Chapter 9

General Discussion

Wineke Armbrust
GENERAL DISCUSSION

Introduction

The prognosis of juvenile idiopathic arthritis (JIA) has improved, especially since the introduction of corticosteroids and disease modifying anti-rheumatic drugs (DMARD’s) as Methotrexate, and biologicals. Such therapies have induced remission in a substantial number of patients, with a much better prognosis and less long-term damage (1-4). Current treatment regimens aim to reach prompt remission in the first year of the disease, since it is assumed that this strategy will improve outcome (5-7). This implies that early treatment with (biological) DMARDs are advocated (8), resulting in an inactive state of the disease in the first year of specialized care for a majority of newly diagnosed patients (9). How these more aggressive treatment regimens will affect long-term outcome regarding disease activity and damage is not yet known, even as it is unclear how patient-reported outcome will be affected by these new strategies.

Patient-reported outcome measures (PROM) are important tools in assessing how patients perceive their psychosocial situation and physical health as a result of the disease itself, combined with the treatment. Data from PROMs has taught us that patients with JIA suffer from pain (10-12), fatigue (13-16) and they feel disabled (17), regardless of the disease status. Other negative outcomes are that patients are less physically active and have lower exercise capacity, independent from disease activity (18-20). For a chronic and unpredictable disease like JIA, the resilience of patients and parents is essential in order to adjust in a physical and mental way to a period of active disease, and to regain normal levels of physical and psychosocial functioning after remission has been reached (21). The role of resilience in the adaptation of parents after a serious illness of their child has been studied (22); however, we do not know the factors that contribute to a successful adjustment to JIA. Also not known is which underlying mechanisms are responsible for the way patients experience their disease, perceive their health, and to what extent they are capable of remaining physically and socially active, and satisfied in periods of active disease as well as in periods of remission. Insight into these mechanisms can teach us more about the psychosocial outcome of patients with JIA. Especially so, because we know that patients’ perceived health and the possibility of deploying a physically active life are not correlated with disease severity; it is important then to discover what other factors contribute to a negative outcome regarding these factors. By understanding underlying mechanisms, interventions can be developed in order improve psychosocial outcome. Insights can be gained by using PROMs in addition to disease activity scores.

AIMS OF THIS THESIS

The focus of this thesis was to report on patient-reported outcome and resilience. This was studied by looking at self-perceived health in children, evaluating socioeconomic outcome, romantic and sexual functioning in young people, and examining fatigue and promotion of physical activity.
1. Disease assessment by patients and their parents compared to that of the physician

One-hundred-and-thirteen patients with longstanding JIA assessed their disease activity higher than their physicians did (Chapter two); arthritis was rarely ever missed by patients, but many evaluated their medical situation as worse than their physicians did. These findings mean that some patients and parents are under the assumption that the disease is active, while some patients are in temporary or longstanding remission. They lack the capacity to overcome a period of illness and to feel that they have recovered, with all the possible consequences that entails on a physical and emotional level. Patients with resilience are thought to be capable of adjusting to an unpredictable disease like JIA living a more sheltered life.

We found that patients who indicated active disease and those who expressed doubt about the disease activity both had high pain scores and experienced functional impairment in executing their daily activities. An important outcome of this study was that the level of pain and or functional impairment was not related to the physician’s assessment of disease activity (Chapter two). In studies on adult patients with rheumatoid arthritis (RA), increased pain as indicated by the patient caused a worsening of the correlation of doctors and patients scores on disease activity (23,24). On the other hand, an increased number of swollen joints caused a much higher physician score (23). So patients and doctors score disease activity differently; patients focus more on pain and disability, while physicians focus more on swelling. Physicians are aware that, in general, pain and disability are not associated with disease activity and severity, but can be explained by pathophysiological and psycho-emotional factors, and do not include this in the assessment of inflammation in joints (11,12,15,25–29). Patients experience pain for a reason that has not totally been revealed yet, but probably disappointment, fear, and the feeling of being different all contribute to the perception of pain (11,15,28,29). In adults with RA, the concept of catastrophizing seems a critical variable in relation to pain (30). Catastrophizing comprises enlargement of pain-related symptoms, worrying about pain, feelings of helplessness, and pessimism about outcomes related to pain. Catastrophizing conflicts with self-efficacy, the feeling that a person can control the course of the condition. In JIA, catastrophizing has not been studied; it is known that higher self-efficacy results in lower pain, indicating that patients believe they can overcome the negative consequences of JIA, and so they possess the ability to adjust to the disease (31).

Assessing active disease (i.e., disease with joint swelling) is needed in order to initiate anti-inflammatory therapy promptly, but it is at least as important to ascertain a state of inactive disease in order to achieve optimal mental and physical functioning. Here agreement between patients, parents, and the physician as to the evaluation of the disease activity is crucial. When a patient thinks his/her disease is inactive, he/she will be relieved, since most adolescents indicate they do not want to be different from their healthy peers (32). The thought that the disease is under control could also stimulate physical activity, which is important, because patients with JIA have an inactive lifestyle and lower exercise capacity (19,20,33). Since we found that patients relate pain and disability to their opinion of the disease being active, interventions must be designed to teach patients how to interpret physical symptoms of their disease.
2. Relationships and sexuality, and satisfaction about these, body image, body dissociation, socioeconomic outcomes, and their interrelations in young people with JIA

Having a chronic condition that is accompanied by physical restraints is likely to affect socioeconomic outcomes. We therefore studied education levels, employment, and income. We found that young people with JIA (n=33, age 18-28 years) had lower income compared to controls, despite a similar level of education and employment level (Chapter three). These results had been found previously, and higher unemployment levels were also found in one study (34–37). A reason for the significantly lower income, as found in this study, might be that the patients work part-time. Patients with JIA suffer from impaired physical capacity, pain, or fatigue (38–40). It is known that exercise capacity (19) and muscle strength, which are needed to sustain a physical workload (41), are decreased in adolescents with JIA. These consequences of JIA could also favor the choice of a job with less physical and mental burden, for which wages are usually lower. We did not ask whether patients had jobs at their educational level or below, or whether they worked part-time. Further studies should aim to study the mental and physical capacities of adolescents in relation to vocational choice in order to find suitable studies and future employment. Close collaboration between schools and healthcare providers is needed to assist patients in finding a suitable job.

We assumed that a chronic relapsing disease like JIA, accompanied with pain, fatigue, and disability, would affect (sexual) relationships and body image negatively. However, young people with JIA had an equal relationship status and indicated that they were as satisfied with their relationships as the controls were. This finding is important, because the more satisfied healthy people are with their relationship status, the more satisfied they are with their lives, and the less distress they experience (42). Chronic diseases can affect relationship status negatively, depending on the stage of life (43). We assume that suffering from JIA before entering into a relationship will lead to a deliberate choice on the part of the patient and his/her partner; finding a partner who accepts all the possible consequences of the disease might lead to relationship satisfaction. Our finding that young people with JIA had similar sexual experiences, and were as satisfied with their sexual status as healthy controls, has also been found in previous studies (35,44). It appears that patients with an unpredictable chronic disease like JIA are not dissuaded from entering into sexual relationships. Follow-up studies are needed in order to evaluate whether these positive findings are retained. In a family with young children, physical strain is higher, which can lead to relational stress in cases where one parent is less physically capable.

We did not find any negative consequences for patients’ body image or awareness of their bodily sensations as compared to healthy controls. A previous study showed a lower body image in adult patients with rheumatoid arthritis (45). In this study, many patients were treated according to older treatment regimens, resulting in visible growth disturbances and physical limitations (46), which might have resulted in lower body image. Apparently a disease like JIA, which has hardly any effect on appearance but does result in feeling different (47), does not hamper body image.
We found that body image was strongly negatively related to body dissociation, indicating that a more negative view of the body is linked to more avoidance of physical sensations and vice versa. In controls, this correlation was weaker. For patients with JIA, a more positive body image was moderately related to greater sexual satisfaction and relationship status satisfaction, while body dissociation was negatively related to their sexual and relationship status satisfaction. The more positively they viewed their body, the greater sexual satisfaction they reported, and the more satisfied they were with being single or partnered. Surprisingly, these associations were not found among controls (Chapter three). These findings indicate that a number of young people with JIA are at risk for negative outcomes regarding body issues, and sexual and relationship satisfaction. In general, a negative body image is associated with depressive symptoms, social anxiety, low self-esteem, and all forms of less optimal self-care (48). It might be that, in a person at risk for impaired body image, and relational and sexual dissatisfaction, having JIA is crucial in determining a negative outcome vis-à-vis these issues. So it is important to identify those persons who lack the capability of feeling good about their bodies and thereby deploying satisfactory relationships, sexual or otherwise, while having a chronic disease like JIA.

3. Fatigue in patients with JIA

Fatigue is a major problem in patients with JIA. In Chapter four, we performed a systematic review showing that fatigue was present in 60-79% of the patients with JIA on 79% of the days. In these patients, fatigue was associated with pain, disease activity, Health-related Quality of Life (HRQoL), sleep disturbances, mood, medication, and stress. Pain was the strongest correlate of fatigue. Disease activity showed only a moderate correlation with fatigue (Chapter four). Fatigue exerted a negative influence on psychosocial health, although it did not affect school attendance. This means that factors other than inflammation contribute to a negative patient-reported outcome, which indicates an approach other than medication.

To assess fatigue, physicians can choose between multidimensional and unidimensional measurements. Multidimensional measurements assess physical, cognitive, and psychosocial dimensions of fatigue in contrast to unidimensional measurements such as the Visual Analogue Scale (VAS) that measure the intensity or frequency of fatigue (49,50). The advantages of multidimensional scales are that they teach us about the different dimensions of fatigue (49,50), which have special interest when predictors and consequences of fatigue are studied (Chapter five). But multidimensional measurements are more time consuming, and their use in an individual patient is not appropriate (49,50). Unidimensional scales like a VAS are easier to assess and can be used in order to study frequency and severity. Unidimensional scales are less suitable for studying underlying mechanisms of fatigue.

In a cross-sectional study on fatigue in 80 patients with JIA, age 8-13, we found that fatigue was present on all days in 60% of the patients (Chapter five), which is similar to previous studies (Chapter four). Few studies exist that compare fatigue of patients with JIA with healthy controls or with other chronic conditions. Data on fatigue in healthy children vary greatly; a postal survey showed a prevalence of severe fatigue of 62/100,000 children
aged 5-19 years (51), whereas a study among adolescents, mean age 14.1 years, showed a prevalence of severe fatigue of 20% in girls and of 9.5% in boys (52). To understand more about fatigue in patients with JIA, it is necessary to study why fatigue is present in JIA and whether it is caused by factors that also contribute to fatigue in healthy children, like puberty.

Based on the results of our study concerning perceived health, physical health, and participation in school and sports, we conclude that a portion of patients perceive negative health consequences from JIA. They suffer from fatigue and pain, and they experience impaired functional ability and believe that the disease is active while it is not. All these perceptions seem to be correlated with each other. It is not known why some patients perceive their health as impaired and feel severely restricted in their functioning, while others feel identical to healthy peers, despite the same disease severity. For the outcome, both short- and long-term, it is important to reveal which patients are at risk for impaired perceived health, and what the reasons for this might be. We found that high self-efficacy was related to low fatigue (Chapter five). Self-efficacy might be a factor that contributes to a patient’s resilience in terms of adjusting to the disease, including its negative symptoms and unpredictable course. Self-efficacy is best assessed within a consideration of contextual factors in order to ascertain whether it plays a moderating, mediating, or other kind of role in the behavior of a person (53). The role of self-efficacy was established as a factor for predicting pain in patients with JIA (31); however, the role of self-efficacy in the perception of other disease-related factors, including fatigue, was not studied (54). Promoting self-efficacy in adolescents is important for the enhancement of skills, relationships, responsibility, and sense of belonging (53). Self-efficacy should be a target in the coaching of patients to deal with the negative consequences of JIA. This should also be part of the care provided in transition clinics where patients care move from pediatric to adult departments.

4. Promoting physical activity in patients with JIA

Patients with JIA are less physically active compared to healthy controls despite the long- and short-term positive effects of PA on physical and mental health (55–60). PA is therefore an important patient-reported outcome measurement.

We compared PA in patients with JIA, measured using the activity diary (AD), to PA measured, using an accelerometer (Actical). Results showed that the AD assessed higher PA levels compared to the Actical (Chapter six), which is in line with results found in other studies (61-63). This discrepancy is caused by overrating of duration and intensity by children when using an AD, by technical issues of the Actical, and because of non-wearing of the device (64-67). For reliable results, assessment of 6-13 days with an AD and 5-7 with an Actical are needed (Chapter six).

For current practice, to evaluate PA in patients, the accelerometer is preferred as an objective measurement. Adjustment for non-wearing should be considered by complementing non-wearing time with data from the AD (Chapter six). In our opinion, an AD can be used in the context of teaching the patient about PA. Filling in a diary, indicating the intensity and duration of certain activities, can give patients insights about their daily
PA (Chapter seven). However, the imprecision of both the accelerometer as well as the diary should be kept in mind when measuring PA.

To promote PA in patients with JIA aged 8-13 years, we developed Rheumates@work (R@W), an interactive, cognitive behavioral and educational program. R@W, whose design is based on Pender’s Health Promotion model, takes 14 weeks and is delivered by Internet, combined with four group-sessions (Chapter seven). The basic concept of this health promotion model consists of the idea that, by enhancing self-efficacy and thereby self-management strategies, barriers can be overcome, whereupon a person can profit from the benefits of the newly learned behavior (68,69).

Patients and parents rated R@W as good and valuable, and the commitment was high (Chapter seven). This level of commitment was high compared to other Internet-based interventions and might have been caused by selection bias (70,71). Only 27% of eligible patients were willing to participate, which is lower than other Internet-based interventions (70,71), indicating that the actual participants were strongly motivated to participate. It is remarkable that so few patients were willing to participate in light of the burden of the disease and the need for supportive care that was expressed by adolescents in previous studies (32,72). A possible explanation is that our target group was younger compared to the adolescents in the other studies where they voiced their needs. The willingness to participate in R@W could be a parent’s decision rather than a patient choice. A future challenge for intervention studies would be to reach younger patients, since an early attempt to change behavior might lead to a better outcome (69). For this, a common goal should be set between parents and patients, on the one hand, and physicians, on the other, not only aimed at improving PA but also at other psychosocial outcome measures, and at a joint decision.

Results of the intervention study R@W showed that PA parameters (measured with the AD) and exercise capacity improved significantly, and were clinically relevant in the intervention group (Chapter eight). However results should be interpreted with caution while the differences between the intervention and controls did not reach significance. The effect of the intervention improved further in the three months after finishing the intervention (in the intervention group), at which point it decreased slightly (Chapter eight). We found that participants starting in winter (winter group) improved significantly more as compared to those who started in the summer (summer group). School attendance also improved significantly, while an effect from R@W on HRQoL was not noted.

What can be learned from these results? First, PA can be seen as a type of behavior, and, in general, it is hard to exert influence in favor of PA in sedentary children (73-76). The ongoing improvement after three months might imply that time is essential in order to induce a behavioral change and that a refresher is needed to maintain the behavioral habits. It would be interesting to retest these participants after one year, again to find out whether the higher PA levels were preserved. Second, the seasonal effect that we found suggests that a program aimed at improving PA should start in the winter to gain maximum benefit. PA is higher in summer; participants who began in winter were bolstered in their effort to improve after finishing R@W in summer; natural seasonal effects might have resulted in long-term consolidation of the improvement from PA outcome measures. It is known that positive experiences in changing behavior are of
major importance in cognitive behavioral theory and self-efficacy strategies (40). Finally, patients indicated that they had appreciated receiving more explicit exercise assignments (78). General recommendations for stimulating PA in daily life, as were given in R@W, might have been too abstract. We suggest including exercise-training elements in a cognitive behavioral program like R@W. This supplement to a program like R@W might also help to overcome the seasonal influence on PA, since exercise devices can be used at home and during the winter (43).

Limitations of these studies
A limitation of our study is the small sample size, which is inherent due to the rarity of a disease like JIA. Furthermore, the low participation grade, as was present in our studies, might have led to a selection bias. Results of R@W should be interpreted with some caution; we found that PA needs to be assessed for 6 to 13 days (Chapter six), and we measured only 7 days.

FUTURE PERSPECTIVES: FROM MEASURING TO IMPROVING PATIENT-REPORTED OUTCOME

Measuring patient-reported outcome
For the purpose of tailor-made treatment regimens, finding biomarkers that predict disease course and medical outcome is crucial. However, it is equally important to recognize those patients who are at risk for impaired patient-reported outcome regarding psychosocial and perceived physical health in order to be able to intervene in an undesirable outcome.

To improve the knowledge about patient-reported outcome, standardized measurements are essential and need to be included in routinely monitoring a patient with JIA in addition to the usual assessment of disease activity (80-82). Ideally, pediatric rheumatologists organized in the PRINTO (Paediatric Rheumatology INternational Trials Organization) and CARRA (Childhood Arthritis & Rheumatology Alliance) should compile a uniform set of measurements that can be used worldwide after translation and validation in various languages. It will be a challenge to determine which instruments are most valid and at what frequency the PROMs should be ased.

In our opinion, these PROMs must satisfy certain requirements. These instruments need to: (1) be easy to apply regarding time expenditure and comprehension; (2) cover all domains that are possibly affected, namely physical (perceived disability, PA, exercise capacity), psychosocial well-being (fatigue, pain, HRQoL, and, from adolescence onwards, sexuality and body issues), participation (school attendance, sport and leisure participation, and, from adult age, occupation), and side effects of treatment and medication; (3) provide information about personal coping skills (self-efficacy, catastrophizing, anxiety, and depression); (4) be generic in comparing patients with JIA with healthy controls and or other chronic diseases; (5) provide a disease-specific section, (6) cover multi- and unidimensional elements; (7) discriminate between those patients
that are most at risk for impaired patient-reported outcome; and (8) evaluate patients’ and parents’ opinions about treatment regimens

How to improve patient-reported outcome?

Patients with chronic conditions make day-to-day decisions as to how to manage their disease; evidence is accumulating that self-management programs are effective in enhancing patient-reported outcome in this group, including in RA and JIA (70,83,84). Results of an Internet-based self-management program, combined with telephone support in adolescents with JIA, showed improvement for pain and knowledge, although no effect was seen for self-efficacy, adherence, HRQoL, and stress post-treatment (70). This program included knowledge, use of medication, symptom management, management of psychosocial consequences, social support, communication, and lifestyle changes. Other self-management programs for patients with JIA are sparse and usually only focus on one aspect of JIA (85).

How to improve self-management?

An accepted definition of self-management is that it refers to the ability of individuals to manage their symptoms, treatment, physical and psychosocial consequences, and lifestyle changes, inherent in living with a chronic condition (86). A central concept in self-management is self-efficacy; confidence in carrying out a behavior necessary to reach a desired goal (69,87). Self-efficacy is enhanced when patients succeed in patient-identified problems; failures will lower this (69). In our opinion patients with JIA, suffering from repeated flares, are at risk for failing self-efficacy strategies, thus leading to negative, catastrophizing thoughts. So, by teaching self-efficacy skills instead of allowing catastrophizing beliefs to overwhelm patients with JIA, patients might develop resilience in coping with the disease.

In patients with JIA, the need for self-management interventions has become clear (88). Patients with JIA expressed interest in e-Health interventions, and shared the urge for more information, self-management strategies, and meaningful social support to manage their disease better (72,89). Self-management could be an opportunity to bridge the gap between a patient’s needs and the treatment goals of healthcare providers, by introducing a patient-professional partnership that involves collaborative care. However, bridging the gap is only possible when a patient’s need for self-managements skills corresponds with the vision of the physician regarding which components self-managements strategies should contain. JIA affects both physical and psychosocial domains, so self-management programs should, in any case, comprise a holistic approach (86). Adolescents with JIA indicate the need for gaining control in managing their illness on their own by gathering information, learning skills to manage the disease, communicating with the doctor, and managing pain and emotions (72). As far as we know, physicians’ opinion regarding the necessary content of self-management program for patients with JIA has not yet been studied. But it is most likely that physicians would include adherence, self-assessment of disease activity, management of disease-related symptoms such as pain and fatigue, and, above all, lifestyle recommendations regarding enhancing PA. The question is whether the priorities of the doctor will correspond to those of the patient,
and, in the case of younger children, with those of the parents. The challenge is to develop self-management programs with a combination of tools addressing the patient’s needs, along with those tools aimed at improving physical outcome as scheduled by the physician in a joint decision. A detailed proposal of such a program for self-management program is proposed in the final paragraph.

**An example of a self-management program for patients with JIA.**

A self-management toolbox (Figure 1) that includes a variety of tools, from which the patient as well as the physician can choose 2 or more items regarding his or her priority at that moment. On every item an e-learning program with assignments, a quiz, and, at the end, a reward upon finishing the module is available. Every e-learning module covers 8 weeks, which is a short time to change behavior. However, while every module contains overlapping issues, iteration will ensure behavioral change and short courses will enhance compliance. E-learning modules are combined with group meetings; this appeared to improve success by means of peer support and adherence. Group meetings are organized two times a year for patients and their parents. These meetings contain education on patient-reported outcome, strategies that can improve this outcome, peer support, and joint activities.

![Toolbox with subjects for self-management interventions](image)

**Figure 1: Toolbox with subjects for self-management interventions**

**Procedure (Figure 2)**

First patients and physicians identify targets for a self-management program, for example, managing fatigue (red phase). Since it is known that fatigue is associated with more negative outcomes, the second step is to identify correlates and consequences of fatigue, which apply to an individual person (check boxes in the green phase). Thereafter, in the third step, goals are set; enhancing self-efficacy strategies and decreasing
catastrophizing are obligatory goals. Patients can set 2-4 more goals for the program (blue phase). Fourth, the self-management program takes place (yellow phase). Patients go through courses with weekly education, assignments, and feedback on these. When needed, goals are adjusted to be sure that patients have a successful experience. Finally, an evaluation takes place, where patients are rewarded and plans are made as to how to hold on to the gains made. Patients are encouraged to join another course in order to maintain their behavioral change.

Figure 2. Schematic representation of a self-management program.
References


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