The Longitudinal Examination of Arthritis Pain (LEAP) Study: Relationships Between Weekly Fluctuations in Patient-Rated Joint Pain and Other Health Outcomes

ADAM HUTCHINGS, MICHAEL CALLOWAY, ERNEST CHOY, MICHELE HOOPER, DAVID J. HUNTER, JOANNE M. JORDAN, YUQING ZHANG, ONUR BASER, STACEY LONG, and LIISA PALMER

ABSTRACT. ***Objective.*** To examine relationships between weekly fluctuations in self-rated joint pain and other health outcomes among adults with osteoarthritis (OA).

Methods. In this observational study, 287 adults (aged ≥ 50 yrs) with hip or knee OA were recruited from 16 medical practices across the United States. Patients were telephoned weekly for 12 weeks to assess pain/stiffness, daily activities/function, productivity, emotional well-being, quality of life, and healthcare utilization. Associations between changes in joint pain levels and other health outcomes were evaluated using a generalized estimating equation model.

Results. The mean (SD) pain score at Week 1 was 4.2 (2.1) on the Western Ontario and McMaster Universities OA index (WOMAC) pain subscale (0 = no pain, 10 = extreme pain); during the study, 49% of patients reported a between-week fluctuation of ≥ 2 points. A 2-point decrease in WOMAC pain subscale score was associated with a 22% decrease in number of days of limited activity/week (ß = –0.107; 95% confidence interval –0.163, –0.051); a 48% decrease in number of days of missed work/week (ß = –0.217; 95% CI –0.395, –0.039); a 14% decrease in number of nights with pain-related sleep interference/week (ß = –0.068; 95% CI –0.109, –0.027). Patients were 1.6 times more likely to contact a healthcare provider when their pain changed from "acceptable" to "unacceptable."

Conclusion. Weekly fluctuations in pain levels and other health outcomes were identified among adults with OA. Decreases in patient-reported pain were associated with improvements in daily activities/functioning and decreases in work absenteeism, sleep interference, and healthcare resource use. (First Release Oct 15 2007; J Rheumatol 2007;34:2291–300)

Key Indexing Terms:

LONGITUDINAL STUDIES   ARTHRITIS   PAIN   QUALITY OF LIFE
ACTIVITIES OF DAILY LIVING   OUTCOME ASSESSMENT   HEALTHCARE

Osteoarthritis (OA) is one of the leading causes of pain and disability in the elderly[1,2]. When OA becomes symptomatic in the knee, as it does in around 13% of adults over 55 years of age[3], the effect is often debilitating[1]. Pain in the knee is a key factor in the decision to seek medical care and an established antecedent to disability[4]. Pain management is, therefore, a major goal of OA treatment[5-7].

Chronic OA joint pain influences patients' functional and social activities, relationships, socioeconomic status, and emotional well-being[8-10]. Chronic pain and functional limitations also contribute to absenteeism and to work related disability[11,12], and patients with OA have elevated healthcare resource use and related costs[13], as high pain levels are associated with increased odds of physician visits and analgesic and antiinflammatory medication use[14].

The effects of chronic pain depend on the patient's perception of pain severity and their coping and management skills[15,16]. Radiographic and magnetic resonance imaging features of OA, such as joint space narrowing and cartilage defects, are moderately associated with pain levels experienced by patients[17-19], while psychological well-being is

strongly correlated with reported knee pain[20,21]. The perception of joint pain is often the result of complex relationships between local peripheral mechanisms[22], central sensitization[23], and psychosocial factors[24,25]. For example, alleviation of pain can positively affect sleep, coping strategies, and mood, which then engender further improvements in pain levels and functional outcomes[26,27]. The relationships are complicated further, considering that perceived pain levels vary across sex and racial groups[28-30], and can fluctuate on a daily[31,32] and monthly[33] basis.

To date, findings from a few longitudinal studies have indicated that longterm fluctuations in OA pain levels relate to quality of life[33-35] and healthcare resource utilization[14,36]; however, direct associations between changes in OA pain levels and a full range of other health outcomes have rarely been studied at intervals of less than 1 month. Greater knowledge of the effect of longitudinal OA pain fluctuations on other health outcomes could lead to reductions in the burden of OA pain for patients, their families, and healthcare services. Therefore the Longitudinal Examination of Arthritis Pain (LEAP) study was conducted to gain a more precise understanding of these relationships. The LEAP study is the first to examine the variability of self-rated OA joint pain and its associations with other health outcomes on a weekly basis, among adults diagnosed with OA.

MATERIALS AND METHODS

Study design. The LEAP study was a longitudinal, observational study conducted in the US between May 1 and December 5, 2005. All patients who met the study eligibility requirements and completed the informed consent process underwent an initial physician interview. Patient-reported pain levels and other health outcomes were then collected using weekly telephone interviews over 12 weeks. The LEAP study was conducted in accordance with US Good Clinical Practice guidelines.

Patients. English-speaking adults aged at least 50 years with physician-diagnosed hip and/or knee OA were eligible for enrollment in LEAP. Patients were recruited across 4 census regions of the US by 12 primary care and 4 rheumatology practices (4 sites in the Northeast, 8 in the South, 1 in the Midwest, and 3 in the West). Sites were selected using specific institutional criteria, to ensure high-quality study conduct and the ability to enroll sufficient numbers of patients with hip and/or knee OA. Participating practices received posters (displayed at the discretion of the site coordinator) to advertise the study and recruit potential participants. Practices received a one-time compensation of $2000 for the cost of contracting, recruiting, and screening activities plus $200 per patient enrolled.

All patients were required to have identified signal-joint pain in a hip or knee on at least 15 out of the 30 days prior to enrollment, and to hear well enough to participate in a telephone interview. Patients received $25 compensation for each weekly questionnaire they completed, up to a total of $325 for the maximum of 13 completed questionnaires. Potential participants were excluded if they had other pain sites or conditions that would interfere with their ability to assess pain in the signal joint, had a prosthesis in the signal joint, had received an intraarticular injection in the signal joint within the 3 months preceding enrollment, were currently participating in a clinical trial, or had taken glucosamine for less than 3 months prior to the enrollment date.

Assessments

Baseline data collection. Baseline data for each patient were obtained during an initial visit to the physician's office, with input from the patient and a clinician familiar with the patient's medical history. Sociodemographic characteristics, clinical characteristics, current therapy, and healthcare resource utilization data were recorded.

Daily rating sheet. Patients were provided with a diary and encouraged to complete structured daily rating sheets to rate their daily pain at its highest, at its lowest, and on average using a scale of 0 (no pain) to 10 (extreme pain). Daily rating sheets also included a question asking whether more or less pain medication than usual was taken on that day. The purpose of the daily rating sheets was to help patients complete their weekly telephone interviews, and thus patients were not instructed how or at what time each day to complete the sheets. The daily rating sheets were not formally collected.

Weekly telephone interview. Weekly telephone interviews were carried out over 12 weeks by 10 trained survey administrators; patients did not have a copy of the interview questions. Interviews took an average of 20 minutes. Patients completed their first interview within about 1 week of study enrollment. Subsequent interviews took place at prearranged times and dates and, if possible, the same interviewer conducted all interviews for a given patient. Patients could miss interviews and remain in the study. Any patient who missed a scheduled interview was contacted twice within 1 day (to complete the missed interview) and 3 times within a week (to schedule the next interview). Patients who missed 2 consecutive interviews received a reminder postcard. These patients, along with any who provided verbal indication that they no longer wished to continue, were no longer contacted by interviewers. However, patients could reinitiate study involvement at any time during the 12-week period by calling a toll-free number.

Each interview was scripted and used an identical questionnaire that covered 6 areas of interest: pain/stiffness, daily activities and function, productivity, emotional well-being, quality of life, and healthcare resource use. The questionnaire was composed of 61 questions: 8 from the 8-item Medical Outcome Study Short-Form health survey (SF-8)[37], 5 from the 5-item Mental Health Inventory (MHI-5)[38], 24 adapted from the Western Ontario and McMaster Universities OA index (WOMAC)[39], and an additional 24 freestanding questions developed specifically to assess pain severity, daily activities, productivity loss, sleep impairment, and use of healthcare services. Use of telephone interviews for the WOMAC and SF-8 are valid methods of obtaining outcome measurements[40,41] and, although use of MHI-5 by telephone has not been validated, respondents generally completed the questions with little or no intervention from an interviewer.

Analytical methods. Baseline data were summarized descriptively for the study population.

Longitudinal pain fluctuations. The patient-rated lowest, highest, and average pain scores provided during each interview were used to calculate weekly pain fluctuations for each patient who completed an interview during a given week. Within-week pain fluctuations were calculated by subtracting the lowest pain score for the given week from the highest pain score for the given week. Between-week fluctuations in WOMAC pain subscale score were also examined.

Multivariable regression analyses. The relationships of pain and pain fluctuations to other health outcomes were examined using multivariable regression analyses. The WOMAC pain subscale score, patient-rated highest weekly pain score, patient-rated average weekly pain score, patient-rated lowest weekly pain score, and the number of days per week when the patient deemed their pain to be manageable, were all individually tested as independent variables in separate models. The patient-rated dichotomous measure ("acceptable"/"unacceptable" pain) was also examined as a predictor of outcome. The WOMAC pain subscale and the "acceptable"/"unacceptable" pain rating proved to be the 2 most consistent predictors of outcome across all domains, and therefore outcome data based on these 2 measures of pain are presented. A 2-point change was considered to be a minimum clinically important difference on the WOMAC pain subscale (an 11-point scale)[42,43]. The other health outcome variables evaluated were daily activities and function, productivity (among workers and nonworkers), emotional well-being (mood, sleep interference), quality of life, and healthcare resource use.

The effect of pain assessed at baseline examination (Week 1) and changes

in pain status over time on each outcome variable were examined using generalized estimating equation models[44], using a binomial link for 0–1 dependent variables, a Poisson link for count data, and a Gaussian link for continuous variables. This approach provides a coefficient for within-subject differences over time (i.e., the average change in an outcome measure of interest associated with a specific change in pain level). In all multivariable regression models, adjustments were made for age, sex, race/ethnicity, marital status, body mass index, comorbidity, education status, medication use, number of years since onset of OA symptoms, WOMAC physical functioning score, and WOMAC stiffness subscale score. The MHI-5 score was considered a potential confounding variable and was controlled in all analyses except mood. Medical insurance coverage was controlled when analyzing the effect of pain status on healthcare resource use[45].

RESULTS

Patient disposition. Of 303 adults screened for possible participation in the LEAP study, 287 were enrolled. The geographic distribution of enrolled patients in the US was 44% South, 28% Northeast, 20% West, and 9% Midwest. Patient retention was high: only 33 patients (11%) did not complete the study and 21 of these withdrew prior to their fourth weekly interview. The most common reasons for patient discontinuation (based on anecdotal evidence from interviewers) were unspecified personal reasons, finding the daily diary and weekly interviews cumbersome, or going on vacation. Among the 279 patients (97%) who completed at least 1 interview, the mean ± SD number of completed interviews was 10.7 ± 2.5; 234 patients (82%) completed 10 or more interviews. The most common reasons for missed interviews were vacation, hospitalization, or forgetting the appointment.

Baseline characteristics. Sociodemographic and clinical characteristics of the enrolled patients are summarized in Table 1 and Table 2, respectively. The healthcare providers most frequently consulted by patients for their OA were orthopedic surgeons (38%), physical therapists (17%), and rheumatologists (10%). At study entry, 91% of patients were taking at least 1 prescription or over-the-counter OA medication. Nonselective nonsteroidal antiinflammatory drugs (NSAID) were most commonly taken (66%). The mean ± SD number of OA medications taken by each patient was 3.7 ± 0.7. The baseline mean ± SD pain intensity rating was 4.4 ± 2.4, indicating moderate pain.

Population characteristics at Week 1. Of 287 enrolled patients, 275 completed interviews at Week 1. Sample mean responses are detailed in Tables 3 and 4. The mean WOMAC pain subscale score at Week 1 was 4.2 (indicating moderate pain). The differences between the mean "average" weekly pain rating (4.5) and the mean lowest (2.7) and mean highest (6.9) weekly pain ratings indicated a within-week pain fluctuation of roughly ± 2 points (on the 11-point daily rating scale). Nonworkers were more likely than workers to report missed work/normal activity: 62% of nonworkers and 33% of workers missed all or part of a day of work/normal activity during Week 1.

Association between pain levels and other health outcomes at Week 1. Cross-sectional associations between pain levels

Table 1. Sociodemographic characteristics of LEAP study patients.

Characteristic	All Patients*, n = 287
Age, mean ± SD yrs	65.0 ± 8.7
Age group, %, yrs	
50–59	28
60–69	40
70–79	24
≥ 80	6
Women, %	70
Race/ethnicity, %	
Non-Hispanic Caucasian	89
Non-Hispanic Black/African American	6
Hispanic	4
Marital status, %	
Married/domestic partner	60
Separated/divorced/widowed/never married	39
Living situation (all residential setting), %	
Alone	27
Spouse/partner	61
Relative/friend	11
Education level, %	
No high school diploma or GED equivalent	10
Completed high school or GED	34
Some college or higher	53
Employment status, %	
Work or volunteer, fulltime	24
Work or volunteer, part-time	23
Retired	41
Disabled	8
Other	3
Health insurance coverage, %	
Private	68
Medicare and no other insurance	45
Other insurance	13
None	3

* Patients are included only in those categories for which they have known values. GED: General Educational Development

(WOMAC pain subscale score and "acceptable"/"unacceptable" pain) and other health outcomes at Week 1 are described in Tables 5 and 6. Lower WOMAC pain subscale scores were associated with lower levels of limited activity, lower levels of missed activity (nonworkers only), less sleep interference, and better quality of life. WOMAC pain subscale scores at Week 1 were not associated with levels of missed work (workers only), mood, or healthcare provider contact (Table 5). A rating of "acceptable" pain was associated with lower levels of limited activity, lower levels of missed activity (nonworkers only), less sleep interference, better quality of life, better mood, and less healthcare provider contact. A rating of "acceptable" pain at Week 1 was not associated with levels of missed work (workers only; Table 6).

Longitudinal fluctuations. Based on all responses given during the study, average pain levels reported by patients over 12 weeks were similar to those described at Week 1. The overall mean scores ± SE were: 3.8 ± 0.04 on the WOMAC pain subscale (2967 responses); 4.3 ± 0.04 on the "average" weekly

Table 2. Clinical characteristics of LEAP study patients.

Characteristic	All Patients*, n = 287
Body mass index, mean ± SD	
Male	31.4 ± 6.4
Female	31.6 ± 7.7
Time since onset of OA symptoms, mean yrs ± SD	10.9 ± 9.2
Signal joint, %	
Right knee	44
Left knee	38
Right hip	10
Left hip	8
OA in signal joint confirmed by radiograph, %	80
Length of time since confirmation, %, mo	
1–6	30
7–24	38
> 24	31
Other sites with OA, mean ± SD	1.9 ± 1.2
Other sites with OA, %	
Knee	68
Hip	36
None	9
Care recieved from OA specialist, %	66
Dietary supplements ever used to treat OA symptoms, %	41
Comorbid conditions, mean ± SD	1.4 ± 1.3
Most common comorbid conditions, %	
Cardiovascular condition (e.g., hypertension, heart attack)	63
Diabetes	15
Respiratory condition (e.g., asthma)	15

* Patients are included only in those categories for which they have known values.

pain rating (2962 responses); 2.6 ± 0.04 on the lowest weekly pain rating (2967 responses); and 6.5 ± 0.04 on the highest weekly pain rating (2968 responses). The mean values and variability of other continuous outcomes reported throughout the study (data not shown) were also consistent with the data reported for Week 1. During the study, patients exhibited a mean ± SD within-week pain fluctuation (the difference between their lowest and highest pain score during the past week) of 3.9 ± 1.9 points. Forty-nine percent of patients reported at least one between-week difference in WOMAC pain subscale score of 2 or more points.

Association between changes in pain levels and other health outcomes. Effects of weekly pain change (as measured by the WOMAC pain subscale score and "acceptable"/"unacceptable" pain ratings over time) on other health outcomes are described in Tables 5 and 6.

Association between changes in WOMAC pain subscale score and other health outcomes. Weekly changes in the WOMAC pain subscale score were associated with changes in the number of days of limited activity each week, number of days with limited productivity (nonworkers and workers) each week, number of nights with sleep interference each week, mood, and quality of life (Table 5). Changes in WOMAC pain subscale score were not associated with changes in healthcare provider contact.

Change in WOMAC pain subscale score was strongly associated with productivity. A 2-point decrease in pain score was associated with a 32% improvement in the number of days of missed activity (nonworkers only) and a 48% improvement in the number of days of missed work (workers only) each week (Figure 1A). No such effect, however, was observed for mood or quality of life.

Association between changes in "acceptable"/"unacceptable" pain and other health outcomes. Changes between ratings of "acceptable" and "unacceptable" pain were associated with differences in the number of days of limited activity each week, the number of days with limited productivity (nonworkers and workers) each week, the number of nights with sleep interference each week, mood, quality of life, and healthcare provider contact (Table 6).

Productivity was again particularly strongly associated with these pain ratings — when pain status changed from "unacceptable" to "acceptable," the number of days of missed work/activity improved by 64% (Figure 1B). Consistent with the observations with the WOMAC pain subscale score, change to a rating of "acceptable" pain had a relatively modest effect on quality of life and mood (degree of change < 5%; Figure 1B).

Healthcare resource use was significantly reduced when pain status changed from "unacceptable" to "acceptable." Patients were 1.6 times more likely to contact a healthcare provider when their pain became "unacceptable." Health insurance status did not significantly affect healthcare resource use.

DISCUSSION

LEAP is the first observational study involving adults with OA to describe longitudinal relationships between frequent (weekly) changes in patient-rated pain levels and other health outcomes. Weekly fluctuations in signal-joint pain scores and other health outcomes were identified over 3 months; these observed reductions in pain intensity were directly associated with increased functionality, decreased sleep interference, increased productivity, improved quality of life, and decreased healthcare resource use. The LEAP study shows that a longitudinal study with weekly contact can be successfully carried out in a US population of adults with hip and/or knee OA. The results broaden the current evidence that changes in chronic pain levels affect other health outcomes, and demonstrate that small changes in OA pain have a significant and contemporaneous impact on personal and socioeconomic outcomes.

The LEAP study population was comparable to populations enrolled in similar OA studies[14,46-48] and resembled US patients who have symptomatic hip OA in terms of sociodemographics and clinical features[47-49]. The population was characterized by high levels of pain medication use, moderate levels of pain, and detectable variations in pain levels. The pain fluctuations were broadly similar to those described

Table 3. Patient-reported health outcomes at Week 1 (baseline).

Domains and Questions	No. of Patients	Mean ± SD or %
Pain/stiffness		
Stiffness, mean ± SD, WOMAC subscale score	274	4.8 (2.3)
Pain, mean ± SD, WOMAC subscale score	275	4.2 (2.1)
Weekly pain rating, mean ± SD of 0 (no pain) to 10 (extreme pain)		
Highest	275	6.9 (2.1)
Average	273	4.5 (2.1)
Lowest	274	2.7 (2.0)
Pain "acceptable" during past week, %	274	69
Pain "manageable" during past week, mean ± SD days/week	274	5.4 (1.9)
Daily activities and function		
Function, mean ± SD WOMAC subscale score	275	3.9 (1.9)
Daily activities limited, mean ± SD days/week	272	1.9 (2.1)
Able to do planned activities due to pain, %	275	
None/little of the time		9
Some of the time		26
Most/all of the time		65
Asked for help with activities due to pain, %	275	
Nearly every day/more than half of days		10
On several days		26
Never		64
Unable to engage in enjoyable activities due to pain, %	274	
Every day		8
2–3 times a week		32
Once/never		60
Productivity		
Entire day of work/normal activity missed due to pain, mean ± SD days/week	274	0.5 (1.2)
Part of a day of work/normal activity missed due to pain, mean ± SD days/week	274	1.1 (1.6)
Emotional well-being		
Mood/emotion, mean ± SD MHI-5 score	272	24.2 (3.9)
Sleep interference due to pain, mean ± SD rating of 0 (slept well) to 10 (unable to sleep)	275	3.4 (2.9)
Woken by pain, mean ± SD nights/week	273	2.4 (2.6)
Woken by pain, mean ± SD times/night	175	2.3 (1.5)
Time to fall back asleep if woken, mean ± SD hours	46	1.7 (1.4)
Quality of life		
Quality of life and general health, mean ± SD SF-8 score	274	44.9 (6.5)

WOMAC: Western Ontario and McMaster Universities OA index; MHI-5: 5-item Mental Health Inventory; SF-8: 8-item Short-Form health survey.

in a study evaluating the reliability of pain flare assessment[50], and similar levels of pain and pain variation have been reported in clinical trials of patients with hip and/or knee OA[31,51]. Importantly, although most patients in our study rated their pain levels as "acceptable," quality of life was lower than that of the general population, as reported previously for patients with symptomatic hip and/or knee OA[14,35,52]. Further, about one in 10 patients reported severe and disabling levels of pain during most days. When pain control was inadequate, patients adopted self-coping approaches to deal with their pain (e.g., limiting their daily activities). Only 10% of patients had consulted a rheumatologist regarding their OA. These results suggest that many patients with OA tolerate a considerable burden of pain through self-coping mechanisms, and that the clinical management of OA pain may be inadequate in a notable subgroup of patients.

Among patients with OA pain, reductions in pain levels of 20% or more (equivalent to a decrease of ~2 points on an 11-point scale) are associated with self-rated improvements in overall clinical status after 5–12 weeks[53]. Although there are presently no standard definitions of pain flare in OA, a 20% variation (equivalent to a 2-point difference on the WOMAC pain subscale or a 20 mm change on a 100 mm scale) seems to be consistent and clinically significant in terms of pain perception and functional impairment[42,43]. In our study, clinically relevant (2-point) reductions in weekly WOMAC pain subscale scores, along with a change in pain rating from "unacceptable" to "acceptable" pain, were consistently associated with substantial improvements in activity, productivity, and sleep — outcomes that are likely to influence indirect healthcare costs[9,13]. Mood and quality of life also improved when pain levels decreased, although the magnitude of change was

Table 4. Healthcare resource use at Week 1 (baseline).

Domains and Questions	No. of Patients	Mean ± SD or %
Healthcare resource use		
Prescription medication taken for pain during past week, %	275	90
Pain relief when medication taken, %	243	
None/mild		30
Moderate		58
Complete		12
Action taken if pain relief was "none" or "mild", %	72	
Reduce activities		71
Try different medication		31
Increase dose		25
Use a cane		24
Get assistance from others		14
Contact doctor		8
Pain medication used, mean ± SD days/week		
Any	253	5.4 (2.3)
Over-the-counter medication	246	3.7 (2.8)
Prescription OA medication	236	3.2 (3.2)
Medications changed by doctor, %	273	6
Contacted healthcare professional during past week, %	275	12
In-person visit		7
Scheduled a visit		3
Telephone discussion		6

Table 5. Association between adjusted WOMAC pain subscale scores and other health outcomes. Outcomes were adjusted for the covariables age, sex, race/ethnicity, marital status, body mass index, comorbidity, WOMAC stiffness score, WOMAC physical functioning score, education status, medication use, number of years since the onset of OA symptoms, and insurance status.

Domains	Week 1 Pain Level ß-coefficient (95% CI)	p	Decrease in Pain Level* ß-coefficient (95% CI)	p
Daily activities and function				
Days of limited activity	0.1192 (0.0223, 0.2161)	0.0159	–0.1070 (–0.1632, –0.0507)	0.0002
Productivity				
Days of missed work (workers)	0.0869 (–0.2246, 0.3984)	0.5845	–0.2170 (–0.3947, –0.0393)	0.0167
Days of missed activity (nonworkers)	0.1706 (0.0135, 0.3277)	0.0333	–0.1441 (–0.2366, –0.0516)	0.0023
Emotional well-being				
MHI-5 score	0.0074 (–0.0089, 0.0236)	0.3760	0.0106 (0.0042, 0.0170)	0.0012
Nights with sleep interference	0.1644 (0.0537, 0.2752)	0.0036	–0.0680 (–0.1089, –0.0271)	0.0011
Quality of life				
SF-8 score	–0.0123 (–0.0209, –0.0038)	0.0049	0.0126 (0.0079, 0.0174)	< 0.0001
Healthcare resource use				
Contact with healthcare provider	0.0870 (–0.1555, 0.3296)	0.4818	–0.1012 (–0.3180, 0.1155)	0.3599

*1-unit decrease (improvement) in WOMAC pain subscale score. WOMAC: Western Ontario and McMaster Universities OA index; MHI-5: 5-item Mental Health Inventory; SF-8: 8-item Short-Form health survey.

smaller than for productivity, activity, or sleep. The associations represent the direct effect of pain, as the models were adjusted for age, sex, race/ethnicity, marital status, body mass index, comorbidity, education status, medication use, number of years since onset of OA symptoms, WOMAC physical functioning score, and WOMAC stiffness subscale score.

The links between changes in pain levels and quality of life observed in this study are consistent with the results of other

Table 6. Association between adjusted "acceptable"/"unacceptable" pain ratings and other health outcomes. Outcomes were adjusted for the covariables age, sex, race/ethnicity, marital status, body mass index, comorbidity, WOMAC stiffness score, WOMAC physical functioning, education status, medication use, number of years since the onset of OA symptoms, and insurance status.

Domains	Week 1 Pain Rating "acceptable" ß-coefficient (95% CI)	p	Change in Pain Rating to "acceptable" ß-coefficient (95% CI)	p
Daily activities and function				
Days of limited activity	–0.5466 (–0.7943, –0.2990)	< 0.0001	–0.3012 (–0.4321, –0.1702)	< 0.0001
Productivity				
Days with limited productivity (workers)	–0.4990 (–1.0722, 0.0742)	0.0880	–0.5051 (–0.9460, 0.0643)	0.0247
Days with limited activity (nonworkers)	–0.5677 (–0.9016, –0.2337)	0.0009	–0.4916 (–0.7122, –0.2709)	< 0.0001
Emotional well-being				
MHI-5 score	0.0615 (0.0194, 0.1037)	0.0043	0.0269 (0.0114, 0.0423)	0.0007
Nights with sleep interference	–0.2763 (–0.5408, –0.0117)	0.0407	–0.1953 (–0.3017, –0.0889)	0.0003
Quality of life				
SF-8 score	0.0541 (0.0349, 0.0733)	< 0.0001	0.0341 (0.0198, 0.0484)	< 0.0001
Healthcare resource use				
Contact with healthcare provider	–0.8463 (–1.3653, –0.3272)	0.0014	–0.4939 (–0.9328, –0.0550)	0.0274

* Change from "unacceptable" to "acceptable" pain rating. WOMAC: Western Ontario and McMaster Universities OA index. MHI-5: 5-item Mental Health Inventory; SF-8: 8-item Short-Form health survey.

studies[34,35,46], including those that have described associations between pain levels, quality of life, and healthcare resource use over periods of 6 months or more[14,36,54]. Thus, quality of life and mood appear to respond to changes in pain levels, albeit more gradually than other outcomes such as productivity. These data emphasize the importance of evaluating patients' current level of OA pain and the frequency with which their pain fluctuates. Management strategies designed to cope with breakthrough pain, such as lifestyle interventions (self-awareness of physical limitations and pacing activities) and healthcare system interventions (cognitive-behavioral therapy and use of rapidly acting analgesia) may also be beneficial to patients with OA pain[55].

Most of the health outcomes examined were dependent on absolute levels and on relative changes in pain, but productivity (workers only) was sensitive only to fluctuations in pain. It may be that workers are reluctant to let pain affect their paid employment, and only miss work when their pain becomes unmanageable[11], whereas nonworkers have more freedom to limit their activities. In support of this, most patients who reported missed work/activity during Week 1 were nonworkers. Interestingly, healthcare provider contact was associated with the pain rating of "acceptable"/"unacceptable," but not with the WOMAC pain subscale score. It is likely that patients cope with small variations in pain by limiting activities and increasing medication usage, and only go to their doctor when their pain management strategies are exhausted and their pain becomes "unacceptable." Overall, the "acceptable"/"unacceptable" pain measure was predictive of change across a range of assessments, highlighting its potential value as a patient-based definition of pain flare. However, since patients who rated their pain as "acceptable" also reported considerable limitations in their work and daily activities, this tool may best be used to complement other clinical pain measures.

Several observations regarding the LEAP study warrant further attention. The fluctuating nature of OA pain means that measurements taken at one point in time may under- or overestimate the overall pain burden of individual patients[33]. The LEAP study was specifically designed to enable within-patient changes in pain levels and other health outcomes to be identified and related over time. Most patients experienced weekly fluctuations in pain scores, which enabled the relationships between pain fluctuations and other health outcomes to be examined. Although relationships between weekly fluctuations in pain levels and other health outcomes were observed, the causality of these associations has not been fully defined. In LEAP, factors not identified in the weekly interviews (e.g., self-coping mechanisms, pain triggers, diurnal variation, subjective stress, and exercise)[56] may have contributed to the reported fluctuations in pain levels and other health outcomes. Repeated administration of identical questionnaires may have influenced patient responses, and the
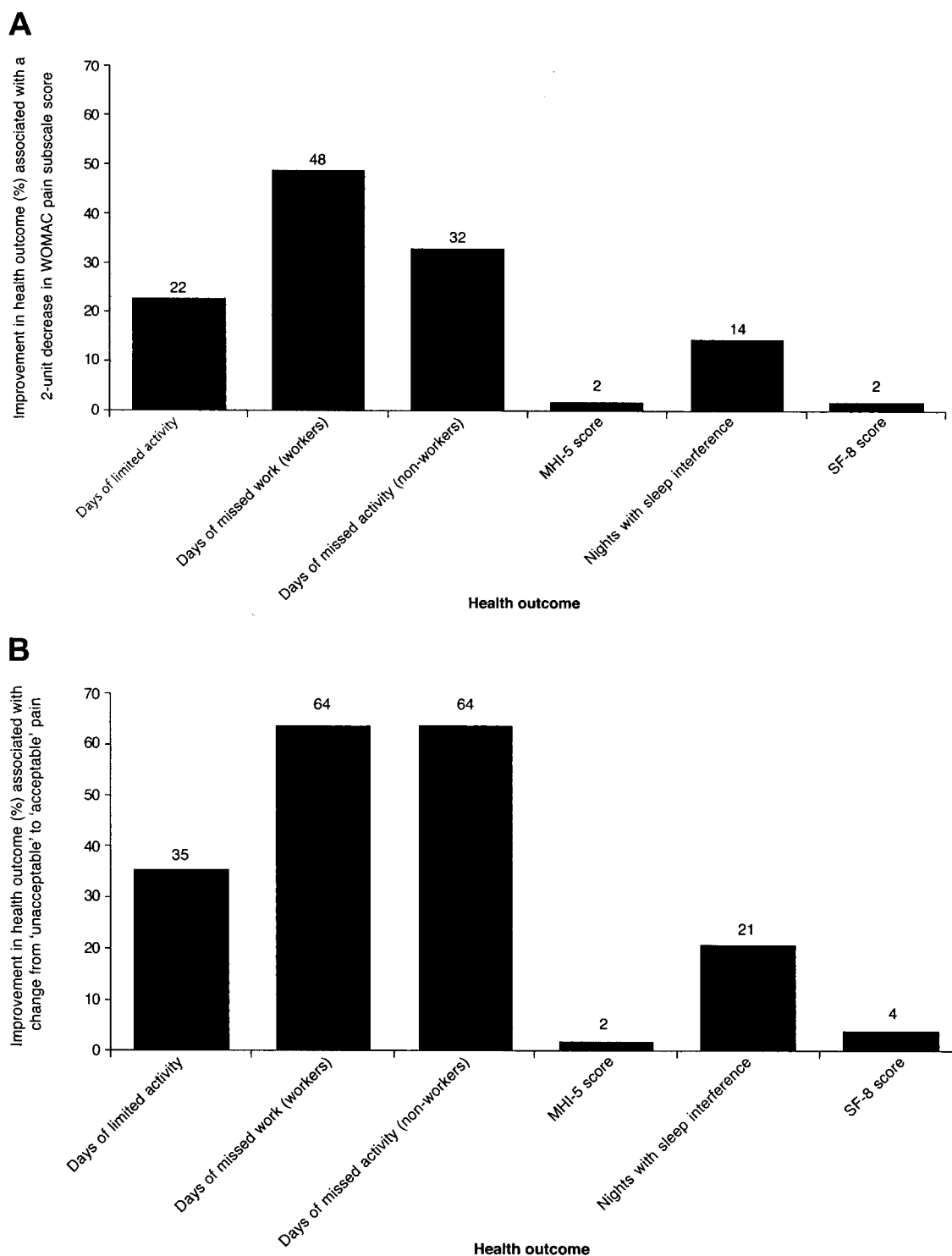
A

B

Figure 1. A. Improvements in other health outcomes associated with a 2-unit decrease in WOMAC pain subscale score. B. Improvements in other health outcomes associated with a change from "unacceptable" to "acceptable" pain rating. WOMAC: Western Ontario and McMaster Universities osteoarthritis index; MHI-5: 5-item Mental Health Inventory; SF-8: 8-item Short-Form health survey.

potential therapeutic effect of the telephone interviews themselves cannot be excluded[57]. Further, Black Americans may report higher levels of OA pain and poorer health outcomes than Caucasians[29,58], but Black Americans and Hispanics were underrepresented in the study population[59]. Finally, the 12-week LEAP study may have limited sensitivity to detect gradual changes. A similarly designed study that considers all of these factors, conducted across seasons (e.g., temporal

overlap of winter and spring) and in additional countries would be informative. Assessing the level of commitment to participate in such a study should be a consideration, since most withdrawals occurred during the early weeks of the study.

In summary, significant and direct associations between weekly fluctuations in patient-rated pain levels, functionality, quality of life, and healthcare resource use were identified among US adults with knee and/or hip OA. A reduction in pain equivalent to 2 points on the WOMAC pain subscale was associated with substantial benefits in productivity and healthcare resource use, and with additional improvements in activity, sleep, and quality of life. This in-depth examination of the relationships between joint pain and other health outcomes should help clinicians gain a better understanding of the daily experience and burden of OA pain.

ACKNOWLEDGMENT

REFERENCES

1. Guccione AA, Felson DT, Anderson JJ, et al. The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. Am J Public Health 1994;84:351-8.
2. Birchfield PC. Osteoarthritis overview. Geriatr Nurs 2001;22:124-30.
3. Felson DT. An update on the pathogenesis and epidemiology of osteoarthritis. Radiol Clin North Am 2004;42:1-9.
4. McAlindon TE, Cooper C, Kirwan JR, Dieppe PA. Knee pain and disability in the community. Br J Rheumatol 1992;31:189-92.
5. Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Arthritis Rheum 2000;43:1905-15.
6. Jordan KM, Arden NK, Doherty M, et al. EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). Ann Rheum Dis 2003;62:1145-55.
7. Zhang W, Doherty M, Arden N, et al. EULAR evidence based recommendations for the management of hip osteoarthritis: report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis 2005;64:669-81.
8. Carr AJ. Beyond disability: measuring the social and personal consequences of osteoarthritis. Osteoarthritis Cartilage 1999;7:230-8.
9. Yelin E, Callahan LF. The economic cost and social and psychological impact of musculoskeletal conditions. National Arthritis Data Work Groups. Arthritis Rheum 1995;38:1351-62.
10. Simpson K, Todd J, Schofield P. Pain in Europe — impact of pain in osteoarthritis. Ann Rheum Dis 2006;65 Suppl II:405.
11. Ricci JA, Stewart WF, Chee E, Leotta C, Foley K, Hochberg MC. Pain exacerbation as a major source of lost productive time in US workers with arthritis. Arthritis Rheum 2005;53:673-81.
12. Bieleman H, Ittersun M, Oosterveld F, van der Schans C, Groothoff J, Reneman M. Functional capacity evaluation (FCE) in an early osteoarthritis cohort. Ann Rheum Dis 2006;65 Suppl II:225.
13. Mapel DW, Shainline M, Paez K, Gunter M. Hospital, pharmacy, and outpatient costs for osteoarthritis and chronic back pain. J Rheumatol 2004;31:573-83.
14. Dominick KL, Ahern FM, Gold CH, Heller DA. Health-related quality of life and health service use among older adults with osteoarthritis. Arthritis Rheum 2004;51:326-31.
15. Ethgen O, Vanparijs P, Delhalle S, Rosant S, Bruyere O, Reginster JY. Social support and health-related quality of life in hip and knee osteoarthritis. Qual Life Res 2004;13:321-30.
16. Creamer P, Lethbridge-Cejku M, Hochberg MC. Factors associated with functional impairment in symptomatic knee osteoarthritis. Rheumatology Oxford 2000;39:490-6.
17. Phan CM, Link TM, Blumenkrantz G, et al. MR imaging findings in the follow-up of patients with different stages of knee osteoarthritis and the correlation with clinical symptoms. Eur Radiol 2006;16:608-18.
18. Sengupta M, Zhang YQ, Niu JB, et al. High signal in knee osteophytes is not associated with knee pain. Osteoarthritis Cartilage 2006;14:413-7.
19. Hayes CW, Jamadar DA, Welch GW, et al. Osteoarthritis of the knee: comparison of MR imaging findings with radiographic severity measurements and pain in middle-aged women. Radiology 2005;237:998-1007.
20. Davis MA, Ettinger WH, Neuhaus JM, Barclay JD, Segal MR. Correlates of knee pain among US adults with and without radiographic knee osteoarthritis. J Rheumatol 1992;19:1943-9.
21. Dieppe P, Altman R, Lequesne M, Menkes J, Pelletier JP, Martel-Pelletier J. Osteoarthritis of the knee: Report of a Task Force of the International League of Associations for Rheumatology and the Osteoarthritis Research Society. J Am Geriatr Soc 1997;45:850-2.
22. Kidd BL, Photiou A, Inglis JJ. The role of inflammatory mediators on nociception and pain in arthritis. Novartis Found Symp 2004;260:122-33,33-8,277-9.
23. Bradley LA, Kersh BC, DeBerry JJ, Deutsch G, Alarcon GA, McLain DA. Lessons from fibromyalgia: abnormal pain sensitivity in knee osteoarthritis. Novartis Found Symp 2004;260:258-70,70-9.
24. Dieppe P, Cushnaghan J, Tucker M, Browning S, Shepstone L. The Bristol 'OA500 study': progression and impact of the disease after 8 years. Osteoarthritis Cartilage 2000;8:63-8.
25. Dieppe PA, Lohmander LS. Pathogenesis and management of pain in osteoarthritis. Lancet 2005;365:965-73.
26. Davis GC. Improved sleep may reduce arthritis pain. Holist Nurs Pract 2003;17:128-35.
27. Lin EH, Katon W, Von Korff M, et al. Effect of improving depression care on pain and functional outcomes among older adults with arthritis: A randomized controlled trial. JAMA 2003;290:2428-9.
28. Xie F, Li SC, Fong KY, et al. What health domains and items are important to patients with knee osteoarthritis? A focus group study in a multiethnic urban Asian population. Osteoarthritis Cartilage 2006;14:224-30.
29. Golightly YM, Dominick KL. Racial variations in self-reported osteoarthritis symptom severity among veterans. Aging Clin Exp Res 2005;17:264-9.
30. Affleck G, Tennen H, Keefe FJ, et al. Everyday life with osteoarthritis or rheumatoid arthritis: independent effects of disease and gender on daily pain, mood, and coping. Pain 1999;83:601-9.
31. Allen KD, Golightly YM, Olsen MK. Pilot study of pain and

coping among patients with osteoarthritis: A daily diary analysis. J Clin Rheumatol 2006;12:118-23.

32. Bellamy N, Sothern RB, Campbell J. Rhythmic variations in pain perception in osteoarthritis of the knee. J Rheumatol 1990;17:364-72.

33. Paradowski PT, Englund M, Roos EM, Lohmander LS. Similar group mean scores, but large individual variations, in patient-relevant outcomes over 2 years in meniscectomized subjects with and without radiographic knee osteoarthritis. Health Qual Life Outcomes 2004;2:38.

34. Majani G, Giardini A, Scotti A. Subjective impact of osteoarthritis flare-ups on patients' quality of life. Health Qual Life Outcomes 2005;3:14.

35. Rabenda V, Burlet N, Ethgen O, Raeman F, Belaiche J, Reginster JY. A naturalistic study of the determinants of health related quality of life improvement in osteoarthritic patients treated with non-specific non-steroidal anti-inflammatory drugs. Ann Rheum Dis 2005;64:688-93.

36. Peters TJ, Sanders C, Dieppe P, Donovan J. Factors associated with change in pain and disability over time: a community-based prospective observational study of hip and knee osteoarthritis. Br J Gen Pract 2005;55:205-11.

37. The SF-8 Health Survey. Internet. Available from: http://www.sf-36.org/tools/sf8.shtml. Accessed June 4, 2007.

38. Veit CT, Ware JE Jr. The structure of psychological distress and well-being in general populations. J Consult Clin Psychol 1983;51:730-42.

39. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: A health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol 1988;15:1833-40.

40. Bellamy N, Campbell J, Hill J, Band P. A comparative study of telephone versus onsite completion of the WOMAC 3.0 osteoarthritis index. J Rheumatol 2002;29:783-6.

41. Qualitymetric Health Outcomes Solutions. Internet. Available from: http://www.qualitymetric.com/products/sf8.aspx. Accessed June 4, 2007.

42. Farrar JT, Portenoy RK, Berlin JA, Kinman JL, Strom BL. Defining the clinically important difference in pain outcome measures. Pain 2000;88:287-94.

43. Pham T, van der Heijde D, Altman RD, et al. OMERACT-OARSI initiative: Osteoarthritis Research Society International set of responder criteria for osteoarthritis clinical trials revisited. Osteoarthritis Cartilage 2004;12:389-99.

44. Diggle PJ, Heagerty PJ, Liang K-Y, Zeger SL. The analysis of longitudinal data. Oxford Statistical Science. New York: Oxford University Press; 2002.

45. Carriere KC, Roos LL, Dover DC. Across time and space: variations in hospital use during Canadian health reform. Health Serv Res 2000;35:467-87.

46. Chacon JG, Gonzalez NE, Veliz A, et al. Effect of knee osteoarthritis on the perception of quality of life in Venezuelan patients. Arthritis Rheum 2004;51:377-82.

47. Felson DT, McLaughlin S, Goggins J, et al. Bone marrow edema and its relation to progression of knee osteoarthritis. Ann Intern Med 2003;139:330-6.

48. Ayral X, Pickering EH, Woodworth TG, Mackillop N, Dougados M. Synovitis: a potential predictive factor of structural progression of medial tibiofemoral knee osteoarthritis — results of a 1 year longitudinal arthroscopic study in 422 patients. Osteoarthritis Cartilage 2005;13:361-7.

49. Osteoarthritis of the hip: State of the condition. American Academy of Orthopaedic Surgeons; 2004. www.aaos.org/Research/documents/OAinfo_hip_state.pdf. Accessed Sept 28, 2007.

50. Scott-Lennox JA, McLaughlin-Miley C, Lennox RD, et al. Stratification of flare intensity identifies placebo responders in a treatment efficacy trial of patients with osteoarthritis. Arthritis Rheum 2001;44:1599-607.

51. Angst F, Ewert T, Lehmann S, Aeschlimann A, Stucki G. The factor subdimensions of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) help to specify hip and knee osteoarthritis. A prospective evaluation and validation study. J Rheumatol 2005;32:1324-30.

52. Salaffi F, Carotti M, Stancati A, Grassi W. Health-related quality of life in older adults with symptomatic hip and knee osteoarthritis: a comparison with matched healthy controls. Aging Clin Exp Res 2005;17:255-63.

53. Farrar JT, Young JP Jr, LaMoreaux L, Werth JL, Poole RM. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. Pain 2001;94:149-58.

54. Ethgen O, Kahler KH, Kong SX, Reginster JY, Wolfe F. The effect of health related quality of life on reported use of health care resources in patients with osteoarthritis and rheumatoid arthritis: a longitudinal analysis. J Rheumatol 2002;29:1147-55.

55. Bennett D, Burton A, Fishman S. Consensus panel recommendations for the assessment and management of breakthrough pain: part 2. Management. Pharmacy Therapeutics 2005;30:354-61.

56. Focht BC, Gauvin L, Rejeski WJ. The contribution of daily experiences and acute exercise to fluctuations in daily feeling states among older, obese adults with knee osteoarthritis. J Behav Med 2004;27:101-21.

57. Rene J, Weinberger M, Mazzuca SA, Brandt KD, Katz BP. Reduction of joint pain in patients with knee osteoarthritis who have received monthly telephone calls from lay personnel and whose medical treatment regimens have remained stable. Arthritis Rheum 1992;35:511-5.

58. Dominick KL, Baker TA. Racial and ethnic differences in osteoarthritis: prevalence, outcomes, and medical care. Ethn Dis 2004;14:558-66.

59. Profile of General Demographic Characteristics: 2000. Washington, DC: U.S. Bureau of the Census, Census 2000.