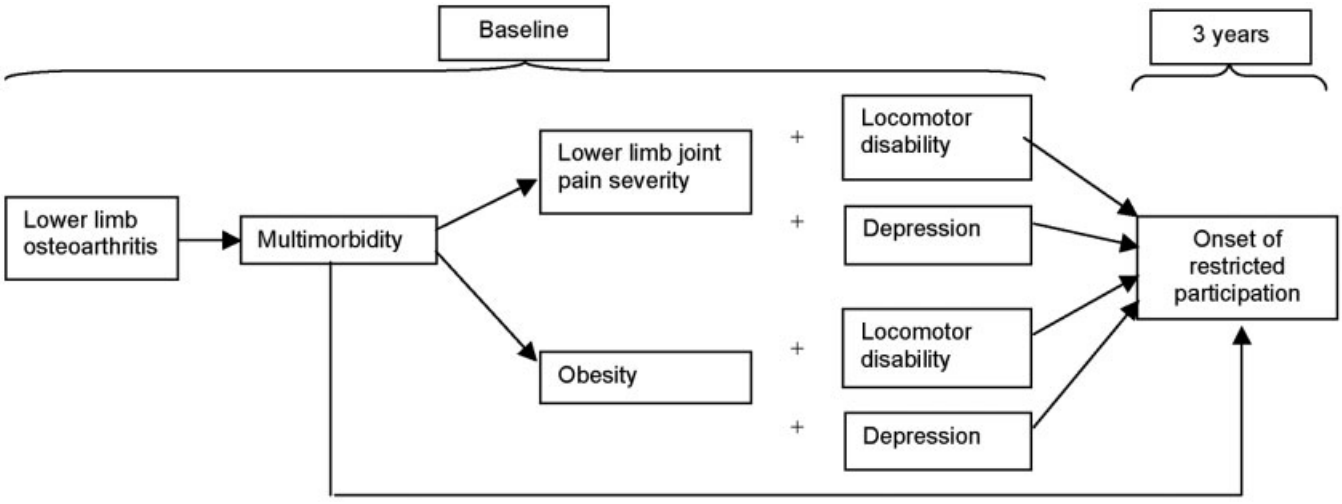

Figure 1. Hypothesized pathways between multimorbidity and the onset of restricted participation among primary care patients with lower extremity osteoarthritis.

those with multimorbidity (18), is the main symptom of lower extremity OA, and may result in reduced participation (6,10).

The second potential mechanism concerns the role of obesity, which, through biomechanical or metabolic routes, may influence the progression of OA (19,20) and health problems, such as cardiovascular disease (21), and lead to the onset of restricted participation. Multimorbidity, pain, and obesity are separately associated with depression and locomotor disability (8,22–24). Depression is associated with poor outcomes for those with OA (25). Locomotor disability refers to the individual's physical capacity to walk or climb stairs. It is proposed in the ICF as part of the mechanism to participation restriction (1). Previous work empirically supports this, but also indicates that older adults with OA continue to participate in social activities despite locomotor disability/physical limitation (6). Therefore, in this study we proposed that the mechanisms whereby multimorbidity, obesity, and severe lower extremity pain might result in the onset of restricted participation are through depression and locomotor disability.

Procedures. Multimorbidity was defined using 2 different methods, the first using self-report of health conditions and impairments, and the second using general practice consultation data. Self-report data were used as they reflect an individual's report of how they appraise the presence of morbidities and are associated with poorer outcomes when compared with objective measures of morbidity (26). General practice consultation data were used to provide a more objective definition of multimorbidity based on the number of morbidities consulted for.

Multimorbidity defined by self-report. Participants were asked to report the presence of 3 common chronic health conditions (chest problems, heart problems, and diabetes mellitus), 2 impairments most commonly associated with disability (deafness and problems with eyesight), and 7 other impairments likely to restrict activity or mobility in older people (falls, memory difficulties, cough with spit, breathless when walking, dizziness, weakness in arms/legs, and raised blood pressure). From these single items, counts of health conditions and impairments were calculated (0–12). The median cut point (which was 2) was used to define multimorbidity (3–12) versus low comorbidity (0–2).

Multimorbidity defined by general practice consultation data. General practitioners in the study populations used the Read system to code all morbidity encounters in actual consultations. 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 were used to identify morbidity, and related to at least 1 consultation for a given morbidity category in the 18-month study period (repeat consultations for the same morbidity were not included). Multimorbidy was defined using a previously validated method; based on a simple count, multimorbidity was defined as ≥4 morbidities (27).

Defining participation restriction. Participation was measured using the Keele Assessment of Participation (KAP) (28), a self-report measure designed to assess participation restriction from the perspective of the individual. Participants were considered to be restricted if they reported participating during the previous 4 weeks "as and when (they) wanted" for "some of the time" or less. At the 6-year followup, incident participation restriction was defined as moving from no restriction at baseline to participation restriction at 6 years. The reliability and validity of the KAP have been established as adequate for providing estimates of perceived participation restriction in population studies (28).

Pathway variables. Obesity, lower extremity pain severity, depression, and locomotor disability were measured at baseline. Based on their body mass index (BMI; calculated from self-reported height and weight), subjects were categorized as normal weight (BMI 20–24.9 kg/m^2) or obese (BMI ≥30 kg/m^2) (29). Results are not presented for overweight (BMI 25–29.9 kg/m^2) because it only contributes 0.7% of the total effect of comorbidity on onset, and there were only 16 participants who were underweight (BMI <20 kg/m^2).

Lower extremity pain severity was measured using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (30) for those with hip and knee pain, and the Foot Disability Index (FDI) (31) for those with foot pain. Responses to the 5 WOMAC pain items are on a 5-point ordinal scale (none/mild/moderate/severe/extreme). The FDI contains 19 items designed to measure the effects of pain on physical activities. FDI responses are on a 3-point scale (none of the time/on some days/on most or every day). Subjects were categorized as having severe lower extremity joint pain if 1) those with hip or knee pain indicated "severe" or "extreme" pain in any of the 5 WOMAC pain items, or 2) those with foot pain indicated foot pain "on most or every day" on any of the items of the FDI pain intensity constructs (i.e., items 10 and 14–17) (32,33).

Depression was measured using the Hospital Anxiety and Depression Scale (HADS). The scale has a range of 0 to 21 and subjects were categorized as noncases (score 0–7) or possible/probable cases (score 8–21) (34). An interval-level score for locomotor disability, which has been devised using 5 items from the Short Form 36 (SF-36) physical functioning subscale (35) that measures limitation in an individual's physical ability to walk and ascend or descend stairs using the Rasch model, was included (36).

Potential confounders. Demographic and socioeconomic factors measured at baseline were included in the analysis as potential confounders of the relationship between pathway variables and onset of restricted participation. Demographic details collected were age and sex. Socioeconomic characteristics incorporated occupational class (manual/nonmanual) (37,38), educational attainment (completed high school only/went onto further education), and perceived adequacy of income (comfortably off/strain getting by on income) (39).

Statistical analysis. *Hypothesis 1: subjects with multimorbidity have an increased risk of the onset of restricted participation.* Logistic regression tested the crude relationship between multimorbidity at baseline and the onset of restricted participation by 3 years, subsequently adjusting for age, sex, occupational class, education, and income.

Hypothesis 2: the relationship between multimorbidity and onset of restricted participation is mediated by obesity, joint pain severity, depression, and locomotor disability. Path analysis (i.e., an extended form of multiple regression that tests whether dependent variables are on a pathway to the occurrence of an outcome [40]) was used to test the proposed mechanisms by examining for mediation of the association between multimorbidity at baseline and incident participation restriction at 3 years by the levels of obesity, lower extremity pain severity, depression, and locomotor disability at baseline. A series of models were built to estimate: 1) the total effect of multimorbidity at baseline on onset of participation restriction by 6 years (no adjustment for other factors), 2) the direct effect (i.e., the effect of multimorbidity on onset of participation restriction adjusting for pathway variables), and 3) the indirect effect (i.e., the reduction in the total effect of multimorbidity on restricted mobility minus the direct effect); this is the "amount" of mediation and the extent to which each factor explains the link between multimorbidity and onset (40,41). The Karlson-Holm-Breen method of decomposition of total effects in a logistic model into a sum of direct and indirect effects was adopted (42,43). The first model examines the total effect of multimorbidity on onset. For model 2, taking the obesity pathway as an example, variables were then added sequentially, i.e., 1) obesity, 2) obesity and depression, 3) obesity and locomotor disability, and 4) obesity, depression, and locomotor disability, in order to estimate which pathway variable has a higher indirect effect. The same pattern was followed for the pain pathway, i.e., 1) pain, 2) pain and depression, 3) pain and locomotor disability, and 4) pain, depression, and locomotor disability. Putative confounders were added to the models for each relevant mechanism and adjusted effects are reported. The analyses were performed first for multimorbidity defined using self-report data and then for multimorbidity defined by consultation data.

RESULTS

Response rates. At baseline, responses were received from 13,986 persons (71% of those mailed) and 10,432 (74.6%) consented to medical record review. From this sample, 2,573 had consulted a general practitioner for OA in the 18 months prior to baseline and indicated hip, knee, or foot pain in the baseline questionnaire (Figure 2), of these, 1,541 had no participation restriction at baseline and formed the potential sample for this analysis. There were 1,053 persons who had full followup data to 3 years (followup 68.3%; reasons for loss to followup were nonconsent to followup [n = 377] and exclusion or nonresponse at 3-year followup [n = 111]). Compared to those who were lost to followup or had incomplete data (n = 488), those included in the analysis were younger (median age 64.6 versus 67.5 years; $P < 0.01$), were more likely to be female (62.2% versus 54.7%; $P = 0.01$), and less likely to have severe lower extremity pain (19.5% versus 46.4%; $P < 0.01$) or be depressed (probable/possible cases: 18.3% versus 30.2%; $P < 0.01$); but there was no difference for multimorbidity (self-report: 27.0% versus 31.2%; $P = 0.09$ and consultation data: 53.2% versus 57.6%; $P = 0.07$) and educational attainment (further education: 9.0% versus 11.7%; $P = 0.12$) or obesity (21.7% versus 22.1%; $P = 0.98$).

Of the 1,053 older adults who had hip, knee, or foot pain, consulted for OA, and were included in the analysis, 181 (17.2%) had incident participation restriction by 3 years. Both definitions of multimorbidity at baseline were associated with incident participation restriction at 3 years; odds ratio (OR) 2.83 (95% confidence interval [95% CI] 2.03–9.94) for multimorbidity defined by self-report and OR 1.59 (95% CI 1.15–2.21) for multimorbidity defined by consultation data. Subjects with multimorbidity defined by self-report were significantly more likely to report severe lower extremity pain, obesity, depression, and locomotor disability at baseline (Table 1). Only locomotor disability was significantly associated with multimorbidity defined by consultation data.

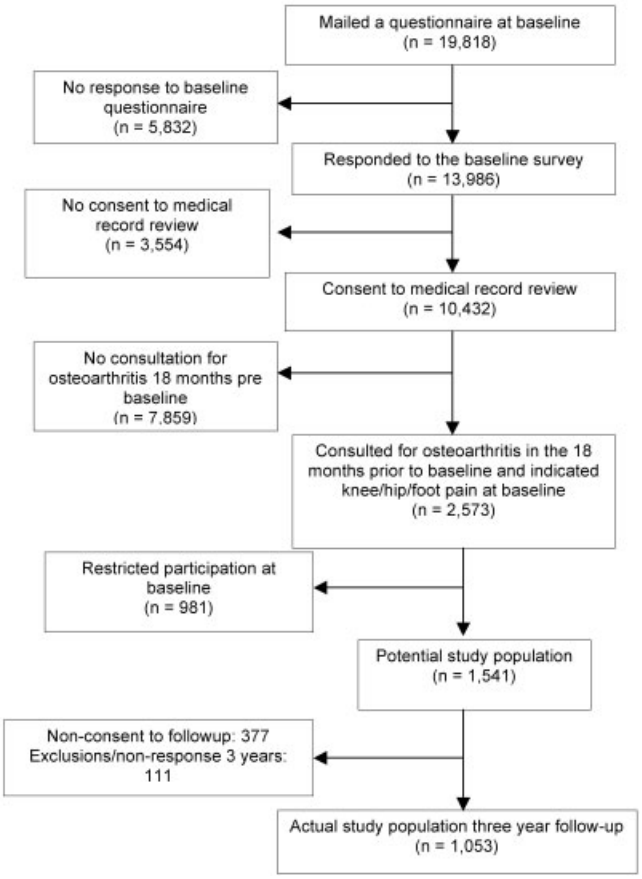

Figure 2. Flow diagram of participants.

Table 1. Characteristics of the study population at baseline*

	Multimorbidity defined by self-report		Multimorbidity defined by consultation data	
	Low comorbidity (0–2) (n = 769)	Multimorbidity (3+) (n = 284)	Low comorbidity (0–3) (n = 507)	Multimorbidity (4+) (n = 546)
Age, years				
50–59	277 (36.0)	68 (23.9)	197 (38.9)	148 (27.1)
60–69	294 (38.2)	104 (36.6)	179 (35.3)	219 (40.1)
≥70	198 (25.6)	12 (39.4)	131 (25.8)	179 (32.8)
Sex				
Male	281 (36.5)	117 (41.2)	199 (39.3)	199 (36.5)
Female	488 (63.5)	167 (58.8)	308 (60.8)	347 (63.5)
Onset of restriction at 3 years				
No	671 (87.3)	201 (70.8)	437 (86.2)	435 (79.9)
Onset	98 (12.7)	83 (29.2)	70 (13.8)	111 (20.3)
Pain				
Non-severe	452 (58.8)	112 (39.4)	287 (56.6)	277 (50.7)
Severe	317 (41.2)	172 (60.6)	220 (43.4)	269 (49.3)
Body mass index, kg/m^2				
Normal	220 (29.4)	56 (20.4)	146 (29.6)	130 (24.5)
Underweight	10 (1.3)	6 (2.2)	7 (1.4)	9 (1.7)
Overweight	360 (48.1)	138 (50.4)	233 (47.2)	265 (50.0)
Obese	159 (21.2)	74 (27.0)	107 (21.7)	126 (23.8)
Depression				
Noncase	684 (88.0)	204 (71.8)	431 (85.0)	457 (83.7)
Possible/probable case	85 (11.1)	80 (28.2)	76 (15.0)	89 (16.3)
Locomotor disability				
Less than or equal to −1.85	500 (65.5)	110 (39.3)	313 (62.6)	297 (54.6)
Greater than −1.85	264 (34.6)	170 (60.7)	187 (37.4)	247 (45.4)

* Values are the number (percentage).

Pathway 1: multimorbidity at baseline and incident participation restriction at 3 years via severe lower extremity pain. The standardized β coefficient for the total effect of the association between multimorbidity at baseline, defined by self-report, and incident participation restriction at 3 years was 0.450 (SE 0.080) (Table 2 and Figure 3). After inclusion of severe lower extremity pain, the direct effect was 0.418 (SE 0.081) and the indirect effect (i.e., the extent of mediation) was 0.032 (SE 0.015). The addition of depression (i.e., severe lower extremity pain and depression) increased the amount of mediation of the effect of multimorbidity on incident participation restriction to 0.065 (SE 0.021). The amount of mediation was greater with the addition of locomotor disability, i.e., severe lower extremity pain plus locomotor disability (0.091 [SE 0.024]); however, the contribution of severe pain decreased to 0.016 (SE 0.015); locomotor disability 0.075 (SE 0.023). The addition of both depression and locomotor disability to severe pain further increased the amount of mediation of the association between multimorbidity at baseline and incident participation restriction at 3 years to 0.115 (SE 0.028); severe pain 0.014 (SE 0.015), depression 0.031 (SE 0.016), and locomotor disability 0.070 (SE 0.023).

The coefficients for the extent of mediation by severe lower extremity pain, depression, and locomotor disability on the association between multimorbidity defined by consultation were lower than when defined by self-report data (e.g., total effect of 0.216 [SE 0.088]; the coefficient for mediation by severe lower extremity pain only was 0.012 [0.009]) (Table 2). However, the proportion of the total effect explained by severe pain, obesity, and locomotor disability was similar for both definitions of multimorbidity. For multimorbidity defined by consultation, depression did not increase the extent of mediation when included with pain or locomotor disability. The addition of locomotor disability decreased the extent of mediation of severe lower extremity pain to 0.006 (SE 0.006).

Pathway 2: multimorbidity at baseline and incident participation restriction at 3 years via obesity. The standardized β coefficient for the total effect of the association between multimorbidity at baseline, defined by self-report, and incident participation restriction at 3 years was 0.294 (SE 0.116). After inclusion of obesity, the direct effect was 0.273 (SE 0.117) and the indirect effect (i.e., the extent of mediation) was 0.020 (SE 0.019) (Table 2). Further addition of depression (i.e., obesity and depression) increased the extent of total mediation to 0.053 (SE 0.032). The addition of locomotor disability (i.e., obesity and locomotor disability) led to a further increase in the amount of mediation (0.098 [SE 0.038]). Including both depression and locomotor disability, in addition to obesity, increased the amount of mediation to 0.119 (SE 0.045), obesity 0.006 (SE 0.020), depression 0.027 (SE 0.031), and locomotor disability 0.086 (SE 0.037).

Table 2. Pathway from multimorbidity to the onset of restricted participation at 3 years via severe pain severity and obesity, with indirect effects disentangled into contributions from each pathway variable*

	Pathway 1: pain severity		Pathway 2: obesity	
	Multimorbidity defined by self-report	Multimorbidity defined by consultation data	Multimorbidity defined by self-report	Multimorbidity defined by consultation data
Mediation by severe pain/obesity only				
Total effect	0.450 (0.080)	0.216 (0.088)	0.294 (0.116)	0.279 (0.125)
Direct effect	0.418 (0.081)	0.204 (0.088)	0.273 (0.117)	0.266 (0.126)
Indirect effect	0.032 (0.015)	0.012 (0.009)	0.020 (0.019)	0.013 (0.013)
Mediation by severe pain/obesity and depression				
Total effect	0.448 (0.081)	0.218 (0.088)	0.290 (0.117)	0.282 (0.126)
Direct effect	0.384 (0.083)	0.206 (0.088)	0.237 (0.121)	0.274 (0.127)
Indirect effect	0.065 (0.021)	0.012 (0.012)	0.053 (0.032)	0.008 (0.016)
Via pain severity	0.028 (0.015)	0.010 (0.008)	–	–
Via obesity	–	–	0.017 (0.019)	0.009 (0.011)
Via depression	0.037 (0.016)	0.002 (0.008)	0.036 (0.028)	−0.002 (0.010)
Mediation by severe pain/obesity and locomotor disability				
Total effect	0.461 (0.081)	0.211 (0.089)	0.312 (0.118)	0.275 (0.127)
Direct effect	0.369 (0.083)	0.179 (0.089)	0.214 (0.121)	0.252 (0.128)
Indirect effect	0.091 (0.025)	0.032 (0.016)	0.098 (0.038)	0.023 (0.023)
Via pain severity	0.016 (0.015)	0.006 (0.006)	–	–
Via obesity	–	–	0.007 (0.019)	0.004 (0.012)
Via locomotor disability	0.075 (0.023)	0.026 (0.014)	0.090 (0.037)	0.020 (0.020)
Mediation by severe pain/obesity, depression, and locomotor disability				
Total effect	0.460 (0.081)	0.210 (0.089)	0.309 (0.118)	0.274 (0.128)
Direct effect	0.345 (0.084)	0.179 (0.089)	0.190 (0.125)	0.254 (0.128)
Indirect effect	0.115 (0.028)	0.031 (0.017)	0.119 (0.045)	0.020 (0.023)
Via pain severity	0.014 (0.015)	0.005 (0.006)	–	–
Via obesity	–	–	0.006 (0.020)	0.002 (0.012)
Via depression	0.031 (0.017)	0.002 (0.007)	0.027 (0.031)	0.000 (0.007)
Via locomotor disability	0.070 (0.023)	0.023 (0.013)	0.086 (0.037)	0.018 (0.018)
Mediation by severe pain, obesity, locomotor disability, and depression				
Total effect	0.425 (0.083)	0.274 (0.128)		
Direct effect	0.304 (0.086)	0.254 (0.128)		
Indirect effect	0.120 (0.029)	0.019 (0.023)		
Via obesity	−0.001 (0.001)	0.001 (0.005)		
Via pain severity	0.015 (0.015)	0.002 (0.012)		
Via depression	0.033 (0.017)	0.000 (0.007)		
Via locomotor disability	0.073 (0.024)	0.019 (0.019)		

With inclusion of all 4 factors, the contribution of severe lower extremity pain and obesity remained low: 0.015 (SE 0.015) and 0.001 (SE 0.001), respectively. Again, locomotor disability made the strongest contribution (0.073 [SE 0.024]).

Similar to that for severe lower extremity pain, the extent of mediation by obesity was lower when multimorbidity was defined using consultation data than when defined by self-report data (0.013 [SE 0.013]) (Table 2). The addition of depression did not increase the extent of mediation. The addition of locomotor disability did increase the amount of mediation (0.023 [SE 0.023]), although the coefficient for obesity remained low (0.004 [SE 0.012]). Inclusion of depression and locomotor disability reduced the coefficient for obesity to 0.002 (SE 0.012).

DISCUSSION

In this longitudinal study of adults ages ≥50 years who consulted primary care with lower extremity OA, 12% of the effect of multimorbidity on incident participation restriction was explained by potentially modifiable factors. Obesity, recognized as a major contributor to the global burden of disability in older adults (44), made little contribution to the onset of restricted participation, and the mechanism from obesity to incident participation restric-

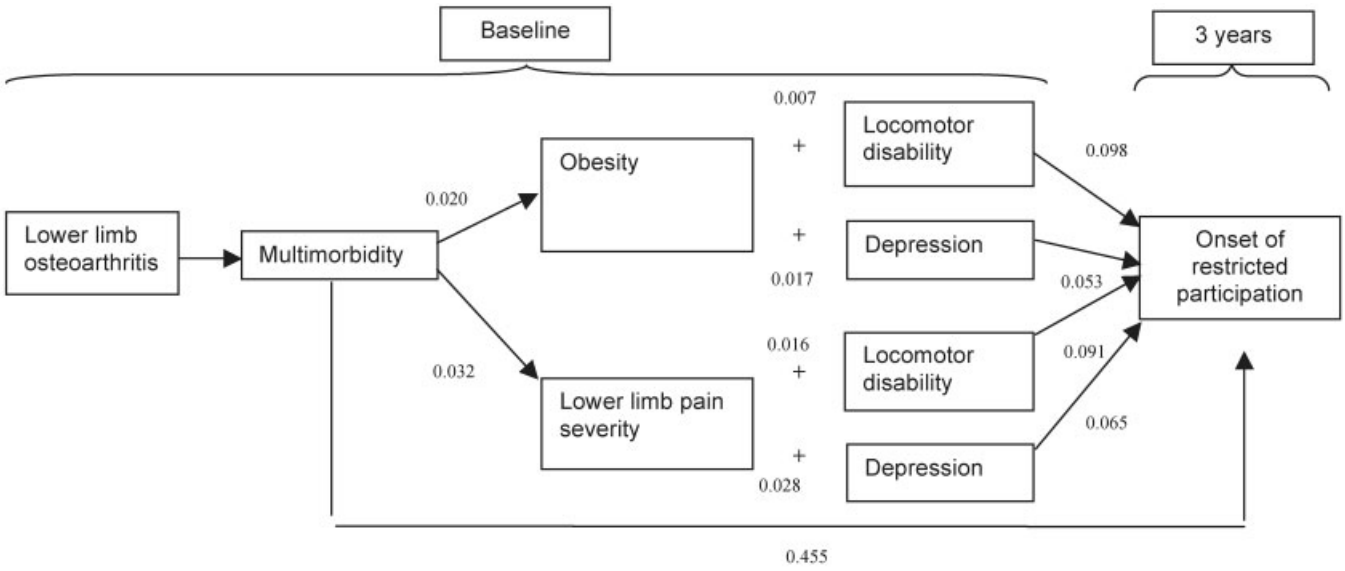

Figure 3. Pathways between multimorbidity, defined by self-report, and the onset of restricted participation among primary care patients with lower extremity osteoarthritis with path coefficients.

tion was primarily through locomotor disability. Lower extremity pain, the main symptom of OA, also explained a small amount of the effect of multimorbidity on future restriction, and much of this effect occurred via the mechanism of locomotor disability and depression. Locomotor disability made the strongest contribution to onset of restriction, followed by depression. This highlights the potential independent roles of both physical and psychological mechanisms in explaining the impact of health conditions and symptoms on participation in social and domestic life.

The majority of the link between multimorbidity and the onset of participation restriction was explained by the direct effect of multimorbidity. This suggests that there are potential mediators that were not considered in this analysis that could explain the link between multimorbidity and onset of restriction. Multimorbidity defined by consultation data had a weaker association with incident participation restriction than multimorbidity defined by self-report. Notably, when multimorbidity was defined by consultation data, depression had little effect. Why this is the case is unclear, although recent studies have shown that a patient-reported high symptom load is associated with poor outcomes, independent of the symptoms reported (45).

Regarding implications for practice and research, these findings highlight potential targets for primary care management for older adults with OA and multimorbidity. The contribution of obesity was small. However, small amounts of weight loss have significant and important effects in improving the symptoms and function in adults with lower extremity OA, although this is often difficult to achieve and maintain (46,47). Medical approaches to managing the symptoms of OA are important and targeting pain per se is going to make some contribution to promoting participation. However, maintaining or improving an individual's physical capacity and managing depression offer the clearest potential targets in terms of their apparent effect in mediating the onset of restriction in patients with combined multimorbidity and OA. Functional rehabilitation and approaches to exercise aimed at improving muscle strength and physical capacity may improve participation to a greater extent than interventions targeting obesity and pain alone, although clearly the latter can contribute in practice to the success of physical and mental rehabilitation.

Management of depression needs to be considered by clinicians when aiming to improve participation and functioning in older adults who have OA. It is often not recognized and undertreated in older adults in primary care, especially in those with chronic physical illness (48). These data suggest that the successful results of trials treating depression in persons with OA (49) can be extended to an effect on improving participation in older people with multiple medical problems alongside their OA. Behavioral and lifestyle approaches to physical activity and exercise could prevent the onset of participation restriction; in addition to maintaining capacity, continuing physical activity may also prevent and reduce the development of pain, depression, and obesity (50,51).

The strength and novelty of this study is the prospective design that enables the identification of mechanisms involved in incident participation restriction. Path analysis allows the testing of hypotheses about specific mechanisms to explain the effect of health conditions and symptoms on outcomes and, in particular, the inclusion of multiple (i.e., secondary) "mediators" that further explain the observed relationships. This builds on previous studies that used nonlinear modeling but did not estimate the direct and indirect effects because summation is not equivocal to the total effect (52). Disentangling the direct and indirect effects with binary data is complex, and this study has employed a novel method to do this. Although this can produce biased estimates, the data were re-

analyzed using an alternative method and produced identical findings (53).

There are limitations to this study. Data on pathway variables were collected by self-report. Although this is susceptible to measurement error, validated instruments (e.g., KAP [28], WOMAC [30], FDI [31], HADS [34], and the SF-36 [35]) were used to measure participation, pain severity, depression, and locomotor disability. There may be some differential reporting for height and weight that may lead to misclassification of BMI, and this is particularly notable in older adults (54). However, we adjusted for sociodemographic factors, which reduces misclassification of BMI and improves the accuracy of estimates of association between self-reported BMI and health outcomes in older people (55). Self-report of morbidities is susceptible to reporting bias. However, although they may not be severe enough to warrant formal diagnosis, self-reported morbidities relate to an individual's perception of health and symptoms, which is associated with poor health and functional outcomes. Bias can also affect consultation data, and neither method of defining multimorbidity can be considered to be the gold standard (56). The approach of categorizing variables to include binary variables may underestimate their effect. A simple count was used to categorize multimorbidity in which all conditions were weighted equally. This approach may be insufficient to fully explain the relationship of co-occurring comorbidities with participation restriction, as it takes no account of the severity of individual conditions or the interaction between co-occurring conditions. The generalizability of the study may be limited by the characteristics of the study sample; the area covered by the study is more deprived in terms of health, education, and employment, but has fewer barriers to housing and services than England as a whole. As in all longitudinal studies there was some attrition and missing data throughout the 3 years. The sample analyzed in this study was younger and healthier than those who were lost to followup, but there was no difference in education levels, multimorbidity, or obesity. Although absolute estimates of the effect of multimorbidity, obesity, lower extremity pain severity, depression, and locomotor disability at onset may be underestimated in our sample, it is unlikely that the main associations will be substantially affected. Finally, there may be other confounders that may be important but were not included in this study.

In conclusion, this observational study suggests that targeting locomotor disability and depression in patients with lower extremity OA and multimorbidity will improve participation in social and domestic life. Given that OA and the chronic diseases that frequently accompany it in older people may often not be amenable to cure, the potential for active management of depression and locomotor disability in these patients to significantly improve participation is important for the primary care of chronic disease in older people. However, the majority of the effect on participation restriction remains unexplained by these common factors. Future studies should aim to identify additional factors that may mediate these relationships, that are amenable to intervention, and that could be tested in intervention studies.

ACKNOWLEDGMENTS

The authors thank the administrative and health informatics staff at Arthritis Research UK Primary Care Centre, Keele University, and the doctors and staff of the participating general practices, as well as Peter Croft for his comments in drafting this paper.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Wilkie had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Wilkie, Blagojevic-Bucknall, Jordan, Lacey, McBeth.

Acquisition of data. Wilkie, Blagojevic-Bucknall, Jordan, Lacey, McBeth.

Analysis and interpretation of data. Wilkie, Blagojevic-Bucknall, Jordan, Lacey, McBeth.

REFERENCES

1. World Health Organization. International Classification of Functioning, Disability and Health. Geneva: World Health Organization; 2001.
2. Holmes WR, Joseph J. Social participation and healthy ageing: a neglected, significant protective factor for chronic non-communicable conditions. Global Health 2011;7:43.
3. Dale C, Prieto-Merino D, Kuper H, Adamson J, Bowling A, Ebrahim S, et al. Modelling the association of disability according to the WHO International Classification of Functioning, Disability and Health (ICF) with mortality in the British Women's Heart and Health Study. J Epidemiol Community Health 2012;66:170–5.
4. Peat G, McCarney R, Croft P. Knee pain and osteoarthritis in older adults: a review of community burden and current use of primary health care. Ann Rheum Dis 2001;60:91–7.
5. Jordan K, Clarke AM, Symmons DP, Fleming D, Porcheret M, Kadam UT, et al. Measuring disease prevalence: a comparison of musculoskeletal disease using four general practice consultation databases. Br J Gen Pract 2007;57:7–14.
6. Wilkie R, Peat G, Thomas E, Croft PR. Factors associated with restricted mobility outside the home in community-dwelling adults ages fifty years and older with knee pain: an example of use of the International Classification of Functioning to investigate participation restriction. Arthritis Rheum 2007;57:1381–9.
7. World Health Organization. The burden of musculoskeletal conditions at the start of the new millennium: report of a WHO Scientific Group (WHO Technical Report Series: 919). Geneva: World Health Organization; 2003.
8. Kadam UT, Croft PR. Clinical comorbidity in osteoarthritis: associations with physical function in older patients in family practice. J Rheumatol 2007;34:1899–904.
9. Wilkie R, Peat G, Thomas E, Croft PR. Factors associated with participation restriction in community-dwelling adults aged 50 years and over. Qual Life Res 2007;16:1147–56.
10. Machado GP, Gignac MA, Badley EM. Participation restrictions among older adults with osteoarthritis: a mediated model of physical symptoms, activity limitations, and depression. Arthritis Rheum 2008;59:129–35.
11. Kadam UT, Jordan K, Croft PR. Clinical comorbidity in patients with osteoarthritis: a case-control study of general practice consulters in England and Wales. Ann Rheum Dis 2004;63:408–14.

12. Schram MT, Frijters D, van de Lisdonk EH, Ploemacher J, de Craen AJ, de Waal MW, et al. Setting and registry characteristics affect the prevalence and nature of multimorbidity in the elderly. J Clin Epidemiol 2008;61:1104–12.
13. Thomas E, Wilkie R, Peat G, Hill S, Dziedzic K, Croft P. The North Staffordshire Osteoarthritis Project-NorStOP: prospective, 3-year study of the epidemiology and management of clinical osteoarthritis in a general population of older adults. BMC Musculoskelet Disord 2004;5:2.
14. National Health Service Information. The clinical terms, version 3 (the READ codes). Birmingham (England): NHS Information Authority; 2000.
15. Doherty M. Risk factors for progression of knee osteoarthritis. Lancet 2001;358:775–6.
16. Ling SM, Xue QL, Simonsick EM, Tian J, Bandeen-Roche K, Fried LP, et al. Transitions to mobility difficulty associated with lower extremity osteoarthritis in high functioning older women: longitudinal data from the Women's Health and Aging Study II. Arthritis Rheum 2006;55:256–63.
17. Jinks C, Jordan KP, Blagojevic M, Croft P. Predictors of onset and progression of knee pain in adults living in the community: a prospective study. Rheumatology (Oxford) 2008;47:368–74.
18. Smith BH, Elliott AM, Hannaford PC, Chambers WA, Smith WC. Factors related to the onset and persistence of chronic back pain in the community: results from a general population follow-up study. Spine 2004;29:1032–40.
19. Aspden RM. Osteoarthritis: a problem of growth not decay? Rheumatology (Oxford) 2008;47:1452–60.
20. Sowers M, Karvonen-Gutierrez CA, Palmieri-Smith R, Jacobson JA, Jiang Y, Ashton-Miller JA. Knee osteoarthritis in obese women with cardiometabolic clustering. Arthritis Rheum 2009;61:1328–36.
21. Kenchaiah S, Evans JC, Levy D, Wilson PW, Benjamin EJ, Larson MG, et al. Obesity and the risk of heart failure. N Engl J Med 2002;347:305–13.
22. Spangenberg L, Forkmann T, Brahler E, Glaesmer H. The association of depression and multimorbidity in the elderly: implications for the assessment of depression. Psychogeriatrics 2011;11:227–34.
23. Jinks C, Jordan K, Ong BN, Croft P. A brief screening tool for knee pain in primary care (KNEST): results from a survey in the general population aged 50 and over. Rheumatology (Oxford) 2004;43:55–61.
24. Vogelzangs N, Kritchevsky SB, Beekman AT, Brenes GA, Newman AB, Satterfield S, et al, for the Health ABC Study. Obesity and onset of significant depressive symptoms: results from a prospective community-based cohort study of older men and women. J Clin Psychiatry 2010;71:391–9.
25. Knoop J, van der Leeden M, Thorstensson CA, Roorda LD, Lems WF, Knol DL, et al. Identification of phenotypes with different clinical outcomes in knee osteoarthritis: data from the Osteoarthritis Initiative. Arthritis Care Res (Hoboken) 2011;63:1535–42.
26. Schwartz CE, Rapkin BD. Reconsidering the psychometrics of quality of life assessment in light of response shift and appraisal. Health Qual Life Outcomes 2004;2:16.
27. Kadam UT, Croft PR, and the North Staffordshire GP Consortium Group. Clinical multimorbidity and physical function in older adults: a record and health status linkage study in general practice. Fam Pract 2007;24:412–9.
28. Wilkie R, Peat G, Thomas E, Hooper H, Croft PR. The Keele Assessment of Participation: a new instrument to measure participation restriction in population studies. Combined qualitative and quantitative examination of its psychometric properties. Qual Life Res 2005;14:1889–99.
29. Department of Health. Health Survey for England. London: the Stationery Office; 1999.
30. Bellamy N. WOMAC Osteoarthritis Index: a user's guide. Ontario (Canada): London Health Services Centre, McMaster University; 1996.
31. Garrow AP, Papageorgiou AC, Silman AJ, Thomas E, Jayson MI, Macfarlane GJ. Development and validation of a questionnaire to assess disabling foot pain. Pain 2000;85:107–13.
32. Jinks C, Jordan K, Croft P. Measuring the population impact of knee pain and disability with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Pain 2002;100:55–64.
33. Roddy E, Muller S, Thomas E. Defining disabling foot pain in older adults: further examination of the Manchester Foot Pain and Disability Index. Rheumatology (Oxford) 2009;48:992–6.
34. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983;67:361–70.
35. Ware JE, Snow KK, Kosinski M, Gandek B. SF-36 health survey: manual and interpretation guide. Lincoln (RI): QualityMetric Incorporated; 1993.
36. Muller S, Thomas E, Peat G. Derivation and testing of an interval-level score for measuring locomotor disability in epidemiological studies of middle and old age. Qual Life Res 2009;18:1341–55.
37. Office for National Statistics. Standard occupational classification. Vol. 2. The coding index. London: Office for National Statistics; 2000.
38. Office for National Statistics. The national statistics socioeconomic classification user manual, version 1. London: Office for National Statistics; 2001.
39. Thomas R. Question bank commentary: income. 1999. URL: http://surveynet.ac.uk/sqb/topics/income/qbcommentary_income_thomas.pdf.
40. Streiner DL. Finding our way: an introduction to path analysis. Can J Psychiatry 2005;50:115–22.
41. Erikson R, Goldthorpe JH, Jackson M, Yaish M, Cox DR. On class differentials in educational attainment. Proc Natl Acad Sci U S A 2005;102:9730–3.
42. Buis ML. Direct and indirect effects in a logit model. Stata J 2010;10:11–29.
43. Karlson KB, Holm A. Decomposing primary and secondary effects: using the Karlson-Holm-Breen decomposition method. Res Soc Strat Mobil 2011;29:221–37.
44. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global burden of disease and risk factors. New York: World Bank and Oxford University Press; 2006.
45. Creed FH, Tomensen B, Davis I, Litlewood A, Chew-Graham C, Macfarlane GJ, et al. Multiple symptom reporting is associated with poor mental and physical health outcomes. J Psychosom Res. In press.
46. Miller GD, Nicklas BJ, Davis C, Loeser RF, Lenchik L, Messier SP. Intensive weight loss program improves physical function in older obese adults with knee osteoarthritis. Obesity (Silver Spring) 2006;14:1219–30.
47. Messier SP, Loeser RF, Miller GD, Morgan TM, Rejeski WJ, Sevick MA, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. Arthritis Rheum 2004;50:1501–10.
48. Chew-Graham C, Kovandzic M, Gask L, Burroughs H, Clarke P, Sanderson H, et al. Why may older people with depression not present to primary care? Messages from secondary analysis of qualitative data. Health Soc Care Community 2012;20:52–60.
49. Lin EH, Katon W, von Korff M, Tang L, Williams JW Jr, Kroenke K, et al, for the IMPACT Investigators. Effect of improving depression care on pain and functional outcomes among older adults with arthritis: a randomized controlled trial. JAMA 2003;290:2428–9.
50. Semanik PA, Chang RW, Dunlop DD. Aerobic activity in prevention and symptom control of osteoarthritis. PM R 2012;4 Suppl:S37–44.
51. Blumenthal JA, Babyak MA, O'Connor C, Keteyian S, Landzberg J, Howlett J, et al. Effects of exercise training on

depressive symptoms in patients with chronic heart failure: the HF-ACTION randomized trial. JAMA 2012;308:465–74.
52. Preacher KJ, Hayes AF. Contemporary approaches to assessing mediation in communication research. In: Hayes AF, Slater MD, Snyder LB, editors. The Sage sourcebook of advanced data analysis methods for communication research. Thousand Oaks (CA): Sage Publications; 2008. p. 13–54.
53. Karlson KB, Holm A. Decomposing primary and secondary effects: a new decomposition method. Res Soc Strat Mobil 2011;29:221–37.
54. Merrill RM, Richardson JS. Validity of self-reported height, weight, and body mass index: findings from the National Health and Nutrition Examination Survey, 2001–2006. Prev Chronic Dis 2009;6:A121.
55. Stommel M, Schoenborn CA. Accuracy and usefulness of BMI measures based on self-reported weight and height: findings from the NHANES & NHIS 2001–2006. BMC Public Health 2009;9:421.
56. Persell SD, Wright JM, Thompson JA, Kmetik KS, Baker DW. Assessing the validity of national quality measures for coronary artery disease using an electronic health record. Arch Intern Med 2006;166:2272–7.