The Impact on Health-Related Quality of Life from Non-Steroidal Anti-Inflammatory Drugs, Methotrexate, or Steroids in Treatment for Juvenile Idiopathic Arthritis

Russ Riddle,1 MS, Christina N. Ryser,1,2 PhD, Anne A. Morton,1 PhD, J. D. Sampson,1 MA, Richard H. Browne,1 PhD, Marilynn G. Punaro,1,2 MD, and Robert J. Gatchel,2 PhD
1Texas Scottish Rite Hospital for Children and 2The University of Texas Southwestern Medical Center at Dallas

Objective To assess and compare the impact of medication treatments on health-related quality of life (HRQOL), family function, and medical status in children with juvenile idiopathic arthritis (JIA). Methods Fifty-seven children diagnosed with JIA were assessed by a pediatric rheumatologist and placed into one of three treatment groups: (1) non-steroidal anti-inflammatory; (2) methotrexate; or (3) steroids via IV methylprednisolone. Questionnaires were administered at baseline and 4-month follow-up. The attending pediatric rheumatologist provided additional medical information. Results Data document the impact of JIA on HRQOL, particularly on physical and pain domains. Steroid patients experienced improved HRQOL at follow-up relative to other groups, despite reporting more problems with side effects. Conclusion These results demonstrate positive benefits of steroids in treating JIA children, despite the greatest incidence of adverse side effects.

Key words health-related quality of life; juvenile arthritis; outcomes.

Quality of life (QOL), as defined by The World Health Organization (WHO), is “the individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” (WHOQOL Group, 1995). Although this definition was originally conceived with mostly adults in mind, child perception of QOL has been gaining increased acceptance in pediatrics (Brunner & Giannini, 2003). Assessment of health-related quality of life (HRQOL), the portion of QOL determined by one's physical health, has been increasingly undertaken in pediatric chronic illness as healthcare professionals agree that traditional endpoints such as symptom reduction are no longer sufficient when evaluating medical outcomes (Gerharz, Eiser, & Woodhouse, 2003; Miller, LeBovidge, & Feldman, 2002; Varni et al., 2002). Monitoring a disease's impact on HRQOL is especially important where the task is to manage rather than cure a disease, particularly since children with a chronic illness have long been shown to have a higher risk for behavior and emotional disorders (Farmer, Marien, Clark, Sherman, & Selva, 2004; Quittner & DiGirolamo, 1998). Specifically, domains of HRQOL can include physical, emotional, and behavioral function, pain and discomfort, and coping (Miller et al., 2002).

The relationship of medical variables to pediatric HRQOL has been difficult to pin down. Jirojanakul, Skevington, and Hudson (2003), for example, failed to find that chronic, acute, or severe illnesses had any direct impact on HRQOL, hypothesizing that HRQOL may be influenced more by one’s expectations of the treatment experience rather than the presence of specific disease factors. Similarly, recent evaluations involving chronic liver disease (Hauser, Holtmann, & Grandt, 2004) and diabetes (Whittemore, Urban, Tamborlane, & Grey, 2003) found that disease severity had little or no impact.
on HRQOL. Other studies, though, have uncovered inverse relationships between severity of disease symptoms and levels of HRQOL in cancer (Barrera et al., 2003) and chronic migraines (Powers, Patton, Hommel, & Hershey, 2003). Associations have also been uncovered among HRQOL, disease status, and emotional difficulties in children with asthma (Sawyer et al., 2000; Vila et al., 2003) and diabetes (Grey, Boland, Yu, Sullivan-Bolyai, & Tamborlane, 1998). Cumulatively, the present lack of agreement in the literature precludes any summary statement that alleviation of disease symptoms in and of itself improves HRQOL.

One area in which assessment of HRQOL is of particular importance is that of juvenile idiopathic arthritis (JIA). The term JIA encompasses multiple types of arthritis, all of which result in joint inflammation. Affecting approximately one child out of every 1,000, JIA can cause considerable pain and discomfort, impacting QOL (American College of Rheumatology, 2004). When evaluating treatments, the Federal Food and Drug Administration (FDA) recently suggested that improvements in HRQOL may be more important to consider than the sole impact of drugs on symptoms such as joint counts and sedimentation rates (Brunner & Giannini, 2003). Understanding cases, then, where symptom improvement is observed while domains of HRQOL either remain the same or worsen, is crucial to facilitating the overall adjustment of these children and their families.

Definitive conclusions regarding health status in JIA have been difficult to make. For example, LeBovidge, Lavigne, Donenberg, and Miller (2003) completed a meta-analysis, finding children with chronic arthritis to be at greater risk for adjustment problems and internalizing symptoms. One example of contrary evidence, however, is found from Gerhardt et al. (2003), who observed families of children with JIA to be at no greater clinically significant risk for disruption in psychosocial functioning than were matched controls. Similarly, Reiter-Purtill, Gerhardt, Vannatta, Passo, and Noll (2003) observed children with more severe JIA to be at a slightly greater risk for social difficulties over a 2-year period, but with small effect sizes. Sallfors, Hallberg, and Fasth (2004), on the other hand, studied 125 children, finding that self-reports of pain and attendance in physical education classes predicted participants' subjective sense of well being. Moreover, pain was found to be a significant factor of HRQOL in a study by Sawyer et al. (2004), where pain levels showed clear and consistent negative relationships with children's physical, social, and emotional HRQOL.

Despite some equivocal results regarding the impact JIA has on HRQOL, what seems clear is that children with JIA face long-term risks for difficulties in adulthood. A recent study of adults who had JIA as children concluded that many still had active disease in adulthood along with higher risks of unemployment (Foster, Marshall, Myers, Dunkley, & Griffiths, 2003). Other analyses have documented similar difficulties with entering the workforce (Flato et al., 2002; Oen et al., 2002). In these evaluations, persons with JIA had greater disability, more bodily pain, and poorer general health than healthy populations. Indeed, entire families can be affected, as they are subject to increased stress from the psychosocial and financial cost of caring for a child with JIA (Akikusa & Allen, 2002; Reisine, 1995).

Studying HRQOL in these children requires that perceived gains in HRQOL take into account not only improvements in JIA symptoms but also occurrence of negative side effects to medications. Three classes of disease medication have been among those most commonly used: non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying rheumatic drugs (DMARDs), and steroid treatments. NSAIDs are typically the first line of treatment for JIA, and although they do lessen pain and stiffness (Chikanza, 2002; Giannini & Cawkwell, 1995), many adverse effects can occur, especially gastrointestinal symptoms (Chikanza, 2002). Methotrexate, the DMARD used here, has been shown to produce greater treatment effects than NSAIDs (Ilowite, 2002), but the potential for side effects can be greater, including effects on blood cells, liver, or skin in isolated cases (Chikanza, 2002; Ilowite, 2002). Finally, steroids often produce the most dramatic improvements in JIA symptoms; however, these changes come with additional risk of increased number and severity of side effects, including behavior changes, headaches, abdominal pain, swollen face, and even growth problems (Chikanza, 2002; Hamilton & Capell, 2001). Further investigation into the impact these drugs and their side effects have on the HRQOL of children with JIA and their families is needed.

This study examined the effect of JIA treatment on HRQOL. Effects of NSAID, methotrexate, and steroid treatments were compared within and across treatment groups, as were the frequency and severity of their side effects. It was hypothesized that the methotrexate group might demonstrate the most positive change in HRQOL relative to the other groups, because of the drug's short-term efficacy profile and its safer side effects profile relative to steroids. Further, it was hypothesized that although the steroid group would experience marked alleviation of JIA symptoms, the
medication’s adverse effects might offset improvements in domains of HRQOL.

Methods
Participants
The original sample consisted of 63 parent–child pairs, consecutively recruited from a local hospital specializing in pediatric rheumatological conditions. Prior approval of this study was received from the appropriate Institutional Review Board, and informed consent was obtained at the beginning of each patient’s clinic visit. Criteria for inclusion in the study were (1) diagnosis of JIA; (2) beginning new medication treatment—NSAIDs, methotrexate, or steroids; and (3) range in age from 1 to 18 years. Criteria for exclusion from the study were (1) presence of any other major illness or disability, as determined by the pediatric rheumatologist and (2) lack of proficiency in the English language prohibiting the administration of study questionnaires.

During the study, two parent–child pairs were dropped because of a change in patient diagnosis and four were lost to follow-up. The remaining 57 pairs completed the study with 22, 20, and 15 in the NSAID, methotrexate, and steroid groups, respectively. Of the children, there were 13 males and 44 females (mean age = 8.1 years, SD = 4.8) whereas parents included 4 males and 53 females (mean age = 36.4 years, SD = 6.4). Children age 4 and younger (n = 20) were too young for self-report measures, so child self-reports for 37 of the 57 children were obtained.

Materials
HRQOL was assessed by using the Pediatric Quality of Life Inventory (PedsQL™, Version 4.0, Generic Core Scales, and Version 3.0, Rheumatology Module (Varni et al., 2002; Varni, Seid, & Kurtin, 2001). These are patient and parent-proxy self-report instruments designed to measure the perceived HRQOL of children ages 5–18. On the Generic Core Scale, a total score is received in addition to scores along physical, school, social, and emotional functioning domains. The PedsQL™ rheumatology module yields scores along dimensions of pain and hurt, daily activities, treatment, anxiety, and communication, as well as a total score. For the generic core, internal consistencies for child reports have ranged from .71 within the school domain to .91 for the total score whereas proxy reports ranged from .79 to .93. For the rheumatology module, internal consistencies for child reports have ranged from .75 within the anxiety domain to .86 for the total score whereas proxy reports ranged from .82 to .91. The generic core scales have successfully discriminated between healthy populations and those with rheumatic disease whereas the rheumatology module distinguished children with fibromyalgia from those with other pediatric rheumatic diseases (Varni et al., 2001; Varni et al., 2002). In this study, Cronbach α coefficients for the generic core total score were .89 and .90 on the child and parent forms respectively, with corresponding coefficients of .87 and .89 for the rheumatology module child and parent total scores.

To assess the number and severity of medication side effects, the lead pediatric rheumatologist generated a side effects checklist based on commonly reported side effects to the study medications. On this instrument, a parent identified how many of 22 potential side effects were experienced by the child “as a result of taking his/her current arthritis treatment medication(s)” (Table I). For each side effect identified, the parent then indicated perceived severity by marking along a 5-cm visual analog scale anchored from “mild” to “severe.” An item was individually scored by measuring the length of the line preceding the test-taker’s mark. In an effort to enhance targeting of clinically significant side effects, ratings less than 1 cm from the left anchor were all scored as zero. A total side effect severity rating was then calculated by summing the severity ratings of all side effects and dividing by 22 (the total number of potential side effects contained in the questionnaire). This instrument yielded an α coefficient of .70.

Other data included the number of active, involved, and limited joints and erythrocyte sedimentation rates, for each patient at both periods. The project’s lead pediatric rheumatologist, who is the director of our pediatric rheumatology clinic, also assigned a disease severity rating to each patient, which was a reflection of her global assessment of disease severity as suggested by medical data such as active joints and sedimentation rates. Ratings ranged from 0 to 10, with 0 indicating absence of disease and 10 representing the most severe disease. Other scale ranges have also been used for this purpose, such as 1–4 or 1–5 (Alsufyani et al., 2004; Selvaag et al., 2003). A 10-point range was chosen here to increase sensitivity to variability in treatment gains within the sample. Before beginning medication treatment, a correlation of −.46 was obtained between the disease severity rating and child-reported generic HRQOL.

Design and Procedure
At Time 1, each patient was prescribed one of the three study medications and assigned to the corresponding group. NSAID and methotrexate children took their
medicines orally whereas steroid children received their medicine in the form of IV methylprednisolone, administered once at Time 1 and again at Time 2. Time 2 assessment occurred 4 months after Time 1 for each child. At Times 1 and 2, children and one of their parents completed the PedsQL™ generic and rheumatology modules, although children 4 years of age and younger did not complete self-reports because they were too young for the instruments used. Parents completed the medication side effects checklist at Time 2. In all cases, the parent completing the Time 1 forms completed the Time 2 forms. Research assistants were available to help a child read and understand questionnaire items when necessary. Data regarding disease status, including the physician’s disease severity rating, were recorded at both the time points.

**Data Analysis**

Repeated measures multivariate analysis of variance (MANOVA) was used to examine differences in change across time among the three groups. Significant interactions were tested with subsequent univariate ANOVA tests and Tukey post hoc tests where necessary. To evaluate relative change apart from the size of the values themselves, a “percent change” score was calculated for each dependent variable by subtracting the baseline score from the follow-up score and dividing by the baseline score, then multiplying by 100. ANOVAs evaluated these percent change scores to examine relative change apart from baseline differences, and Tukey multiple comparison methods were employed when \( p < .05 \).

Two methods were used to evaluate side effect scores. First, ANOVA was used to compare total side effect severity scores across medication groups. Additionally, the number of severity ratings greater than 1.0 was recorded for each side effect. The number of such endorsements by medication group was analyzed by using the Wilcoxon rank-sum test.

**Results**

Table I presents means and standard deviations for the original, unmodified severity ratings as well as frequencies of endorsements at greater than the 1.0 level for each side effect within each medication group. Tables II and III present means, standard deviations, and percentage.
change across time, where applicable, for the HRQOL and medical variables.

**HRQOL**

**Child Report**

For generic HRQOL, repeated measures MANOVA revealed a significant main effect for time [Wilks's Λ = .46, approximated $F(5, 28) = 6.72, p = .001$] as well as a significant time–medication group interaction [Wilks's Λ = .51, approximated $F(10, 56) = 2.27, p = .026$]. Subsequent univariate ANOVA tests indicated significant interactions for the total $F(2, 32) = 7.27, p = .002$ and physical $F(2, 32) = 10.70, p = .001$ generic HRQOL scores. ANOVA comparisons of the groups at Time 1 indicated that the three groups had different total and physical HRQOL scores, $F(2, 38) = 10.52, p = .001$ and $F(2, 38) = 12.53, p = .001$, respectively, with Tukey post hoc tests showing the steroid group to have lower total and physical generic HRQOLs than the NSAID.

### Table II. Means and Standard Deviations for PedsQL Generic Core and Rheumatology Modules, with Average Percentage Change over Time

<table>
<thead>
<tr>
<th></th>
<th>NSAID</th>
<th>Methotrexate</th>
<th>Steroid</th>
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<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Average percentage change</td>
</tr>
<tr>
<td><strong>Generic PedsQL™</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child</td>
<td>80.1</td>
<td>85.2</td>
<td>+9.7</td>
</tr>
<tr>
<td>Parent</td>
<td>76.1</td>
<td>77.5</td>
<td>+4.2</td>
</tr>
<tr>
<td><strong>Physical</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child</td>
<td>75.7</td>
<td>78.5</td>
<td>+31.3</td>
</tr>
<tr>
<td>Parent</td>
<td>67.7</td>
<td>71.8</td>
<td>+21.2</td>
</tr>
<tr>
<td><strong>Emotional</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Child</td>
<td>83.6</td>
<td>95.9</td>
<td>+35.1</td>
</tr>
<tr>
<td>Parent</td>
<td>76.2</td>
<td>81.9</td>
<td>+14.9</td>
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<tr>
<td><strong>Social</strong></td>
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<td></td>
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</tr>
<tr>
<td>Child</td>
<td>88.6</td>
<td>86.4</td>
<td>–3.5</td>
</tr>
<tr>
<td>Parent</td>
<td>85.0</td>
<td>83.8</td>
<td>–5.0</td>
</tr>
<tr>
<td><strong>School</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child</td>
<td>75.5</td>
<td>68.6</td>
<td>+20.8</td>
</tr>
<tr>
<td>Parent</td>
<td>74.2</td>
<td>75.8</td>
<td>+16.6</td>
</tr>
<tr>
<td><strong>Rheumatology PedsQL™</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child</td>
<td>82.0</td>
<td>86.9</td>
<td>+10.2</td>
</tr>
<tr>
<td>Parent</td>
<td>70.8</td>
<td>75.7</td>
<td>+18.5</td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child</td>
<td>66.1</td>
<td>75.7</td>
<td>+14.6</td>
</tr>
<tr>
<td>Parent</td>
<td>53.1</td>
<td>61.5</td>
<td>+20.5</td>
</tr>
<tr>
<td><strong>Activities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child</td>
<td>91.8</td>
<td>94.5</td>
<td>+12.1</td>
</tr>
<tr>
<td>Parent</td>
<td>84.1</td>
<td>87.9</td>
<td>+7.9</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child</td>
<td>85.2</td>
<td>89.6</td>
<td>+5.3</td>
</tr>
<tr>
<td>Parent</td>
<td>67.0</td>
<td>75.0</td>
<td>+36.7</td>
</tr>
<tr>
<td><strong>Worry</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child</td>
<td>78.0</td>
<td>85.6</td>
<td>+16.0</td>
</tr>
<tr>
<td>Parent</td>
<td>78.3</td>
<td>78.4</td>
<td>+10.6</td>
</tr>
<tr>
<td><strong>Communication</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Child</td>
<td>83.3</td>
<td>82.6</td>
<td>+24.9</td>
</tr>
<tr>
<td>Parent</td>
<td>84.9</td>
<td>76.7</td>
<td>–10.5</td>
</tr>
</tbody>
</table>

### Table III. Means, Standard Deviations, and Percent Change for the Medical Status Markers

<table>
<thead>
<tr>
<th></th>
<th>NSAID</th>
<th>Methotrexate</th>
<th>Steroid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Average percentage change</td>
</tr>
<tr>
<td><strong>Active joints</strong></td>
<td>2.8</td>
<td>2.0</td>
<td>–40.0</td>
</tr>
<tr>
<td><strong>Involved joints</strong></td>
<td>3.2</td>
<td>2.0</td>
<td>–36.6</td>
</tr>
<tr>
<td><strong>Limited joints</strong></td>
<td>3.7</td>
<td>3.1</td>
<td>–9.6</td>
</tr>
<tr>
<td><strong>Sedimentation rate</strong></td>
<td>22.6</td>
<td>22.1</td>
<td>+9.1</td>
</tr>
<tr>
<td><strong>Disease severity</strong></td>
<td>2.2</td>
<td>1.1</td>
<td>–44.5</td>
</tr>
</tbody>
</table>
MANOVA indicated no difference between the groups at Time 2 for either domain [Wilks's Λ = .84, F(4, 64) = 1.48, p = .220]. Percent change in HRQOL across time was not the same among the three groups as indicated by ANOVA comparisons of percent change for the generic [F(2, 32) = 10.3, p = .001] and physical [F(2, 32) = 5.41, p = .009] domains. Tukey post hoc tests indicated that the steroid group experienced greater positive change relative to baseline in the areas of overall and physical domains of HRQOL than the NSAID and methotrexate groups.

For rheumatological HRQOL, repeated measures MANOVA revealed a significant main effect for time [Wilks's Λ = .39, approximated F(5, 27) = 8.62, p = .001] as well as a significant time–medication group interaction [Wilks's Λ = .48, approximated F(10, 54) = 2.40, p = .02]. Subsequent univariate ANOVA tests indicated significant interactions for the total [F(2, 31) = 4.02, p = .03] and pain [F(2, 31) = 5.98, p = .006] rheumatological HRQOL scores. ANOVA comparisons of the groups at Time 1 indicated that the three groups had different total and pain HRQOL, [F(2, 38) = 6.06, p = .005 and F(2, 38) = 8.04, p = .001, respectively], with Tukey post hoc tests showing the steroid group to have poorer total rheumatological HRQOL scores than the NSAID group and poorer pain rheumatological HRQOL than the NSAID and methotrexate groups. MANOVA indicated no difference among medication groups at Time 2 for either domain [Wilks's Λ = .86, approximated F(4, 62) = 1.22, p = .313]. ANOVA comparisons of percent change indicated differences in change in total rheumatological HRQOL across time relative to baseline [F(2, 32) = 4.10, p = .026]. Tukey post hoc tests indicated that the steroid group experienced greater positive change than both NSAID and methotrexate groups relative to baseline in the area of overall rheumatological HRQOL.

**Parent Report**

For generic HRQOL, repeated measures MANOVA revealed a significant main effect for time [Wilks's Λ = .51, approximated F(5, 29) = 5.53, p = .001] as well as a significant time–medication group interaction [Wilks's Λ = .51, approximated F(10, 58) = 2.36, p = .02]. Subsequent univariate ANOVA tests indicated significant interactions for the total [F(2, 33) = 4.26, p = .023], physical [F(2, 33) = 4.81, p = .015], and school [F(2, 33) = 5.91, p = .006] generic HRQOL scores. ANOVA comparisons at Time 1 indicated that the three groups had different scores for total [F(2, 44) = 10.64, p = .001], physical [F(2, 44) = 11.03, p = .001], and school [F(2, 44) = 4.09, p = .023] HRQOL scores, with Tukey post hoc tests showing the steroid group to have lower generic HRQOL than the NSAID and methotrexate groups in all three domains. MANOVA indicated no difference between the groups at Time 2 [Wilks's Λ = .81, approximated F(6, 68) = 1.29, p = .275]. ANOVA comparisons of percent change indicated that change in parent reports was not the same among the three groups in total [F(2, 30) = 5.41, p = .01], physical [F(2, 48) = 4.19, p = .021], and school [F(2, 33) = 3.46, p = .043] HRQOL scores. Tukey post hoc tests indicated that for children who took steroids, parents perceived greater positive change in total HRQOL than either the NSAID or methotrexate groups and greater physical and school HRQOL percentage change than the NSAID group.

For rheumatological HRQOL, repeated measures MANOVA revealed a significant main effect for time [Wilks's Λ = .51, approximated F(5, 26) = 4.97, p = .003] as well as a significant time–medication group interaction [Wilks's Λ = .42, approximated F(10, 52) = 2.86, p = .007]. Subsequent univariate ANOVA tests indicated significant interactions for the rheumatological total HRQOL score [F(2, 30) = 6.16, p = .006] and pain [F(2, 30) = 7.97, p = .002] rheumatological HRQOL scores. ANOVA comparisons at Time 1 indicated that the three groups had different rheumatology total and pain HRQOL scores, [F(2, 58) = 6.75, p = .002 and F(2, 58) = 7.37, p = .001, respectively], with Tukey post hoc tests showing the steroid group to have poorer total rheumatological HRQOL scores than the NSAID group and poorer pain rheumatological HRQOL than both NSAID and methotrexate groups. MANOVA indicated no difference among medication groups at Time 2 for either domain [Wilks's Λ = .96, approximated F(4, 102) = .47, p = .754]. ANOVA comparisons of percent change indicated differences in percent change across time within total rheumatological HRQOL [F(2, 52) = 4.16, p = .021] and rheumatological pain HRQOL [F(2, 46) = 3.78, p = .03] relative to baseline. Tukey post hoc tests indicated the steroid group experienced greater positive change than the NSAID group relative to baseline in both total and pain-related rheumatological HRQOL.

**Medical Variables**

**Change in Disease Status**

Tests of disease status involved evaluations of number of active, involved and limited joints present, disease severity rating, and sedimentation rates. Repeated measures MANOVA revealed a significant main effect for time [Wilks's Λ = .33, approximated F(5, 43) = 17.35, p = .001] as well as a time–medication group interaction [Wilks's Λ = .40, approximated F(10, 86) = 4.98, p = .001].
Subsequent univariate ANOVA tests yielded significant interactions for sedimentation rate \([F(2, 47) = 28.62, p = .001]\), active joints \([F(2, 47) = 6.19, p = .004]\), involved joints \([F(2, 47) = 4.95, p = .011]\), and limited joints \([F(2, 47) = 3.57, p = .036]\). ANOVA comparisons at Time 1 indicated that the three groups differed in disease status as defined by sedimentation rate \([F(2, 57) = 20.91, p = .001]\), number of active joints \([F(2, 57) = 4.75, p = .012]\), and number of involved joints \([F(2, 57) = 4.09, p = .022]\) as well as in disease severity \([F(2, 53) = 11.80, p = .001]\). Tukey post hoc tests showed children in the steroid group at Time 1 to have higher sedimentation rates than the NSAID and methotrexate groups and greater numbers of active and involved joints than the NSAID group. Additionally, the three groups all differed from each other in disease severity and number of active joints at Time 1, with the steroid group displaying more severe disease characteristics than the methotrexate group which was more severe than the NSAID group. Moreover, MANOVA indicated no difference between the groups in disease status at Time 2 \([\text{Wilks’s } \Lambda = .80, \text{approximated } F(10, 92) = 1.07, p = .395]\). ANOVA comparisons of percent change indicated that the three groups experienced differential changes in sedimentation rate \([F(2, 35) = 12.30, p = .001]\), active joints \([F(2, 35) = 5.62, p = .008]\), and involved joints \([F(2, 35) = 5.61, p = .008]\). Tukey post hoc tests indicated that children taking the steroid medication had greater improvements relative to baseline in sedimentation rates than the NSAID and methotrexate groups and greater improvements in active and involved joint counts than the NSAID group.

Side Effect Severity
ANOVA indicated that the total side effect severity scores were not the same for each medication group, \([F(2, 52) = 6.16, p = .004]\). Tukey post hoc tests showed that the steroid group had significantly greater total severity scores than the NSAID group, with an additional trend toward higher severity scores than the methotrexate group. Wilcoxon rank-sum tests, comparing the number of clinically significant endorsed side effects between groups, indicated that the steroid group possessed more side effects than the NSAID group \([z = −.585, p = .028]\). As Table I illustrates, the most common clinically significant side effects endorsed by children in the steroid group were swollen face, fatigue, and indigestion.

Discussion
This study is one of the first to address how medications for JIA and their associated side effects may impact variables such as HRQOL. Its examination of how side effects contribute to HRQOL can provide helpful information to rheumatologists and pediatricians who may be considering the use of a particular medication to treat their patients. All of this information may improve physicians’ ability to inform families of what they might expect with a given medication treatment, not only medically, but psychosocially.

Results showed that children varied in their health status before treatment. Children in the steroid group tended to have higher sedimentation rates and ratings of disease severity and greater numbers of active and involved joints. These children received also received lower scores on measures of overall generic and rheumatological HRQOL as well as on the physical and pain subdomains. Our findings bolster conclusions from other studies of children with JIA (LeBovidge et al., 2003; Sawyer et al., 2004) which have shown an association between JIA symptoms and HRQOL or psychosocial functioning. Such findings held true for both parent and proxy report, as high levels of patient–parent agreement were observed. Not surprisingly, children with more severe disease have lower health-related qualities of life.

Children who received steroids generally made the most improvements among medical status markers during the 4-month period. These children displayed greater improvements in sedimentation rates relative to baseline than participants from the other two medication groups and greater improvements in active and involved joint counts than the NSAID group. Such improvements did not come without a price, however, as children in the steroid group experienced a greater number of impactful side effects than children in the NSAID group and reported greater severity of side effects than NSAID patients with an added trend toward experiencing greater severity than those from the methotrexate group.

When forming hypotheses for this study, it was anticipated that symptom improvement might be offset by adverse effects of medications. Surprisingly, despite being impacted by the most severe side effects, results showed that the steroid group demonstrated the greatest positive changes overall in HRQOL when compared with the other groups. Furthermore, self-reported gains in HRQOL came within domains that one could argue are most highly related to JIA, including total scores from both the generic and rheumatological modules in addition to physical and pain subdomains. Taken collectively, it appears that the benefits of this treatment have outweighed the negative effects with this sample, at least initially.
There are two possible reasons for this finding. One rationale considers the acute nature of steroid treatment. Whereas NSAIDs and methotrexate can sometimes take several months to bring about the most positive health-related changes, steroids bring about physical changes much more quickly (Cassidy, 2001; Chikanza, 2002). A second potential explanation relates to the methotrexate group, as these children reported similar levels of indigestion and nausea, and more vomiting, than the steroid group. Any delay in treatment response combined with the presence of bothersome side effects could have contributed to superiority of the steroid group.

Of course, the occurrence of negative side effects to medications can add to the already significant stress with which families with a chronically ill child must cope. Because the most vulnerable families tend to be those whose child’s medical care requirements are larger than the available resources (Farmer et al., 2004; McCormick, Stemmler, & Athreya, 1986), any treatment complication that may necessitate further contact with a healthcare provider could increase stress within the family or impact HRQOL. Routinely charged with helping a family learn ways to cope with the stress of chronic illness, pediatric psychologists can play an additional role in helping one deal with side effects to medications. For example, children in this study who received steroid treatment often reported stomach aches, difficulty in eating, swollen face, headaches, or fatigue. These effects can cause pain, general physical discomfort, or possibly increase one’s self-consciousness about physical appearance or abilities. Relaxation training, biofeedback, guided imagery, and cognitive reframing are among the tools that may be useful to help a child and family learn to cope with complications of treatments for JIA.

The study design presents some limitations. For example, the 4 months between baseline and follow-up may be too short to detect treatment effects. One suggestion for future research is a longer follow-up interval (e.g., 6 months to 1 year) which would provide valuable information regarding whether the current results changed or remained the same over time. In addition, the study sample was limited to English-speaking participants. Results may not generalize to some children and families in other ethnicities. The addition of samples of children with other chronic illnesses might further enhance the potential generalization of findings, as documentation of the impacts of treatment for chronic illness on HRQOL continues to be needed (Gerharz et al., 2003; Miller et al., 2002; Varni et al., 2002).

At any rate, continued discussion of medication effects is necessary, given the fundamental mistrust of medication on the part of some parents (Akikusa & Allen, 2002). Our data suggest that some degree of adverse treatment effects is tolerable as long as treatment benefits are concurrently perceived. As JIA is a long-term disease that can go into remission and return, one’s subjective assessment of the overall impact of treatment likely takes into account the accumulation of past and present experiences of symptom relief. Nausea and abdominal pain, for example, may be less tolerable where mild disease fails to remit, than in other instances where more severe disease improves. Research which helps answer these questions will help determine if treatments are actually improving the lives of these children or merely replacing some problems with others.

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