Clinically Important Improvement in Function Is Common in People with or at High Risk of Knee OA: The MOST Study

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ABSTRACT. ***Objective.*** To calculate the frequency of clinically important improvement in function over 30 months and identify risk factors in people who have or are at risk of knee osteoarthritis (OA).
Methods. Subjects were from the Multicenter Osteoarthritis (MOST), a longitudinal study of persons with or at high risk of knee OA. We defined minimal clinically important improvement (MCII) with the Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) physical function using 3 different methods. Baseline risk factors tested for improvement included age, sex, educational attainment, presence of radiographic knee OA (ROA), the number of comorbidities, body mass index (BMI), knee pain, walking speed, isokinetic knee extensor strength, depressive symptoms, physical activity, and medication usage. We used logistic regression to evaluate the association of baseline risk factors with MCII.
Results. Of the 1801 subjects (mean age 63 yrs, BMI = 31, 63% women), most had mild limitations in baseline function (WOMAC = 19 ± 11). Regardless of how defined, a substantial percentage of subjects (24%–39%) reached MCII at 30 months. Compared to their counterparts, people with MCII were less likely to have ROA and to use medications, and were more likely to have a lower BMI, less knee pain, a faster walking speed, more knee strength, and fewer depressive symptoms. After adjustment, MCII was 40% to 50% less likely in those with ROA, and 1.9 to 2.0 times more likely in those walking 1.0 meters/second faster than counterparts.
Conclusion. Clinically important improvement is frequent in people with or at high risk of knee OA. The absence of ROA and a faster walking speed appear to be associated with clinically important improvements. (J Rheumatol First Release April 15 2010; doi:10.3899/jrheum.090989)

Key Indexing Terms:
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The natural history of knee pain and osteoarthritis (OA) often leads to difficulty performing functional activities[1], yet a number of persons maintain a high level of functioning[2], improve[3,4], or recover from previous limitations[5]. While this may seem contrary to the chronic progressive nature of OA, large observational studies from the past decade confirm this[2,6,7]. Closer examination of these studies reveals, however, that the magnitude or clinical significance of improvement is largely unknown. In particular, it is not clear how much of the improvement in these and other studies represents change that is relevant to the patient or healthcare provider.

Beaton and others have emphasized the need to differentiate between improvements in outcome that are merely statistically significant versus those that are clinically meaningful or important[8]. One method to qualify the clinical significance of improvement is to use a minimal clinically important improvement (MCII) threshold, which represents the smallest improvement that is important from the subject's perspective[9]. Although different thresholds of MCII for the Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) physical function scale have been reported[9,10], to date only one study with 44 subjects has examined the longitudinal occurrence of MCII in function in people with symptomatic hip or knee OA. That study found that 8 subjects had meaningful improvement as

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measured by the WOMAC physical function scale over 5 years[11]. We studied the frequency of clinically important improvement within a larger cohort of people with knee OA.

There is much literature examining risk factors of functional decline for persons with knee OA, but little is known about factors related to improvement. Research has identified these factors with decline in function in people with knee pain, symptomatic knee OA, and older individuals: age[4,12], body mass index (BMI)[12-15], pain at baseline[4,12-14,16], and walking speeds[17,18]. It is not clear whether these factors for decline are also associated with clinically important improvements in function. In particular, we are interested in identifying baseline risk factors associated with MCII to help clinicians better identify which of their patients evaluated for the first time are likely to make future improvements in function. Additionally, recognizing modifiable baseline risk factors associated with improvement may provide therapeutic targets for interventions to bring about functional gains. We will examine whether factors of decline are also important for meaningful improvement in function.

Our purpose was to examine the frequency of clinically important improvement in WOMAC physical function over 30 months using 3 definitions of MCII in people with or at risk of symptomatic knee OA with existing limitations in function, and to examine baseline factors associated with clinically meaningful improvement.

MATERIALS AND METHODS

Participants were recruited from the Multicenter Osteoarthritis (MOST) study, a large multicenter prospective cohort study of 3026 community-dwelling persons who were at high risk of developing symptomatic knee OA at baseline. MOST was designed to evaluate the effects of a variety of potential risk factors on the occurrence and progression of radiographic and symptomatic knee OA. Subjects aged 50 to 79 years were recruited from Birmingham, Alabama, and Iowa City, Iowa, USA. Baseline assessments took place between May 2003 and March 2005, and followup assessments 30 months later. Participants were defined as being at risk of developing knee OA based on known risk factors, including older age, female sex, previous knee injury or operation, and high body weight. A more detailed description of recruitment and sampling for MOST has been published[19].

We focused on MOST subjects with at least a minimal degree of self-reported functional limitation at baseline to permit us to study possible improvement in these limitations. We defined this as a baseline WOMAC physical function score of at least 4/68, which is consistent with a previous definition of minimal limitation in function[2]. We anticipated that subjects undergoing a knee or hip replacement would likely improve in function. But we wanted to focus on the natural history of functional improvement uninfluenced by these surgical procedures, so we excluded those who underwent a new total knee or hip replacement after the baseline assessment.

The MOST study protocol was approved by the institutional review boards at the University of Iowa, University of California San Francisco, University of Alabama, and Boston University Medical Center.

Outcome measures. We selected 3 definitions of MCII for WOMAC physical function. Our rationale for choosing these definitions was that they were anchored to patient-based indicators of improvement and defined meaningful improvement relative to baseline WOMAC physical function scores. All MCII definitions were dichotomous outcomes (improved/not improved) and were decreases in WOMAC physical function scores because lower scores on WOMAC represent less limitation. The first 2 definitions, MCII 26% and MCII Tertile, were estimated from a study of 1362 people with knee pain reporting a "good, satisfactory effect with occasional episodes of pain or stiffness" following a 4-week course of nonsteroidal antiinflammatory drug (NSAID)[9]. The last definition, MCII 17%, was from a study of 192 people with knee OA who underwent 3 to 4 weeks of inpatient rehabilitation[10].

MCII 26% and MCII 17% defines meaningful improvement as a 26% and 17% decrease in WOMAC physical function (final value minus baseline value/baseline value), respectively, with a minimum absolute decrease of 2 out of 68. For instance, a baseline WOMAC physical function score of 30 would need a 5.1-point decrease to meet meaningful improvement for MCII 17% criteria, and a 7.8-point improvement to meet MCII 26% criteria.

MCII Tertile defines meaningful improvement as absolute values (final value minus baseline value) dependent on baseline WOMAC physical function scores. We considered those with a decrease of 3.6, 8.0, and 13.9 out of 68 to reach meaningful improvement within low, medium, and high baseline tertile categories, respectively. These cutoff values came from the study of a 4-week course of NSAID in persons with knee pain[9].

Baseline risk factors. All participants underwent bilateral weight-bearing posteroanterior (PA) and lateral fixed-flexion radiographic evaluation of the knee[19]. We noted the presence or absence of radiographic knee OA (ROA) in either knee. We defined ROA based on radiographic findings in either tibiofemoral or patellofemoral joints. For the tibiofemoral joint this was a Kellgren and Lawrence (KL) grade > 2, and for the patellofemoral joint an osteophyte score > 2, or any joint space narrowing score > 2 with any osteophyte, sclerosis, or cyst score of > 1 on a lateral plain-view radiograph[20,21]. The interrater reliability-weighted κ for the KL grade at baseline was 0.80. For persons with ROA, we noted whether subjects had ROA in 1 or both knees.

Subjects self-reported age in years, sex, and educational attainment as attending some college or not. Comorbidities were estimated as none or 1 or more with a validated self-report measure, the modified Charlson comorbidity index[22]. BMI was classified according to the World Health Organization categories[23] and computed from standardized weight and height assessments. Knee pain (by visual analog scale) in the more painful knee was used for analysis and was quantified as the average knee pain over the past 30 days as measured on a horizontal line with 0 and 10 as endpoints. Walking speed was measured continuously in meters/second (m/s) from walking at a usual pace over 20 meters. Knee strength was classified in tertiles using the weaker knee as a data point, and was calculated from the mean of 4 isokinetic knee extensor torque repetitions at 60˚/s measured in Newton-meters. Depressive symptoms were classified by risk of significant depressive symptomatology measured with the Center for Epidemiologic Studies Depression Scale (CES-D: 0–60) ≥ 16[24]. Physical activity was measured in tertiles with the Physical Activity Scale for the Elderly (PASE: 0–360)[25].

We also examined whether subjects were or were not taking medications or had a steroid injection up to the baseline assessment. Specifically, we asked subjects if they took the following medications for arthritis every day or almost every day: aspirin, ibuprofen, acetaminophen, COX-2 inhibitors, or other NSAID. We also asked whether subjects had a steroid injection, such as cortisone, in either knee in the past 12 months from the baseline assessment.

Statistical analysis. To examine differences between people with and without clinically meaningful improvement, means and 95% CI were applied for continuous variables and odds ratios and chi-squared tests for categorical variables. We used multiple logistic regression for each of the 3 definitions of MCII, mutually adjusting for all baseline risk factors. We applied the Hosmer-Lemeshow goodness-of-fit statistics to examine the regression models.

We investigated the association between the following baseline risk factors with clinically meaningful improvement based on existing evidence linking them to changes in function[1,2,19,26-28]: age, sex, educational attain-

ment, ROA, comorbidities, BMI, knee pain, walking speed, knee extensor strength, depressive symptoms, physical activity, and medications. We performed additional analyses restricted to those with ROA at baseline, given that these subjects may have a different frequency of improvement and associated risk factors from those without ROA. We examined the same baseline risk factors with the addition of the presence of ROA in 1 or both knees.

RESULTS

Of the 3026 subjects from the MOST study at baseline, 782 had WOMAC physical function scores less than 4, and 20 did not have complete data. At the 30-month followup, 187 had a new total hip or knee replacement, 31 were lost to followup, and 205 did not have complete data or did not complete the 30-month assessment, leaving 1801 subjects for analysis (Figure 1). Compared to those included for analysis, the excluded sample (n = 1225) had a lower percentage of women (56% vs 63%), fewer people with ROA (52% vs 59%), and fewer people with comorbidities (40% vs 45%; all $p < 0.05$). There was no difference in age, education, or BMI. The most frequently missing risk factor among the 1801 included in the analyses was ROA status (n = 15) followed by level of education (n = 13).

Of the included subjects, the mean age was 62.7 years (SD 8.0). Most were women (63%), had some college education (71%), had ROA (59%), had no comorbidities (55%), and were overweight (BMI = 30.8, SD 6.0 kg/m^2). A little over one-third reported taking medication for arthritis or having a steroid injection in either knee at baseline (39%). Most subjects had mild to moderate limitations in function (mean WOMAC 18.7, SD 11.2). Subject characteristics and baseline data are listed in Table 1. Using different definitions of MCII, clinically meaningful improvement occurred in 615 (34%) for the MCII 26% method, 704 (39%) for the MCII 17% method, and 425 (24%) for the MCII Tertile method. There were 425 subjects meeting criteria for all 3 definitions of MCII. The percentage of subjects meeting MCII across the range of baseline WOMAC physical function scores is depicted in Figure 2.

Table 1. Subject characteristics and modifiable factors at baseline (n = 1801).

Characteristic	
Age, yrs (SD)	62.7 (8.0)
Women, n (%)	1135 (63)
Some college, n (%)	1279 (71)
ROA, n (%)	1045 (58.5)
Patellofemoral ROA, n (%)	80 (4.5)
Tibiofemoral ROA, n (%)	604 (33.8)
Patellofemoral and tibiofemoral ROA, n (%)	361 (20.2)
Comorbidities, n (%) none	991 (55)
BMI, kg/m^2 (SD)	30.9 (6.0)
Knee pain, VAS 0–10 (SD)	3.0 (2.2)
Walking speed, m/s (SD)*	1.18 (0.2)
Knee strength, Newton meters (SD)**	68 (36)
Depressive symptoms, CES-D 0–60 (SD)	8 (7.7)
Physical activity, PASE 0–360 (SD)	171 (87)
Arthritis medications or steroid injection, n (%)***	698 (39)
Baseline WOMAC physical function score, 4–68 (SD)	18.7 (11.2)

* Walking speed measured in meters per second over a 20-meter walk at a usual pace. ** Isokinetic knee extensor strength. Weaker value of 2 knees used for analysis. *** Arthritis medication taken every day or almost every day including aspirin, ibuprofen, acetaminophen, COX-2 inhibitors, or other nonsteroidal or antiinflammatory medications, or a steroid injection, such as cortisone, in either knee in the past 12 months. ROA: radiographic knee osteoarthritis; BMI: body mass index; VAS: visual analog scale; CES-D: Center for Epidemiologic Studies Depression Scale; PASE: Physical Activity Scale for the Elderly; WOMAC: Western Ontario McMaster Universities Osteoarthritis Index.

Baseline risk factors associated with meaningful improvement. For risk factors at baseline measured continuously, people with clinically important improvement had statistically significant lower BMI, faster walking speeds, and fewer depressive symptoms across all 3 MCII methods, less knee pain for the MCII 26% and MCII Tertile methods, and

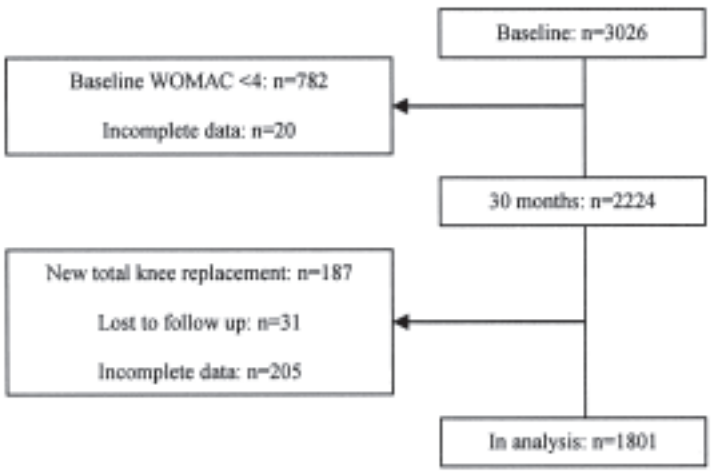

Figure 1. The progress of subjects from baseline to 30 months. WOMAC: Western Ontario McMaster Universities Osteoarthritis Index.

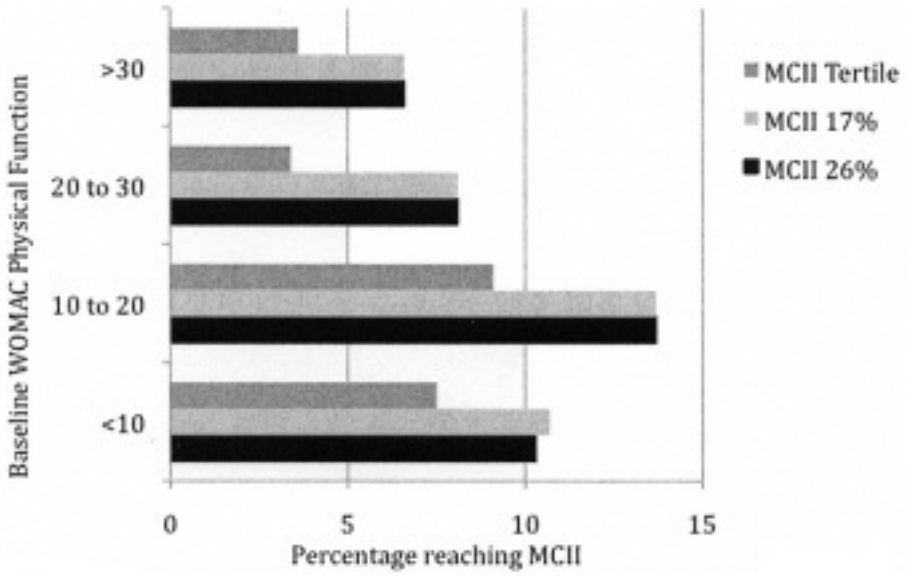

Figure 2. Percentages of subjects with meaningful improvement by minimal clinically important improvement (MCII) 26%, MCII 17%, and MCII Tertile by baseline WOMAC physical function score groups. MCII percentages refer to decrease in WOMAC physical function to reach meaningful clinically important improvement. Tertile refers to 3.6, 8.0, and 13.9 out of 68 for those in low, medium, and high baseline WOMAC physical function tertiles, respectively. WOMAC: Western Ontario McMaster Universities Osteoarthritis Index.

more knee strength using the MCII Tertile method, compared to their counterparts (Table 2). For risk factors measured categorically, people with ROA were 40% to 60% less likely to have clinically important improvement across all 3 MCII methods, and people with at least some college education were 1.3 times more likely to have clinically important improvement for the MCII 26% and Tertile methods compared to their counterparts. People who take arthritis

Table 2. Differences (without MCII and with MCII) and 95% CI in risk factors measured continuously at baseline between those with and without minimal clinically important improvement (MCII). All improvements indicated are mean (SD). Data in bold type represent $p < 0.05$.

	MCII Definitions								
	MCII 26%*			MCII 17%**			MCII Tertile***		
	Minimal Improvement	No Minimal Improvement	Difference (95% CI)	Minimal improvement	No Minimal Improvement	Difference (95% CI)	Minimal Improvement	No Minimal Improvement	Difference (95% CI)
Age, yrs	62.17 (8)	62.7 (8)	0.0 (–0.8, 0.8)	62.7 (8.0)	62.7 (8.0)	0.0 (–0.7, 0.8)	62.5 (7.6)	62.8 (8.1)	0.3 (–0.5, 1.2)
BMI, kg/m^2	**30.2 (5.8)**	**31.2 (6.0)**	**1.0 (0.4, 1.6)**	**30.3 (5.8)**	**31.2 (6.1)**	**0.9 (0.3, 1.5)**	**30.0 (5.6)**	**31.1 (6.1)**	**1.1 (0.5, 1.8)**
Knee pain (VAS 0–10)	**2.8 (2.3)**	**3.2 (2.3)**	**0.4 (0.2, 0.6)**	3.0 (2.3)	3.1 (2.3)	0.1 (–0.9, 3.5)	**2.8 (2.3)**	**3.2 (2.3)**	**0.4 (0.2, 0.7)**
Walk speed, m/s	**1.21 (0.2)**	**1.17 (0.2)**	**–0.04 (–0.06, –0.02)**	**1.20 (0.2)**	**1.17 (0.2)**	**–0.03 (–0.06, –0.02)**	**1.22 (0.2)**	**1.17 (0.2)**	**–0.05 (–0.07, –0.03)**
Knee strength, Newton-meters	70.7 (36.1)	67.1 (35.8)	–3.6 (–7.3, 0.0)	70.1 (36.3)	67.1 (35.8)	–2.9 (–6.5, 0.6)	**73.0 (35.5)**	**66.9 (36.1)**	**–6.1 (–10.3, –2.1)**
Depressive symptoms (CES-D 0–60)	**7.3 (7.3)**	**8.5 (8.0)**	**1.2 (0.5, 2.0)**	**7.4 (7.3)**	**8.5 (8.0)**	**1.1 (0.4, 1.8)**	**7.4 (7.4)**	**8.3 (7.9)**	**0.9 (0.1, 1.7)**
Physical activity (PASE 0–360)	175.8 (90.7)	169.6 (85.1)	–6.2 (–14.7, 2.3)	173.8 (89.9)	170.4 (85.3)	–3.4 (–11.7, 4.8)	177.1 (93.5)	170.0 (85.0)	–7.1 (–16.5, 2.5)

* 26% decrease in WOMAC physical function to reach MCII. ** 17% decrease in WOMAC physical function to reach minimal clinically important improvement. *** 3.6, 8.0, and 13.9 out of 68 for those in low, medium, and high baseline WOMAC physical function tertiles, respectively. WOMAC: Western Ontario McMaster Universities Osteoarthritis Index; BMI: body mass index; VAS: visual analog scale; CES-D: Center for Epidemiologic Studies Depression Scale; PASE: Physical Activity Scale for the Elderly.

medication or who had had a steroid injection in the last 12 months were 20% to 40% less likely to have clinically important improvement across all 3 MCII methods compared with their counterparts (Table 3).

After mutual adjustment for all risk factors, ROA status and walking speed remained associated with MCII across all 3 methods of estimating MCII. People with ROA were 40% to 50% less likely to have clinically important improvement compared to those without ROA, and people able to walk 1.0 m/s faster than their counterparts were 1.9 to 2.0 times more likely to have clinically important improvement (Table 4).

Analysis including only those with ROA. Of the 1045 subjects with ROA, 470 (45%) had ROA in 1 knee and 575 (55%) had ROA in both knees. Clinically meaningful improvement occurred in 288 (28%) for the MCII 26% method, 346 (33%) for the MCII 17% method, and 179

Table 3. Odds of minimal clinical important improvement (MCII) and 95% CI for risk factors measured categorically at baseline. Higher odds represent higher likelihood of meaningful improvement. Data in bold type represent confidence intervals that do not cross 1.0.

	MCII Definitions					
	MCII 26%*		MCII 17%**		MCII Tertile***	
	Minimal Improvement (%)	OR (95% CI)	Minimal Improvement (%)	OR (95% CI)	Minimal Improvement (%)	OR (95% CI)
Women	34	1.0 (reference)	39	1.0 (reference)	23	1.0 (reference)
Men	34	1.0 (0.8, 1.2)	38	1.0 (0.8, 1.2)	25	1.2 (0.9, 1.5)
No college	30	1.0 (reference)	36	1.0 (reference)	20	1.0 (reference)
At least some college education	**36**	**1.3 (1.1, 1.6)**	41	1.2 (1.0, 1.5)	25	**1.4 (1.1, 1.8)**
ROA absent	43	1.0 (reference)	47	1.0 (reference)	33	1.0 (reference)
ROA present	**27**	**0.5 (0.4, 0.6)**	**33**	**0.6 (0.5, 0.7)**	**17**	**0.4 (0.3, 0.5)**
No comorbidities	36	1.0 (reference)	41	1.0 (reference)	24	1.0 (reference)
One or more comorbidities	31	1.0 (1.0, 1.0)	36	1.0 (1.0, 1.0)	22	1.0 (1.0, 1.0)
No arthritis medications or steroid injection	37	1.0 (reference)	41	1.0 (reference)	26	1.0 (reference)
Arthritis medications or steroid injection	**28**	**0.7 (0.5, 0.9)**	**35**	**0.8 (0.6, 1.0)**	**17**	**0.6 (0.5, 0.8)**

* 26% decrease in WOMAC physical function to reach meaningful clinically important improvement. ** 17% decrease in WOMAC physical function to reach meaningful clinically important improvement. *** 3.6, 8.0, and 13.9 out of 68 for those in low, medium, and high baseline WOMAC physical function tertiles, respectively. ROA: radiographic knee osteoarthritis; WOMAC: Western Ontario McMaster Universities Osteoarthritis Index.

Table 4. OR and 95% CI among all subjects for risk factors associated with minimal clinically important improvement (MCII) in WOMAC physical function mutually adjusted for other factors*; with higher OR representing greater likelihood of MCII.

			MCII Definitions		
		n	MCII 26%**	MCII 17%†	MCII Tertile††
ROA	Absent	756	1.0 (reference)	1.0 (reference)	1.0 (reference)
	Present	1045	0.6 (0.4, 0.7)	0.6 (0.5, 0.7)	0.5 (0.4, 0.6)
Walking speed, m/s	OR of MCII per 1.0 m/s	1801	1.9 (1.0, 3.4)	1.9 (1.1, 3.3)	2.0 (1.0, 3.9)
No. of subjects included in logistic models			1768	1768	1768
p, Hosmer-Lemeshow test, 8 degrees of freedom			0.08	0.61	0.32

* Mutually adjusted for age, gender, education, comorbidities, body mass index, knee pain, knee strength, depressive symptoms, physical activity, and medication usage at baseline. ** 26% decrease in WOMAC physical function to reach minimal clinically important improvement. † 17% decrease in WOMAC physical function to reach minimal clinically important improvement. †† 3.6, 8.0, and 13.9 out of 68 for those in low, medium, and high baseline WOMAC physical function tertiles, respectively. ROA: radiographic knee osteoarthritis; WOMAC: Western Ontario McMaster Universities Osteoarthritis Index.

(17%) for the MCII Tertile method. People with clinically important improvement had faster walking speeds and were more likely to have ROA in 1 knee across all 3 methods of estimating MCII, fewer depressive symptoms for the MCII 26% and MCII 17% methods, and less knee pain and a lower BMI for the MCII 26% and MCII 17% methods, respectively, compared to their counterparts (data not shown). After mutual adjustment, we found persons in the highest strength tertile to be 1.9 to 2.2 times more likely to have clinically meaningful improvement across all 3 methods of estimating MCII compared with those in the lowest strength tertile (Table 5).

DISCUSSION

A substantial percentage of subjects (24%–39%) in our study had clinically important improvements in WOMAC physical function 30 months after initial assessment. People who had clinically important improvement had a lower BMI, faster walking speeds, and fewer depressive symptoms across all 3 definitions of MCII unadjusted for other risk factors. After mutual adjustment for other risk factors, people who improved walked faster and did not have radiographic evidence of knee OA at baseline compared with those who did not improve.

The MCII allows one to estimate how many people had clinically meaningful improvement, and represents the smallest improvement in score that can be regarded as important. Limiting investigation of longitudinal changes to group-level analysis, such as mean change and SD summary statistics, may create a perception that subjects' functional status is fixed. For instance, Botha-Scheepers and colleagues recently reported little change in functional limitations in a cohort of 115 people with symptomatic knee and hip OA over 2 years, as evidenced by a mean increase of 2.2 (SD 12.7) in WOMAC physical function[29]. We found similar mean change in WOMAC physical function (mean 0.7, SD 9.8), but our evaluation of change at the level of the individual revealed a large percentage of people with substantial improvement. Improvements in functional limitation have been reported. Most recently, Ayis and Dieppe found that 107 (19.6%) of 545 subjects with functional limitation at baseline had improvement when measured 8 years later, although these changes were not necessarily measured at a level of clinically meaningful improvement[14].

Our study findings reveal that people with ROA had at least a 40% reduction in odds of clinically important improvement in function across all 3 definitions of MCII, compared with those without ROA. Several studies support the notion that ROA influences changes in function. Roos and colleagues found that the presence of tibiofemoral OA was predictive of decline in sport and recreation activities 4 to 10 years later[30], and Davis and coauthors reported people with ROA at baseline were more likely to report difficulty with mobility-related activities 10 years later than those without ROA[31]. While some studies did not find an association between ROA status and function[32,33], several possibilities exist for this association in our study. First, we had ample power and heterogeneity of age to detect this association. We included 1801 people who were at least 50 years of age. Second, our primary outcome was clinically meaningful improvement in function, which was not used in previous studies[32,33]. Lastly, our study took knee radiographs with a standing fixed-flexion body position that has been shown to have high test-retest reliability[34]. Other studies used a full-extended position of the knee[32,33], which has been shown to be less reliable and accurate with estimating the severity of radiographic changes in the knee than a standing fixed-flexion body position[35].

Walking speed over 20 meters was also found to be associated with meaningful improvement in function across all 3

Table 5. OR and 95% CI among persons with ROA at baseline for risk factors associated with minimal clinically important improvement (MCII) in WOMAC physical function mutually adjusted for other factors*; higher OR representing greater likelihood of MCII.

	Mean (SD)	n	MCII Definitions MCII 26%**	MCII 17%†	MCII Tertile††
Knee strength, Newton meters					
Low	27.1 (9.7)	316	1.0 (reference)	1.0 (reference)	1.0 (reference)
Medium	54.75 (8.1)	313	1.5 (1.0, 2.2)	1.4 (1.0, 2.0)	1.6 (1.0, 2.6)
High	104.0 (28.3)	315	1.9 (1.1, 3.0)	1.7 (1.1, 2.7)	2.2 (1.2, 4.0)
No. of subjects included in logistic models			935	935	935
p, Hosmer-Lemeshow test, 8 degrees of freedom			0.18	0.31	0.37

* Mutually adjusted for age, gender, education, comorbidities, body mass index, knee pain, depressive symptoms, physical activity, ROA in 1 or both knees, and medication usage at baseline. ** 26% decrease in WOMAC physical function to reach minimal clinically important improvement. † 17% decrease in WOMAC physical function to reach minimal clinically important improvement. †† 3.6, 8.0, and 13.9 out of 68 for those in low, medium, and high baseline WOMAC physical function tertiles, respectively. WOMAC: Western Ontario McMaster Universities Osteoarthritis Index; ROA: radiographic knee osteoarthritis.

definitions of MCII. This is consistent with other studies, which show that slow walking speed in older adults is associated with a variety of adverse outcomes including incident functional limitation[18], hospital admission[36], and mortality[37-39]. Our findings extend walking speed as a marker of meaningful improvement in younger adults over the age of 50 years with or at high risk of knee OA. The speed of walking can be considered an estimate of walking ability. Given that the WOMAC physical function subscale measures self-reported difficulty with walking and several tasks for which walking is prerequisite, we expected faster walking speeds to be associated with clinically important improvement in function.

Certainly it is plausible that interventions that took place over 30 months may be responsible for subsequent meaningful improvements in function. Our cohort had mild to moderate limitations in function at baseline, as evidenced by a mean WOMAC physical function score of 18.7. Hence most study subjects would not have been referred for physical rehabilitation. We found persons taking prescription medication or those who had a steroid injection by the baseline examination to be less likely to have meaningful improvements in function in the unadjusted analysis. It is likely that these individuals had greater functional involvement and were thus less likely to improve. The association of persons starting to take medications over the 30-month period with meaningful improvement in function would be confounded by indication[40].

There are some limitations in our study. First, we employed cutoff values for MCII from studies that used patient-anchored definitions of meaningful improvements, and not other anchoring methods such as clinician or consensus cutoffs. Second, Gill and colleagues have recently suggested that fluctuations between states of ability and inability are much higher when outcomes are measured monthly compared to longer assessment intervals[41]. Since we calculated change in WOMAC physical function using only 2 reference points, baseline and 30 months, it is possible that the proportion of those with transient meaningful improvement on a monthly basis may be even more common than we estimated over 30 months. Future studies should employ repeated measures within shorter time intervals to investigate the cumulative frequency of meaningful improvement and time course of fluctuations in function. Third, we measured function using a self-report instrument, and lower rates of improvement have been reported for performance-based measures compared to self-report measures[33]. Future study should incorporate both self-report and performance-based outcomes to measure function better. Fourth, we used only 1 measure, the visual analog scale, to estimate knee pain, a method that may underestimate the ability of knee pain to predict meaningful improvements in function. We were reluctant to use the WOMAC pain score as a modifiable factor because of its high correlation with the WOMAC physical function score[42]. Fifth, potential bias may exist in our estimate of 24%–39% of subjects achieving MCII. We excluded those with new total joint replacements, and included those who had or were at high risk of symptomatic knee OA. Also, it is important to note that the percentage of those with meaningful improvement will naturally be higher using the MCII 17% cutpoint compared with MCII 26%, given that less change is needed for meaningful improvement. Sixth, we arbitrarily selected a WOMAC physical function cutoff of 4/68 to represent those with at least a minimal amount of functional limitation. We have analyzed the data using other cutoffs (range 3–6) and found similar percentages of recovery across all methods of calculating MCII. Lastly, we did not differentiate between persons who had 1 versus 2 painful knees, which could have an effect on meaningful improvement in function. Future research should investigate whether persons with 1 painful knee are more likely to have meaningful improvement in function compared with those with 2 painful knees.

Meaningful improvement is common among those with generally mild to moderate self-reported limitations in function who have or are at high risk for knee OA over a 30-month period. Our study found a robust percentage of people to have these improvements irrespective of the method used to estimate improvement. We emphasize that our definition of meaningful improvement excluded those with unchanged or worsening WOMAC physical function scores over 30 months. People without radiographic evidence of knee OA and those with fast walking speeds are more likely to have improvements than those with ROA and slower walking speeds. Healthcare providers may want to consider these risk factors when determining who may benefit from therapeutic intervention.

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