

Is Complementary and Alternative Healthcare Use Associated with Better Outcomes in Children with Juvenile Idiopathic Arthritis?

KARINE TOUPIN-APRIL, DEBBIE EHRMANN FELDMAN, MARIA VICTORIA ZUNZUNEGUI, MARTIN DESCARREAU, PETER MALLESON, and CIARÁN M. DUFFY

ABSTRACT. *Objective.* The objectives of this study were (1) to examine the association between the use of complementary and alternative healthcare (CAHC) and subsequent health outcomes; and (2) to explore the association between CAHC use and adherence to conventional treatments in children with juvenile idiopathic arthritis (JIA).

Methods. A cohort of children with JIA (n = 182, mean age 10 yrs) who attended outpatient clinics were followed for one year. We evaluated the use of CAHC, health-related quality of life (HRQOL), global health, physical functioning, pain, and disease severity at 3-month intervals. We also evaluated perceived adherence to treatments. General estimating equations were performed to determine the association between use of CAHC and subsequent outcomes while controlling for possible confounders.

Results. CAHC was used by 36.4% of participants over the 12-month period. Use of CAHC was associated with subsequent lower global health and physical functioning despite higher adherence to prescribed medications as assessed by the rheumatologist ($p < 0.05$). Use of CAHC was not associated with subsequent improved HRQOL or decreased pain or disease severity.

Conclusion. Children with JIA who use CAHC do not have improved outcomes, at least over the relatively short term. Nevertheless, they seem to be more adherent to conventional treatment according to the rheumatologist. (First Release Sept 1 2009; J Rheumatol 2009;36:2302–7; doi:10.3899/jrheum.081295)

Key Indexing Terms:

JUVENILE IDIOPATHIC ARTHRITIS
ALTERNATIVE MEDICINE

LONGITUDINAL STUDIES

COMPLEMENTARY THERAPIES
QUALITY OF LIFE

In juvenile idiopathic arthritis (JIA), a relatively common chronic condition in children, use of complementary and alternative healthcare (CAHC) varies between 34% and 92%¹⁻⁵. Despite its high use, little is known about the effectiveness of CAHC in this population. Parents of children with JIA have reported a high level of effectiveness⁴. Only a few randomized controlled trials (RCT) have evaluated specific types of CAHC. One RCT indicated that massage

may decrease anxiety and pain in juvenile arthritis, as reported by the child, parents, and physician⁶, and another showed that calcium supplements may lead to better outcomes⁷. Although RCT are essential to evaluate efficacy of CAHC, they may not take into account important aspects of the treatment such as nonadherence to conventional treatments, interactions between CAHC and medication, and variation of disease severity over time.

From the Département de médecine sociale et préventive and Groupe de Recherche Interdisciplinaire en Santé, Université de Montréal and Centre de recherche interdisciplinaire en réadaptation, Montreal; Département de Chiropratique, Université du Québec à Trois-Rivières, Trois-Rivières; Division of Rheumatology, Department of Pediatrics, University of British Columbia, Vancouver, British Columbia; and Division of Rheumatology, Department of Paediatrics, Montreal Children's Hospital of the McGill University Health Centre and McGill University, Montreal, Quebec, Canada.

Supported by the Canadian Institutes of Health Research, the Sick Kids Foundation, the Canadian Arthritis Network, and The Arthritis Society. K. Toupin-April was supported by a graduate training award from the Canadian Arthritis Network and the Canadian Institutes of Health Research. D. Ehrmann Feldman holds a New Investigator Award from The Arthritis Society. Dr. Duffy holds the Sessenwein Award for Research, Department of Paediatrics, McGill University.

K. Toupin-April, OT, PhD, Département de médecine sociale et préventive and Groupe de Recherche Interdisciplinaire en Santé, Université de Montréal and Centre de recherche interdisciplinaire en réadaptation;

D. Ehrmann Feldman, PT, PhD, Associate Professor, École de Réadaptation and Groupe de Recherche Interdisciplinaire en Santé, Université de Montréal; Montreal Children's Hospital of the McGill University Health Centre, and Centre de recherche interdisciplinaire en réadaptation; M.V. Zunzunegui, PhD, Professor, Département de médecine sociale et préventive and Groupe de Recherche Interdisciplinaire en Santé, Université de Montréal; M. Descarreaux, DC, PhD, Professor, Département de Chiropratique, Université du Québec à Trois-Rivières; P. Malleison, MB, BS, MRCP, FRCPC, Professor, Division of Rheumatology, Department of Pediatrics, University of British Columbia; C.M. Duffy, MB, BCh, MSc, FRCPC, Professor and Director, Division of Rheumatology, and Associate Physician in Chief, Department of Paediatrics, Montreal Children's Hospital of the McGill University Health Centre and McGill University.

Address correspondence to K. Toupin-April, University of Ottawa, 1 Stewart Street, Room 201, Ottawa, Ontario K1N 6N5, Canada; E-mail: ktoupina@uottawa.ca

Accepted for publication May 12, 2009.

Before undertaking a RCT, aimed at measuring the efficacy of a treatment under controlled conditions, it is useful to conduct a prospective observational study in order to assess the use of several types of CAHC and associated outcomes as observed in clinical practice. Following the children over time is of interest especially in diseases like JIA because of its chronic aspect, the variability of disease severity over time, and the fact that using CAHC could interfere with standard treatments or diminish adherence. To date, all observational studies assessing CAHC use in children with JIA have been cross-sectional¹⁻⁵.

The objectives of our study were to investigate health outcomes related to the use of CAHC, for four 3-month intervals over a 12-month period, and to evaluate the association between CAHC use and adherence to prescribed medications. We hypothesized that CAHC would be associated with better health outcomes since parents of children with JIA have reported a high level of effectiveness⁴.

MATERIALS AND METHODS

Study population. The study population consisted of parents of children with JIA aged 2 to 18 years who attended the arthritis outpatient clinics at the Montreal Children's Hospital and the British Columbia Children's Hospital in Vancouver. Ethics approval was obtained from the 2 institutions and all participating parents signed a consent form.

Data collection. Parents were asked to answer questionnaires during their visits to the arthritis clinic. They could complete them either at the clinic, or at home and return them by mail. Questionnaires were administered at baseline and 3, 6, 9, and 12 months. Relevant demographic and medical data were abstracted from the medical chart.

Measures. The main predictor of outcomes to be tested was the parents' report of use of CAHC by their child. Parents answered a CAHC Questionnaire that asked if they used CAHC for their child in the previous 3 months and whether they believed that CAHC was useful in improving their child's condition. Many CAHC practitioners and products were addressed: chiropractor, acupuncturist, osteopath, massage therapist, homeopath, naturopath, hypnotist, reflexologist, spiritual healer, dietary changes and supplements (including special diets and vitamins), folk remedies, and other (for which the parent was asked to specify). This questionnaire was pilot-tested and appeared to have reasonable measurement properties in both English and French.

Health outcomes included health-related quality of life (HRQL), global health, physical functioning, and pain as rated by the parents, as well as disease severity rated by the rheumatologist. These health outcomes were chosen because they are part of the core set of outcomes important to measure in children with JIA when conducting a trial⁸. HRQL was measured by the total score of the Juvenile Arthritis Quality of Life Questionnaire (JAQQ)⁹⁻¹¹. The JAQQ assesses HRQL of children with JIA in the past 2 weeks⁹⁻¹¹. It includes 4 domains (gross motor function, fine motor function, psychosocial function, and general symptoms) and a section assessing pain and global health. The global score ranges from 1 to 7, lower scores indicating less difficulty performing activities. The JAQQ has been validated in French and English¹¹ and has excellent sensitivity to change⁹ and good construct validity¹¹. There is also good agreement between parents and children¹². The child's global health since the last assessment is scored on a 5-point Likert scale, from -2 (much worse health) to 2 (much better health), and pain in the past week is scored on a 100-mm visual analog scale (VAS). Physical functioning was measured by the global score of the Child Health Assessment Questionnaire (CHAQ)¹³⁻¹⁵. The CHAQ evaluates physical functioning over the past week in children with

JIA. Questions are grouped in categories such as dressing and grooming, eating, walking, and activities. The overall score varies from 0 (no disability) to 3 (completely disabled)¹³. The CHAQ is a valid and reliable instrument in French and English¹⁴⁻¹⁶. Rheumatologists also rated the children's disease severity using the active joint count, which scores the number of joints with active inflammation¹⁷.

Other outcomes of interest were adherence to prescribed medications according to the child's rheumatologist and adherence to prescribed medications and exercises according to the parents. The Clinical Information Questionnaire was completed by the treating rheumatologist and used to describe the child's disease and its treatment, including a 100-mm VAS evaluating treatment adherence. The degree of adherence to prescribed medications and exercises in the past 3 months according to parents was measured by 2 questions included in the Parent Adherence Report Questionnaire (PARQ) and scored on a 100-mm VAS¹⁸. The PARQ has been validated in English and French and has good construct validity¹⁸.

Some variables may influence the outcomes measured in this study. These include age of the child and disease duration, which were collected from the medical charts. Also, economic hardship was measured by the Economic Hardship Questionnaire, which describes the availability of finances for basic needs (such as healthcare)^{19,20}. The computed score is a sum of 10 questions scored on a 4-point Likert scale. Higher scores indicate more economic hardship.

Analysis. Descriptive statistics were used to describe CAHC use at 3-month intervals. We investigated outcomes related to CAHC use, using generalized estimating equations (GEE)²¹. GEE models account for within-subject correlations among repeated measurements, making standard errors of the parameter estimates valid and improving power.

Our first objective addressed health outcomes subsequent to CAHC use, therefore health outcomes were evaluated at the end of any 3-month period in which the children could have used CAHC. Models were adjusted for the outcome of interest (HRQL, physical functioning, or pain) and disease severity before the period in which the children had used CAHC (baseline value), since those variables may have affected their use of CAHC²² and subsequent outcomes such as HRQL²³. The GEE models were also adjusted for age, disease duration, and economic hardship during the period in which the children could have used CAHC, since those may be related to CAHC use^{2,24,25}. We also adjusted for adherence to prescribed medication and exercises according to parents during the period in which the children could have used CAHC since these may be related to health outcomes such as HRQL²³. Regarding our second objective, the association between adherence to treatment and CAHC use, adherence outcomes were evaluated during the period in which the children could have used CAHC as it was considered that parents might diminish their adherence to conventional care while their child was receiving CAHC.

RESULTS

Two hundred thirty-five subjects consented to participate in the study and 182 parents of children with JIA returned the questionnaires (120 in Montreal and 62 in Vancouver), corresponding to a response rate of 76.43% for Montreal and 63.92% for Vancouver. The main reason cited for refusal to participate was lack of time to complete the questionnaires. There were no differences between participants and nonparticipants at baseline except for mean active joint count, which was higher in participants ($p = 0.001$). Most participants' characteristics were similar over time, and losses to followup were not different between children who used CAHC before the study and those who did not. Concerning the types of arthritis at baseline, 40.4% of children had oligoarthritis, 20.3% polyarthritis, 9% systemic arthritis,

10.1% enthesitis-related arthritis, 11.2% psoriatic arthritis, and 9% had another type of arthritis. Among children included in the study at baseline, 73.3% were prescribed medications and 75.6% were prescribed exercises. The most used medications were nonsteroidal antiinflammatory drugs (NSAID; 53.9% of participants), followed by disease-modifying antirheumatic drugs (DMARD; 41.1%), corticosteroids (8.3%), and tumor necrosis factor- α inhibitors (4.4%). CAHC use ranged between 10% and 24% for the various 3-month intervals, and 36.4% of participants used it at least once over the 12-month period. The most common types of CAHC used were special diets, chiropractic, and naturopathy, and parents perceived a slight to moderate improvement with CAHC²⁶. A description of the cohort is summarized in Table 1.

According to the GEE analyses concerning health outcomes, use of CAHC was associated with subsequent lower global health ($\beta = -0.79$, 95% CI $-1.58, -0.00$, $p < 0.05$) and physical functioning ($\beta = 0.93$, 95% CI $0.22, 1.63$, $p < 0.05$; Table 2). CAHC use was not associated with improved HRQOL or decreased pain or disease severity.

For most health outcomes, the baseline value of the outcome of interest was strongly associated with subsequent values (Table 2). For example, baseline level of physical functioning was very strongly associated with subsequent physical functioning. Other variables associated with the outcomes of interest included child's age, disease duration, and adherence to conventional treatments according to their parents. Longer disease duration was associated with lower health and HRQOL. Older child's age and higher adherence to exercises were associated with better health, while higher adherence to prescribed medications was associated with a lower perception of global health.

The GEE analyses also showed that users of CAHC had a higher adherence to prescribed medications as perceived

by the rheumatologist than nonusers ($\beta = 7.49$, 95% CI $1.35, 13.64$, $p < 0.05$; Table 3). However, CAHC use was not associated with parent reports of adherence to prescribed medications and exercises. Some variables were associated with the parent report of adherence to exercises. The baseline value of adherence to prescribed exercises according to parents was associated with subsequent adherence, while more economic hardship was associated with lower adherence to prescribed exercises.

DISCUSSION

We conducted a longitudinal observational study of the use of CAHC in children with JIA and its association with outcomes over a one-year period. The findings suggest that children who used CAHC had a subsequent lower level of global health and physical functioning than those who did not use CAHC. Since children with higher disease severity might be more likely to use CAHC²², our analysis adjusted for disease severity and the outcomes of interest prior to CAHC use in order to reduce the possibility of these as predictors rather than outcomes of CAHC.

One explanation for our findings could be that using CAHC while at the same time continuing with a conventional treatment regimen may be time- and energy-consuming for the child and his family. This combination of treatments could heighten stress and fatigue of parents and children and also reduce their leisure time, which could in turn lead to worse health outcomes for children with JIA, especially those that include a psychological component and symptoms such as fatigue²⁷. Also, parents who used CAHC for their child may perhaps pay more attention to the child's symptoms as an attempt to monitor the results of such interventions.

A number of other variables were associated with health outcomes. Older child's age was associated with better per-

Table 1. Characteristics of the sample of children with JIA at baseline and 6 and 12 months.

Characteristic	Baseline, n = 180	6 Months, n = 128	12 Months, n = 109
Sex female, n (%)	124 (68.9)	93 (73.2)	75 (70.8)
Age, yrs, mean (SD)	10.2 \pm 4.4	10.1 \pm 4.6	10.6 \pm 4.4
Cultural background, Canadian, n (%)	132 (76.3)	89 (77.4)	72 (77.4)
Maternal education, higher than high school, n (%)	93 (60.8)	64 (57.7)	57 (64)
Income, n (%)			
< \$ 45,000 CAN	33 (25)	29 (30.5)	24 (28.2)
\$ 45,000–75,000 CAN	47 (35.6)	35 (36.8)	25 (29.4)
> \$ 75,000 CAN	52 (39.4)	31 (32.6)	36 (42.4)
Active joint count, mean \pm SD	1.8 \pm 3.7	1.3 \pm 3.3	1 \pm 2.9
Disease duration, yrs, mean \pm SD	4.2 \pm 3.6	4.6 \pm 3.5	4.8 \pm 3.2
Health-related quality of life, mean \pm SD	2.2 \pm 1.2	1.8 \pm 1.1*	1.8 \pm 1*
Use of complementary and alternative healthcare, n (%)	34 (19.8)	20 (16.1)	12 (11.4)

* $p < 0.05$

Table 2. Health outcomes of complementary and alternative healthcare (CAHC) use † over a 12-month period (GEE analysis). Beta coefficients (95% confidence intervals) represent change in the outcome per unit change in the independent variable.

Variables	Global Health β (95% CI)	HRQOL ^{††} β (95% CI)	Outcomes Physical Function ^{††} β (95% CI)	Disease Severity β (95% CI)	Pain β (95% CI)
CAHC use	-0.79 (-1.58, -0.00)*	0.28 (-0.33, 0.89)	0.93 (0.22, 1.63)*	0.16 (-0.59, 0.91)	7.50 (-14.09, 29.08)
Child's age	0.07 (0.02, 0.13)*	-0.03 (-0.08, 0.02)	-0.02 (-0.21, 0.17)	-0.02 (-0.12, 0.08)	0.44 (-0.97, 1.85)
Disease duration	-0.10 (-0.18, -0.03)**	0.08 (0.01, 0.14)*	0.06 (-0.01, 0.14)	-0.03 (-0.16, 0.10)	1.30 (-0.98, 3.58)
Economic hardship	-0.01 (-0.07, 0.05)	0.01 (-0.03, 0.06)	-0.03 (-0.11, 0.05)	-0.05 (-0.14, 0.05)	0.49 (-0.48, 1.46)
Disease severity at baseline (active joint count)	0.08 (-0.04, 0.20)	0.04 (-0.06, 0.14)	0.04 (-0.11, 0.18)	1.07 (0.69, 1.45)***	-0.43 (-2.06, 1.20)
Parents' report of adherence to medications	-0.02 (-0.03, -0.00)**	-0.00 (-0.01, 0.00)	0.00 (-0.01, 0.01)	-0.00 (-0.02, 0.02)	0.05 (-0.16, 0.25)
Parents' report of adherence to exercises	0.01 (0.01, 0.02)**	0.00 (-0.01, 0.01)	-0.00 (-0.01, 0.01)	0.01 (-0.00, 0.02)	-0.11 (-0.32, 0.10)
HRQOL at baseline ^{††}		0.46 (0.23, 0.69)***			
Physical functioning at baseline ^{††}			0.66 (0.36, 0.97)***		
Pain at baseline					0.22 (0.02, 0.42)*

† Adjusted for all variables in the table. †† Higher score = more difficulty in performing activities. * p < 0.05, ** p < 0.01, *** p < 0.0001. GEE: generalized estimating equation; HRQOL: health-related quality of life.

Table 3. Adherence to conventional treatment as an outcome of complementary and alternative healthcare (CAHC) use (adjusted for all variables in the table) over a 12-month period (GEE analysis). Beta coefficients (95% confidence intervals) represent change in the outcome per unit change in the independent variable.

Variables	Adherence to Medications (rheumatologist report) β (95% CI)	Adherence to Medications (parent report) β (95% CI)	Adherence to Exercises (parent report) β (95% CI)
CAHC use	7.49 (1.35, 13.64)*	-8.22 (-23.56, 7.11)	-13.85 (-31.23, 3.53)
Child's age	0.04 (-1.30, 1.38)	-0.47 (-1.41, 0.46)	0.05 (-1.65, 1.76)
Disease duration	0.35 (-0.98, 1.68)	-1.41 (-2.89, 0.06)	1.39 (-0.41, 3.19)
Economic hardship	0.18 (-0.87, 1.23)	0.12 (-0.32, 0.56)	-1.09 (-1.95, -0.22)*
Disease severity at baseline (active joint count)	0.08 (-0.53, 0.68)	-0.08 (-0.68, 0.52)	0.28 (-2.08, 2.65)
Adherence to medications at baseline (rheumatologist report)	0.06 (-0.13, 0.24)		
Adherence to medications at baseline (parent report)		(0.28 (-0.00, 0.56))	
Adherence to exercises at baseline (parent report)			0.63 (0.44, 0.82)***

* p < 0.05, ** p < 0.01, *** p < 0.0001. GEE: generalized estimating equation.

ceived health, possibly because children learn how to cope with their disease over time. Longer disease duration was associated with lower health and HRQOL, which may be explained by the effect of arthritis on the children's joints and surrounding anatomical structures, which is consistent with previous findings in children with JIA¹². Higher adherence to prescribed exercises was associated with better health, while higher adherence to medications was associated with lower perception of global health. This may indicate that exercises have a positive influence on the child's health, consistent with previous results²³, while adherence to medications may bring a higher burden of care, especially if medications are difficult to administer (e.g., subcutaneous administration of methotrexate) and if side effects occur.

Adherence to prescribed medications was perceived to be higher in children who used CAHC than in nonusers, by the

rheumatologist. Parents who used CAHC for their child may be the ones who are the most involved in their child's treatment since they seem to be actively searching for the best treatments, according to the rheumatologists. Therefore, parents could be more adherent to conventional treatments than nonusers, even while using CAHC. This is consistent with other findings that suggest that users of CAHC do not simply reject all conventional care but want to try all possible treatment options^{3,28,29}. Parents may perhaps become more adherent to conventional care if CAHC does not meet their expectations. Also, because children with higher disease severity may be more likely to use CAHC²², they may also use more conventional care. Interestingly, our results indicate that although CAHC use was associated with physician perception of parental adherence, it was not associated with parents' reports of adherence to conventional treat-

ments. This discrepancy between parents' and rheumatologists' perceptions may be explained by the fact that parents assess their current adherence by comparing it to their usual adherence, while rheumatologists base their opinion on the impression given by parents on their involvement in their child's care when meeting with them at the clinic. Therefore, rheumatologists may perceive parents to be more adherent to conventional care when in fact they are more actively using all treatments available for their child as well as monitoring their health outcomes. In a previous analysis, we have shown that users of CAHC perceived a lower degree of helpfulness of prescribed medications²⁶. Despite this perception, it appears that parents who use CAHC for their children continue to adhere to conventional treatment and truly use these as complementary and not alternative treatments.

Economic hardship was associated with lower adherence to prescribed exercises according to parents, possibly because these parents are more distressed and may lack the time and energy to help their child follow an exercise regimen.

Study limitations. The instrument used to evaluate the use of CAHC in this study has not been validated; however, it was pilot tested with 10 families, and was easy to administer and acceptable to parents. It lists most types of CAHC and includes the opportunity for the respondent to indicate other types of CAHC. Nonetheless, certain types of CAHC may be missing and some categories of CAHC are very broad. Thus, we may have underestimated CAHC use.

There may be a memory bias with respect to CAHC use in the past 3 months. Even though we did not validate the CAHC instrument, our previous experience validating the adherence to treatment questionnaire indicated that the 3-month "window" was valid for studying adherence¹⁸.

A selection bias may also occur because parents were recruited at the arthritis clinic, therefore precluding the participation of parents who completely rejected conventional medicine. There may also be a social desirability bias, in that parents may tend to say they use less CAHC and adhere more to conventional care than they actually do. We tried to minimize this bias by having parents complete the questionnaire in complete confidentiality.

The findings of this longitudinal study could be biased due to cases lost to followup over the one-year period (n = 71). However, most participants' characteristics stayed stable over time (except HRQOL, which was better at 6 and 12 months than baseline), and losses to followup were not different between CAHC users and nonusers. We cannot be certain that factors act only as outcomes of CAHC since they may also predict the use of CAHC. However, our analyses adjusted for outcomes of interest before the occurrence of use of CAHC, which may diminish this possibility.

It should also be noted that although this was a longitudinal study of CAHC use in children with JIA, the study was conducted over a one-year period, which is relatively short

for a disease as chronic as JIA. Data collection was done at intervals of 3 months and therefore precluded us from assessing variations of disease severity during these intervals. Further, our study could not determine causation and does not substitute for an RCT. RCT are needed to determine the efficacy of each type of CAHC used by children with JIA.

Children with JIA who use CAHC tended to have lower subsequent global health and physical functioning, but seemed to be more adherent to conventional care than nonusers, according to the rheumatologist. These results may indicate that using CAHC as well as following conventional treatments may constitute an additional effort for the child's family or that parents may pay closer attention to the child's symptoms when using CAHC. However, rheumatologists' perception of high adherence to prescribed medications by parents who use CAHC for their child is a reassuring finding for health practitioners.

Our study represents a first step in understanding the influence of use of CAHC on outcomes in JIA over a period of time. Although there is a need for RCT to assess the efficacy of CAHC in JIA, this exploratory study of CAHC use as observed in clinical practice did not show an improvement in health outcomes in children using CAHC. Further research should include RCT and investigation of outcomes of CAHC use over a longer period of time. Information should be sought from both parents and children, since children may have different perceptions of effectiveness than their parents.

ACKNOWLEDGMENT

The authors thank Dr. Garbis Meshefedian for his assistance with the statistical analysis and Dr. Peter Tugwell for his comments.

REFERENCES

1. Southwood TR, Malleson PN, Roberts-Thomson PJ, Mahy M. Unconventional remedies used for patients with juvenile arthritis. *Pediatrics* 1990;85:150-4.
2. Hagen LE, Schneider R, Stephens D, Modrusan D, Feldman BM. Use of complementary and alternative medicine by pediatric rheumatology patients. *Arthritis Rheum* 2003;49:3-6.
3. Feldman DE, Duffy C, De Civita M, et al. Factors associated with the use of complementary and alternative medicine in juvenile idiopathic arthritis. *Arthritis Rheum* 2004;51:527-32.
4. Zebracki K, Holzman K, Bitter KJ, Feehan K, Miller ML. Brief report: use of complementary and alternative medicine and psychological functioning in Latino children with juvenile idiopathic arthritis or arthralgia. *J Pediatr Psychol* 2007;32:1006-10.
5. Rouster-Stevens K, Nageswaran S, Arcury TA, Kemper KJ. How do parents of children with juvenile idiopathic arthritis (JIA) perceive their therapies? *BMC Complement Altern Med* 2008;8:25.
6. Field T, Hernandez-Reif M, Seligman S, et al. Juvenile rheumatoid arthritis: benefits from massage therapy. *J Pediatr Psychol* 1997;22:607-17.
7. Lovell DJ, Glass D, Ranz J, et al. A randomized controlled trial of calcium supplementation to increase bone mineral density in children with juvenile rheumatoid arthritis. *Arthritis Rheum* 2006;54:2235-42.

8. Giannini EH, Lovell D, Felson DT, Goldsmith CH. Preliminary definition of improvement in juvenile arthritis. *Arthritis Rheum* 1997;40:1202-9.
9. Duffy C, Arsenault L, Watanabe Duffy K, Paquin J, Strawczynski H. Relative sensitivity to change of the Juvenile Arthritis Quality of Life Questionnaire on sequential followup [abstract]. *Arthritis Rheum* 1995;Suppl 38:S178.
10. Duffy C, Arsenault L, Watanabe Duffy K, Paquin J, Strawczynski H. Validity and sensitivity to change of the Juvenile Arthritis Quality of Life Questionnaire (JAQQ) [abstract]. *Arthritis Rheum* 1993;Suppl 36:S144.
11. Duffy CM, Arsenault L, Duffy KN, Paquin JD, Strawczynski H. The Juvenile Arthritis Quality of Life Questionnaire — development of a new responsive index for juvenile rheumatoid arthritis and juvenile spondyloarthritis. *J Rheumatol* 1997;24:738-46.
12. Toupin April K, Ehrmann Feldman D, Platt RW, Duffy CM. Comparison between children with juvenile idiopathic arthritis (JIA) and their parents concerning perceived quality of life. *Qual Life Res* 2006;15:655-61.
13. Bruce B, Fries JF. The Stanford Health Assessment Questionnaire: dimensions and practical applications. *Health Qual Life Outcomes* 2003;1:20.
14. Singh G, Athreya B, Fries J, Goldsmith D. Measurement of health status in children with juvenile rheumatoid arthritis. *Arthritis Rheum* 1994;37:1761-9.
15. Singh G, Athreya B, Fries J, Goldsmith D, Ostrov B. Measurement of functional status in juvenile rheumatoid arthritis [abstract]. *Arthritis Rheum* 1990;Suppl 33:S15.
16. Pouchot J, Ruperto N, Lemelle I, et al. The French version of the Childhood Health Assessment Questionnaire (CHAQ) and the Child Health Questionnaire (CHQ). *Clin Exp Rheumatol* 2001;19 Suppl 23:S60-S65.
17. Pediatric Rheumatology Collaborative Study Group. Methodology for studies of children with juvenile rheumatoid arthritis. *J Rheumatol* 1982;9:107-55.
18. De Civita M, Dobkin P, Feldman D, Karp I, Duffy C. Development and preliminary reproducibility and validity of the Parent Adherence Report Questionnaire: A measure of adherence in juvenile idiopathic arthritis. *J Clin Psychol Med Settings* 2005;12:1-12.
19. Lempers JD, Clark-Lempers DS, Simons RL. Economic hardship, parenting and distress in adolescence. *Child Dev* 1989;60:25-39.
20. Clark-Lempers DS, Lempers JD, Netusil AJ. Family financial stress, parental support, and young adolescents' academic achievement and depressive symptoms. *J Early Adolesc* 1990;10:21-36.
21. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics* 1986;42:121-30.
22. Rosenberg AM. Treatment of juvenile rheumatoid arthritis: approach to patients who fail standard therapy. *J Rheumatol* 1996;23:1652-6.
23. Toupin April K, Ehrmann Feldman D, Zunzunegui M, Duffy CM. Association between perceived treatment adherence and health-related quality of life in children with juvenile idiopathic arthritis: perspectives of both parents and children. *Patient Pref Adher* 2008;2:1-8.
24. Spigelblatt L, Laine-Ammara G, Pless IB, Guyver A. The use of alternative medicine by children. *Pediatrics* 1994;94(6 Pt 1):811-4.
25. Davis MP, Darden PM. Use of complementary and alternative medicine by children in the United States. *Arch Pediatr Adolesc Med* 2003;157:393-6.
26. Toupin April K, Ehrmann Feldman D, Zunzunegui MV, Descarreaux M, Malleson P, Duffy CM. Longitudinal analysis of complementary and alternative health care use in children with juvenile idiopathic arthritis. *Compl Ther Med* 2009;17:208-15.
27. Cohen MH, Kemper KJ. Complementary therapies in pediatrics: a legal perspective. *Pediatrics* 2005;115:774-80.
28. Thomas KJ, Carr J, Westlake L, Williams BT. Use of non-orthodox and conventional health care in Great Britain. *BMJ* 1991;302:207-10.
29. Ernst E, Willoughby M, Weihmayr T. Nine possible reasons for choosing complementary medicine. *Perfusion* 1995;8:356-9.