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Self-Reported Pain and Disease Symptoms Persist in Juvenile Idiopathic Arthritis Despite Treatment Advances:

An Electronic Diary Study

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Abstract

Objective—To use electronic diaries (e-diaries) to determine whether pain, stiffness, and fatigue continue to be common, disabling symptoms in children with juvenile idiopathic arthritis (JIA) despite the use of aggressive treatments in contemporary medical management.

Methods—Fifty-nine children with JIA (ages 8–18 years) provided ratings of pain, stiffness, and fatigue intensity and functional limitations using a smartphone e-diary 3 times each day for 1 month. Medication information was collected via parent report and checked for accuracy by chart review. Descriptive analyses were conducted to determine typical symptom intensity, frequency, and variability. Multilevel modeling was used to analyze associations between symptoms and functional outcomes and between medication use and symptom intensity.

Results—Children reported moments of pain in 66% of e-diary entries. No children were entirely pain-free across the reporting period. In 31% of all e-diary entries the visual analog scale score for pain was >40 (high pain intensity), with 86% of children reporting a high level of pain at least once during the study period. The mean ratings of pain, stiffness, and fatigue intensity were in the mild-to-moderate range. Medication class was not a reliable predictor of differences in symptom intensity, even though 79% of children were prescribed a disease-modifying antirheumatic drug and 47% were prescribed a biologic agent. Moments of higher pain intensity and higher stiffness intensity were each uniquely predictive of higher concurrent functional limitations.

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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 published. Dr. Schanberg 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.

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Conclusion—Self-reported pain, stiffness, and fatigue continue to be common in children with JIA, despite contemporary advances in treatment strategies, including use of biologic agents. These findings are surprisingly consistent with previous results from research using daily paper diaries in the pre-biologics era. There remains a pressing and ongoing need to optimize pain and symptom management in JIA.

Juvenile idiopathic arthritis (JIA) is characterized by periods of disease flare that are often accompanied by pain, fatigue, debilitating morning stiffness, and difficulty performing activities at home and at school. Previous research has consistently demonstrated that pain is a common, clinically significant symptom in children with JIA, with many children experiencing persistent pain despite stable disease activity (1–7). Our previous studies found that children reported having pain and stiffness on 70% of days, with 25% of children with polyarticular arthritis reporting pain intensity in the highest range of the pain scales (8). The presence of pain substantially impacts the lives of children with JIA, reducing performance of routine physical tasks and participation in social or school activities (8–11). Greater fluctuations in pain intensity have been associated with lower quality of life in children with JIA (12), and pain was an important determinant of physical and psychosocial well-being in a cross-sectional study of 3,167 children with JIA from 30 countries (6).

Despite the strength of evidence supporting the persistence of pain in children with JIA, the majority of this research was conducted prior to recent advances in pharmacotherapy. In our original diary study (8), which highlighted the daily frequency and intensity of JIA pain, 73% of children were treated with methotrexate and only 17% with a biologic agent. Since that time, clinical trials, consensus treatment plans, and treatment guidelines all have called for more aggressive JIA treatment involving utilization of biologic agents (13–15). Although pain has not been studied as an independent measure of drug efficacy and has been demonstrated to have a weak relationship with indices of disease activity (1,16–19), it has been identified as a quality indicator of JIA care (20) and is important to investigate in the context of treatment advances.

Technology has also advanced beyond paper diary methods for measuring pain and functioning in the context of a child's daily life. Specifically, smartphones (phones with advanced computing capability) afford ease in obtaining repeated measures of pain within and across days and improves the quality of the self-reported data through prompts and automatic time-stamping (21–23). The use of mobile devices for capturing self-reported data via electronic diaries (e-diaries) has been validated in children with arthritis and effectively captures current symptom reports (24–27).

In the present study, we assessed the pain experience of children with JIA being treated with current pharmacotherapies in the contemporary biologics era. Specifically, we examined temporal relationships between pain, daily symptoms, and daily functional outcomes in children with JIA, using self-reported data from e-diaries completed 3 times daily. The first aim was to describe current patterns of pain and other symptoms, including frequency and intensity, in children with JIA. The second aim was to describe the associations between use of different medication classes and pain and symptom intensity. Finally, the third aim was to determine whether pain alone or in combination with stiffness and fatigue could be used to

predict functional limitations in children with JIA. We hypothesized that a combination of momentary pain and other symptoms would be predictive of higher functional limitations at any given time.

PATIENTS AND METHODS

Participants

Study participants were recruited between August 2010 and May 2011 from a pediatric rheumatology clinic at an academic medical center in the southeastern United States. Children between the ages of 8 and 18 years who were diagnosed as having JIA were recruited for the study if they reported experiencing joint pain within the 6 months prior to study recruitment. Children were excluded if they were 1) diagnosed as having a comorbid disorder affecting their current pain and functioning (e.g., mood disorder, fibromyalgia, pervasive developmental disorder), 2) known to have significant cognitive impairment or illiteracy that would limit understanding of study measures, 3) non-English speaking, 4) physically unable to complete the e-diaries, or 5) not currently attending school (e.g., not enrolled or on academic breaks).

Ninety-three families were approached for recruitment into the study. Of those approached, 19 (20%) declined to participate due to time constraints on the day of the clinic visit, lack of interest, or self-perceived inability to complete the study activities once enrolled. Of the 74 families who consented to participate, additional screening identified 3 families as ineligible based on the exclusion criteria. Four participants withdrew prior to study completion due to time constraints or difficulties with wireless signal reliability (for transmitting daily diary responses). Eight additional participants were removed from the study by the principal investigator due to persistent lack of consistency in diary completion. There were no differences in sex, age, or disease activity between the group of children who completed the study and those who did not complete the study.

The final sample comprised 59 children (44 girls) ages 8–18 years (mean ± SD age 13.30 ± 2.78 years). Those children who had at least 25 repeated measurements were included in the data analysis, which is an adequate number for obtaining reliable parameter estimates in hierarchical linear analyses (28,29). The majority of participants self-identified their race as Caucasian (73%), followed by black or African American (11%) and mixed racial background (5%), reflecting the race and ethnicity of the clinic population. Three patients (6%) self-identified as Hispanic. The school grade ranged from third grade to twelfth grade, with 93% of children attending public schools and the remainder attending private schools. No children in the study were being homeschooled. Of the sample, 11% were classified by the pediatric rheumatologist as having minimal disease activity, while 42%, 43%, and 4% were classified as having mild, moderate, and severe disease activity, respectively. The primary caregiver was predominantly the biologic mother for most of the children (86%).

The majority of children in the sample had been prescribed disease-modifying antirheumatic drugs (DMARDs), as determined by chart review (79%) or based on caregiver report (54%). Biologic agents were the next most commonly prescribed medication, as verified by chart review (47%) or by caregiver report (32%). In addition, caregiver reports indicated that 32%

of children were being treated with nonsteroidal antiinflammatory drugs (NSAIDs), while chart review revealed that 38% of children had been prescribed routine NSAIDs, with 7% taking NSAIDs as needed. Few children in this sample were taking opioids (<3%).

Procedure

Patients scheduled for evaluation in the pediatric rheumatology clinic were prescreened by a research assistant and reviewed by the study rheumatologist (LES). A study information letter was sent to the families of potential participants ~1 week before a scheduled appointment. During the baseline study visit, interested families provided written informed consent (and written assent for children ages ≥12 years) according to local Institutional Review Board requirements. Enrolled children and caregivers independently completed computerized baseline self-report measures. The children were then trained to use customized e-diaries on a smartphone (T-Mobil Dash) and completed a sample entry while being supervised by a research assistant. Information on typical times for starting school, coming home from school, dinner, and bedtime was gathered from each family in order to program audible alerts to cue the child to complete a diary entry 3 times during the day (morning, afternoon, and evening). Children were not cued during school hours, because of school policies pertaining to phone use.

After completing the baseline assessments and e-diary training, participants took home the smartphones and a printed instruction manual. Participants were instructed to complete 3 surveys per day at the cued times, for a total of 28 days. Data were automatically uploaded from the phone to a password-secured internet server through the phone's wireless data plan. Families received standardized, weekly calls from the research assistant to promote e-diary completion and address barriers to e-diary completion. At the end of the diary period, smartphones were returned in a prepaid mailer given to families at enrollment. Children were reimbursed for participation based on number of completed e-diary entries ($0.25/completed entry, with a $0.50 bonus for completing all entries on a given day and a $1.25 bonus for completing a full week's worth of diary entries, for a possible total of $10.00).

E-diary measures

Pain intensity—Current pain intensity was quantified using a horizontal visual analog scale (VAS) with the anchors of "no pain" to "worst possible pain." A 50-mm horizontal line (one-half filled in with blue color) was shown on the smartphone screen, and children were asked to move the filled-in portion of the line to represent their current level of pain. Children received a warning message reminding them to select their current pain level if they did not move the line from the original starting point. Scores were transformed to a 0–100 scale to be consistent with the typical metric for VAS scoring. Consistent with methods used in our previous paper diary study (8), pain intensity scores of ≥3 (of 100) were used to derive the number of days children experienced pain (pain frequency). This electronic VAS has been previously validated for the measurement of pain intensity in children and adolescents with JIA (25).

Pain location—Respondents were shown an image of a skeleton with numbered circles at major body areas (e.g., head, hands, arms, hip and knee, feet) and asked to indicate where

the pain was currently occurring. This image was adapted from paper versions of a pain body map used previously in children with JIA (8). A zoomed-in image of painful areas of the body was then provided and children were asked to identify specific painful joints within each body area. The sum total of painful areas (among 7 body areas) was used for the analyses.

Pain duration—The duration of pain was quantified using a 4-point ordinal scale. Children were asked to indicate the duration of current pain, ranging from “a few minutes” to “more than 4 hours.” A “not applicable” option also was provided.

Pain unpleasantness—Children reported the extent to which the pain was bothering them by moving the filled portion of a 50-mm horizontal line (one-half filled in with blue color) displayed on the smartphone screen, with the anchors of “not bothering me at all” to “bothering me a lot.” Scores were transformed to a 0–100 scale.

Functional limitations—Social, academic, and physical functional limitations were assessed using questions derived from the Activity Scale for Kids (30) and the Child Activity Limitations Questionnaire (31). Children were asked to report the extent of difficulty they were having with each of 8 items during each daily time interval, using a 4-point scale ranging from “not very difficult” to “extremely difficult.” The items varied in the morning, afternoon, and evening assessments based on the activities likely to occur at those times. For example, a question about difficulties putting on clothes was asked in the morning assessment only, whereas questions about social or school activity limitations were asked at the afternoon and evening times. An additive summary score was calculated for each time point, with higher scores indicating greater overall functional limitations.

Stiffness and fatigue intensity—The intensity of current stiffness and intensity of current fatigue were quantified in a manner similar to that used to quantify pain intensity, using a horizontal VAS with the anchors of “no stiffness” to “a lot of stiffness” for evaluation of stiffness intensity and the anchors of “not at all tired” to “very tired” for evaluation of fatigue intensity. A 50-mm horizontal line (one-half filled in with blue color) was shown on the smartphone screen, and children were asked to move the filled-in portion of the line to represent their current level of stiffness or fatigue. Scores were transformed to a 0–100 scale.

Stiffness and fatigue duration—The duration of current stiffness and fatigue was quantified using a 4-point ordinal scale, ranging from “a few minutes” to “more than 4 hours.” A “not applicable” option also was provided.

Baseline measures

Joint count and disease activity—Each participant’s pediatric rheumatologist completed an active joint count for each child, consisting of the number of swollen and tender joints and the number of joints in which range of motion was limited (32). In addition, the child’s disease activity was rated on a 0–3 scale, ranging from minimal (score of 0) to severe (score of 3).

Medications—Information on current medications was gathered at the time of the initial study visit. Both caregiver-reported medications and medication lists from chart review were used in the data analyses to differentiate between the scheduled use of prescription NSAIDs and the as-needed use of NSAIDs. Caregiver-reported medications were classified into 1 of 5 categories for analyses: NSAIDs or acetaminophen, DMARDs (methotrexate, lenalidomide), opioids (oxycodone, methadone), biologics (etanercept, infliximab, adalimumab, abatacept, anakinra, and rituximab), and vitamin D and/or calcium. Medications ascertained from chart review were classified similarly, except for the differentiation between scheduled and as-needed NSAIDs.

Statistical analysis

For the first aim of the present study, to describe patterns of pain and other symptoms in patients with JIA, descriptive statistics (expressed as the mean ± SD) were used to summarize typical levels and variability of symptom intensity and symptom duration within and across days. The proportion of days in pain and proportion of moments with high pain intensity (VAS score >40 of 100) were also calculated. A series of hierarchical multilevel models were used to evaluate the extent to which symptoms were associated with medication use and functional limitations. Multilevel models account for the nesting of observations (multiple measurements within each child) (33,34). Multilevel analyses were specified using the SAS Mixed procedure program (35). A serial autocorrelation residual variance structure was applied to all models to account for the fact that responses obtained closer together in time are more similar than those obtained further apart.

For models evaluating the extent to which average symptom levels differed as a function of medication class, all classes of medication were entered simultaneously as predictors, and physician-reported disease activity was specified as a covariate. For models evaluating the relationship between symptoms (pain, fatigue, and stiffness) and functional limitations, age and physician-rated disease activity were included as covariates, and symptom intensity values were added in a hierarchical approach in order to identify the unique effect of each symptom on functional limitations. In these models, intensity values for pain, fatigue, and stiffness were centered such that a child's mean symptom intensity score (on 100-mm VAS) was entered in the models; this permitted determination of the extent to which deviations from a child's average symptom intensity at a given moment is associated with increased or decreased functional limitations at that same moment.

RESULTS

Descriptive statistics

Children in the study completed a total of 3,258 e-diary entries. This represents a 66% completion rate, which is similar to that in our e-diary pilot study (26). Children reported experiencing pain (VAS score ≥3 of 100) in 66% of all moments. Across all days, the children's endorsed levels of pain intensity and pain unpleasantness were similar ($r = 0.91$, $P < 0.01$), suggesting that the measures captured a similar aspect of the pain experience. The average score for stiffness intensity was 24 ± 25 and fatigue intensity was 43 ± 28 (mean ± SD on 100-mm VAS) in all children across all moments.

Children reported having pain (VAS score ≥3 of 100) on 72% of all diary days, and the mean ± SD number of days of self-reported pain during the study was 18.8 ± 8.9. No children were entirely pain-free across the reporting period, and in individual children, the number of pain days during the study period ranged from 1 to 28. On any given pain day, the mean ± SD pain intensity score was 36 ± 23, stiffness intensity score was 33 ± 24, and fatigue intensity score was 49 ± 25. In 31% of all e-diary entries, children endorsed the level of pain as being "high pain" (pain intensity score of >40 on 100-mm VAS, as defined in prior studies [1,8]). The majority of children (n = 50 [86%]) reported experiencing high pain at some point during the study period. The mean pain intensity score fell within the high range (>40 of 100) for a subgroup of children (n = 13 [22%]). When children experienced pain, they most often reported a pain duration of >4 hours. In contrast, at times when children reported experiencing stiffness or fatigue, they reported a duration of a few minutes.

As shown in Table 1, the mean pain intensity ratings across the morning, afternoon, and evening entries were not significantly different. However, as expected, the mean stiffness intensity score for children in this study was highest in the morning. Children experienced the highest intensity of fatigue in the evening and lowest intensity of fatigue in the afternoon. In comparison with the morning ratings of fatigue, the evening fatigue intensity was significantly higher and afternoon fatigue intensity was significantly lower, across all children and all e-diary entries.

There were significant correlations between all daily symptoms and functional limitations (Table 2). The correlations between pain and other daily symptoms or functional limitations spanned from medium (e.g., r = 0.37, $P < 0.01$ for correlation with number of painful joints) to large (e.g., r = 0.73, $P < 0.01$ for correlation with stiffness intensity). These findings supported our observations from the analyses of temporal associations among the factors.

Models testing the effects of medication on symp-toms

There was a consistent finding that the intensity of pain, stiffness, or fatigue did not reliably vary as a function of medication class (neither those verified by chart review nor those reported by the parent). For example, children prescribed biologic drugs had pain intensity scores comparable with those of children who were not prescribed biologic drugs ($t[47] = -1.25$, $P > 0.05$). The one exception to this pattern of findings was in children receiving a regular regimen of NSAIDs.

Children who were regularly scheduled to take NSAIDs had significantly lower fatigue intensity scores compared with children who were not taking NSAIDs ($t[47] = -2.18$, $P < 0.05$). In summary, when we based our analysis on whether or not a child had been prescribed DMARDs or biologic agents to manage JIA, we did not detect any differences in the symptom intensities reported in the e-diaries.

Hierarchical models testing the effects of momentary symptom intensity on functional limitations

As shown in Table 3, the association of disease activity with functional limitations was significant, indicating that children with more severe disease could be expected to experience higher functional limitations. Age was not a predictor of functional limitations. The intercept for the model indicates that the expected value of functional limitations was 3.68 for a child at the average age and disease activity of the sample.

Pain intensity at any given moment was a significant predictor of functional limitations; during times when children had higher than their usual pain intensity, they could be expected to have greater functional limitations ($t[3,040] = 19.76$, $P < 0.0001$). The number of painful body locations reported at any given time was a predictor of functional limitations at that time, above and beyond the effects of pain intensity ($t[3,039] = 8.44$, $P < 0.0001$). This finding indicates that it was important to consider not only pain intensity but also the number of painful areas of the body when predicting how well a child might function at any given time.

In addition, the intensity of stiffness at any given time was a predictor of functional limitations at that time, above and beyond the effects of disease activity, pain intensity, and painful locations ($t[3,038] = 2.60$, $P < 0.05$). Children who typically experienced more stiffness also had greater functional limitation scores ($t[49] = 3.36$, $P < 0.05$). In contrast, fatigue experienced at any time was not predictive of functional limitations at that time, when analyses were controlled for disease activity, pain, number of painful areas, and stiffness ($t[3,037] = -1.71$, $P = 0.09$).

DISCUSSION

The results of this study indicate that pain continues to be a significant concern for children with JIA, occurring frequently and associated with significant functional difficulties. These findings regarding pain intensity and frequency are remarkably consistent with our previous study findings using paper diaries (8), despite the current advances in treatments for JIA and the large number of children in this study who were prescribed biologic agents relative to that in the previous sample. Children also reported high levels of fatigue, particularly on pain days, and there were moderate correlations between fatigue, pain, and stiffness. When added as a final predictor in models containing demographic and other daily symptoms, fatigue intensity did not account for any additional variance in functional limitations, despite the high levels of fatigue reported by the children on a daily basis.

An important contribution of this study was the examination of daily patterns of pain and symptoms using technologically advanced data collection methods. E-diaries allowed examination of differences in the children's reported symptoms across mornings, afternoons, and evenings. Findings indicated that, on average, stiffness intensity was highest during the morning, fatigue intensity was highest during the evening, and pain intensity was similar across time periods. The use of repeated measures of momentary pain and other symptoms via e-diaries offers many advantages, such as preventing backfilling and the ability to examine patterns of associations between symptoms and behaviors as they occur.

Using e-diaries, we were able to examine ways in which disease activity and current medication class might be used to predict symptom intensity reports. In analyses controlled for the level of disease activity, we failed to detect significant differences in the children's daily symptoms based on prescribed medication class. The only exception was a significant difference in fatigue intensity related to the scheduled use of NSAIDs; children taking scheduled NSAIDs had lower fatigue intensity ratings than those who were not taking scheduled NSAIDs. The failure to detect consistent differences in the daily symptom report based on medication class is notable, particularly given that many children in this study were treated with biologic drugs. Children with JIA often are prescribed medications from a combination of classes, and the method of analysis did not consider clusters of medications or prescribing patterns, due to concerns regarding loss of statistical power.

Although these results are consistent with recent findings (36), it is possible that other individual differences or moderating factors (e.g., stress, disease duration, mood) might have influenced daily symptoms; none of these were controlled for in our analyses. Nevertheless, these results raise new questions about the effectiveness of contemporary aggressive therapy in preventing or limiting disease symptoms. Moreover, the severity of disease activity may not be as well controlled as is often presumed by health care providers, when disease activity is determined solely on the basis of physical examination and laboratory assessment. Persistent pain may also be attributable to changes in pain processing in the central nervous system (central sensitization) that remain after resolution of the inflammatory component of the disease, and current therapies do not target this aspect of pain.

Our study also investigated the influence of pain and other symptoms on functioning in children with JIA. We hypothesized that a combination of more intense pain and other symptoms at a given time would be a predictor of higher functional limitations at that time. As expected, pain intensity was a predictor of concurrent functional limitations. Individual variations in stiffness intensity were also predictive of functional limitations, beyond the influence of pain intensity and disease activity. However, momentary fatigue intensity was not predictive of functional limitations, despite the high level of fatigue reported by children in the study. It is possible that children are more willing or able to tolerate fatigue and it does not impact activity involvement, or perhaps fatigue occurs as a delayed effect of activity involvement. Our measurement of fatigue was limited to a single item on each e-diary inquiring about tiredness, which likely did not fully capture the nuances of fatigue as a disease symptom. Additionally, a common symptom-reporting method was used (the VAS), increasing the potential influence of method invariance on children's reporting practices, and possibly contributing to the detected results (37). Further research into the cause, nature, and role of daily fatigue is needed, as this is a symptom not previously well studied in JIA and not currently part of routine treatment response criteria. Taken together, these findings indicate that it is important for health care providers to consider children's overall symptom report in the context of functional limitations; assessing and treating pain intensity alone may not fully explain or alleviate children's functional impairment.

Routine assessment and treatment of pain, stiffness, and fatigue intensity should be part of the clinical care regimen, along with the assessment of treatment efficacy in clinical trials for children with JIA. There are brief tools available for capturing symptom reports at clinic

visits (38,39) in order to guide pain management approaches and track treatment outcomes. In addition, pain and disease symptoms should be examined independently of other disease activity measures in clinical trials. Currently, little is known about the direct effect of specific medications on pain and other disease symptoms. While our study did not show a difference between classes of medication and the symptoms report, we aggregated all biologic agents together. It may be that specific biologic agents are better than others at treating specific disease symptoms or that future medications may prove to be more successful than those currently available for treating pain, fatigue, and stiffness. Additionally, it is important to note that pain and other symptoms appear to be related and that interventions addressing one symptom (e.g., pain) may promote reductions in other symptoms and improve functioning.

Our findings indicating that the prescribed class of medication had little effect on daily symptom intensity, in conjunction with existing evidence showing that disease factors only partially account for changes in pain intensity, once again highlight the pressing and often overlooked need to incorporate nonpharmacologic interventions into the care of children with JIA. Cognitive behavioral therapy, including pain coping and self-management, is an empirically supported treatment targeting pain and associated health outcomes in children with JIA (40,41) and other childhood chronic illnesses, such as sickle cell disease (42), functional abdominal pain (43), and headache (44). However, non-pharmacologic services are not widely available and, historically, have not been covered by insurance. Access is often limited to financially secure families served in major academic medical centers with comprehensive mental health resources. Therefore, alternative methods of service delivery are needed for broader dissemination of pain-coping skills training to children with JIA.

The increased use of e-health tools is a promising avenue for service delivery. This study and others have shown that children with JIA can easily use handheld devices to track symptoms and behaviors (24–27). Most children and adolescents in the United States own, or have frequent access to, cellular phones, often smart-phones. As of February 2012, nearly one-half (46%) of adults in the United States were smartphone users (45). Smartphones offer a promising method for delivering a variety of medical and psychosocial pain and arthritis treatments. Smartphone applications can also prospec-tively assess treatment outcomes in the child’s typical environment, rather than depending on a return clinic visit for posttreatment assessment. Smartphones can capture in-the-moment reports, and provide immediate feedback and recommendations targeting symptom reduction and improved functioning. For example, smart-phone applications could teach children in-the-moment coping techniques and prompt practice in response to current symptoms. Recruitment and retention may be promoted by incorporating participant feedback during development (24), and by implementing brief interventions with a short reporting period coupled with the motivation of potential direct benefits from participation. We are currently piloting a smartphone application to test the feasibility and effectiveness of a mobile self-management program for improving the health outcomes of children with JIA.

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Table 1

Aggregate patterns of symptoms across the day

	Time of e-diary entry*			
	Morning	**Afternoon**	**Evening**	**F**
Pain intensity score	26.6	26.0	26.4	0.153
Stiffness intensity score	26.5†‡	23.6‡§	23.5†§	4.65¶
Fatigue intensity score	42.6†‡	36.8§	48.1§	37.98#
No. of painful joints	4.2	3.9	4.0	0.377
No. of painful body areas	2.0	2.0	2.1	0.493

*Values are the mean.

†Significantly different versus afternoon.

‡Significantly different versus evening.

§Significantly different versus morning.

¶$P < 0.05$.

#$P < 0.0001$.

Table 2

Bivariate correlations between daily symptoms and behaviors

		Pearson's correlation coefficient				
	Mean ± SD (range)	**Stiffness intensity**	**Fatigue intensity**	**Functional limitations**	**No. of painful body areas**	**No. of painful joints**
Pain intensity score	26.3 ± 27.5 (0–100)	0.73*	0.48*	0.49*	0.63*	0.37*
Stiffness intensity score	24.4 ± 25.2 (0–100)		0.49*	0.46*	0.45*	0.17*
Fatigue intensity score	42.6 ± 28.2 (0–100)			0.26*	0.30*	0.17*
Functional limitations score	3.9 ± 7.3 (0–32)				0.37*	0.13*
No. of painful body areas	1.1 ± 1.5 (1–7)					0.80*
No. of painful joints	3.9 ± 5.4 (1–66)					

*$P < 0.0001$.

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Table 3

Hierarchical multilevel models assessing predictors of functional limitations*

Level, predictor	B	*t*
Step 2		
Age	−0.16	−0.89
Disease activity	2.08	3.09†
Step 3		
Pain intensity		
Within-child	0.11	19.76‡
Between-child	0.12	6.94‡
Step 4		
No. of painful body areas		
Within-child	0.99	8.44‡
Between-child	0.004	0.01
Step 5		
Stiffness intensity		
Within-child	0.019	2.60†
Between-child	0.10	3.36†
Step 6		
Fatigue intensity		
Within-child	−0.01	−1.71
Between-child	0.008	0.16

*The initial step of each model contained no predictors, in accordance with the procedures detailed by Raudenbush and Bryk (34).

†$P < 0.05$.

‡$P < 0.0001$.