Disease activity and dropout in young persons with juvenile idiopathic arthritis in transition of care: a longitudinal observational study

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Abstract

Objective

Reaching a certain age, juvenile idiopathic arthritis (JIA) patients in paediatric care are transferred to adult care. An increased disease activity after transfer and increased dropout has been suggested, however, evidence is scarce. Our aim is to determine whether the process of transition is associated with increased disease-activity and dropout, and to identify associated factors.

Methods

During a 3-year prospective transition cohort study, paediatric patients (14–17yrs) were transferred to adult care. Paediatric (10–13yrs) and adult JIA patients (18–27yrs) were used as control groups. Demographic and disease-related items were obtained yearly. Non-parametric tests were used to compare differences between the groups and mixed models to evaluate disease activity over time, measured by JADAS27 and DAS28. Dropout was defined as not attending the clinic for 2 consecutive visits.

Results

Groups did not differ regarding baseline variables of subtype, gender, uveitis, ANA-, RF- or HLA B27-positivity and current or past DMARD use. Median disease activity was not different between groups during follow-up. Transfer was not associated with disease activity. Dropout rate was 12%, and was significantly higher in patients under transition (22%) compared with paediatric (3%) and adult care (10%). Patients who dropped out had significantly lower disease activity at baseline and were using less MTX, but did not differ regarding subtype, ANA, RF and HLA-B27.

Conclusion

The process of transition in JIA is not associated with an increase in disease activity, however, this period carries a risk for dropout especially in patients with low disease activity.

Key words

adolescents, juvenile idiopathic arthritis, transition, disease activity, dropout, DMARD

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Introduction

When children with chronic diseases reach adulthood, transition to adult health care is common practice. Transition is defined as 'the purposeful, planned movement of adolescents and young adults with special health care needs from child-centered to adult-oriented health care systems' (1).

Several barriers to successful transition have been described, which can be patient-related, parent-related or process-related. Patient-related barriers are poor adherence, inadequate self-advocacy skills or a reluctance to leave services with known and trusted staff (2, 3). Another barrier may be that parents are not always capable of releasing control when their adolescent child is transferred (2). An essential procedure-related barrier is the transfer of a complete medical record (4). In addition, paediatric care providers can have, like parents, difficulties in releasing their patients. Inadequate preparation of patients and parents by paediatric services may lead to inadequate self-management (5). Growing insight reveals that adult care-providers require specific skills and knowledge in adolescent medicine (6). When ignored, this may result in poor satisfaction of the adolescent with the new treatment team (5, 7, 8). All these barriers may lead to increased disease activity or undesirable dropout (8). Indeed, studies evaluating adult outcomes of patients with juvenile rheumatic diseases after transitional process describe increased disease activity and discontinuation of care in more than half of the patients (9, 10). For that reason, changes in disease activity has been proposed as one of the quality indicators in the EULAR guidelines for transitional care (11). However, studies describing longitudinal disease activity during transition in juvenile idiopathic arthritis (JIA) patients are scarce and mainly retrospective (10). We therefore set up a prospective transition cohort study in JIA patients who were to be transferred to adult care during the observational period. Our aim was to determine whether the process of transition is associated with increased disease activity and dropout. And if this is the case, to identify factors associated with increased disease activity and dropout during transition.

Patients and methods

Study design and patient selection

We conducted a prospective observational three-year follow-up cohort study. All consecutive patients between 2005 and 2008 with JIA (classified by the International League Against Rheumatism criteria ILAR) (12), in the age of 10–27 years were asked to participate. According to local protocols, aiming for a transparent, transferable and positive labelled transition, paediatric patients are transferred between the age of 16 to 18 years to adult care. Patients, aged 14–17 years at study onset were transferred at some point during the three-year follow-up from the paediatric to the adult clinic (transition group). Patients in the age range of 10–13 years at study-onset were treated at the paediatric clinic only (paediatric group) and JIA-patients in the age of 18–27 years were treated at the adult clinic (adult group) only. These paediatric and adult care groups were used as control groups. Patients were included and followed at the out-patient clinics of the paediatric or adult departments of Immunology & Rheumatology at the University Medical Center (UMC) Utrecht, as appropriate. If patients had to be seen at another hospital, clinical assessment and disease activity parameters were obtained from the attending paediatric or adult rheumatologist. All patients first seen before the publication of the ILAR criteria for JIA were reclassified using these criteria. A total of 176 patients gave informed consent. Medical ethics committee of the UMC Utrecht approved all study procedures.

Clinical assessment

At baseline, demographic and disease-related variables were determined. JIA was divided into 4 subtypes: systemic disease, oligopersistent disease, polyarticular course disease and other subtypes.

Joint assessment (number and location of swollen, tender and active joints), physician's global assessment (range 0–10), patient's global assessment (range 0–100) and erythrocyte sedimen-

Table I. Demographic and disease specific variables at baseline of the study of the three patient groups.

% (n) OR median (IQR)	Paediatric care n=63	Transition n=64	Adult care n=49	*p*-value
Patients (%)	36% 36%	28% 0,46		
Age (years)	11.6 (1.4)	15.6 (2.2)	20.8 (4.2)	<0.01*
Female gender	60% (38)	69% (44)	71% (35)	0.42
JIA subtype				0.47
Systemic	6% (4)	13% (8)	22% (11)	
Oligoarthritis	32% (20)	17% (11)	25% (12)	
Polyarthritis	56% (35)	58% (37)	45% (22)	
ERA and PsA	6% (4)	13% (8)	8% (4)	
ANA+ (n =172)	63% (38)	58% (37)	49% (23)	0.38
RF+ (n=163)	5% (3)	11% (6)	17% (8)	0.12
HLA B27 (n=78)	17% (4)	25% (9)	47% (9)	0.08
Uveitis	19% (12)	9% (6)	14% (6)	0.27
Disease duration (years)	5.8 (6.0)	8.7 (9.1)	11.8 (8.1)	<0.01*
DMARD in history				
MTX	79% (50)	86% (55)	67% (33)	0.06
Biologicals	8% (5)	19% (12)	18% (9)	0.16
Glucocorticoids	18% (11)	27% (17)	31% (15)	0.24
Current DMARD				
MTX	64% (40)	64% (41)	53% (26)	0.43
Biologicals	8% (5)	16% (10)	12% (6)	0.41
Glucocorticoids	8% (5)	3% (2)	2% (1)	0.26
Disease activity[#]				
JADAS27	3.6 (5.6)	3.9 (7.6)	4.6 (7.8)	0.88
DAS28	2.1 (1.0)	2.2 (1.5)	2.3 (1.6)	0.30

[#]Disease activity scores were available in 48 patients in the transition group, in 50 patients in the paediatric group and in 30 patients in the adult group. Differences are calculated between the three patient groups. *Significant at a *p*-level of <0.05.

tation rate (ESR) were recorded. An active joint was defined as either a swollen joint or a joint with loss of range of motion with joint pain or tenderness (13). Disease activity was measured with paediatric (JADAS27 (14)) as well as with an adult assessment tool (DAS28 (15)) at both treatment locations. Juvenile Arthritis Disease Activity Score (JADAS) is composed of the physician global assessment of disease activity, measured on a 10-cm visual analogue scale (VAS) where 0 is no activity and 10 is maximum activity; patient global assessment of well-being, measured on a 10-cm VAS where 0 is very well and 10 is very poor; count of joints with active disease; and erythrocyte sedimentation rate (ESR). JADAS27 includes the following joints: cervical spine, elbows, wrists, metacarpophalangeal joints (from first to third), proximal interphalangeal joints, hips, knees, and ankles (14). Disease activity score is a weighed compound score of the total number of a selected group of swollen and painful or tender joints (both range 0–28), assessment of patient's global assessment (range 0–100) and the erythrocyte sedimentation rate (ESR). DAS28 includes the joints shoulders, elbows, wrists, MCP 1–5, PIP 1–5 and knees (15). Disease activity and use of current DMARD medication were recorded annually.

Transition and dropout

The process of transition, which starts approximately one year before and ends one year after transfer, was coordinated by our transition-coordinator. This specialist rheumatology-nurse is responsible for process-related items during transition, *e.g.* monitoring appointments at adult care, and counselling of patients and parents, including enhancing self-management. Within our hospital, all care providers, including paediatric and adult rheumatologists, are allowed to read all parts of the electronic patient file of other departments, when a patient comes under their care. Patients in the transition group should have at least one appointment at the paediatric and one at the adult department during the observational period. Visit number was recoded as time-point to transfer. The last visit before transfer is recoded as minus one, the first visit after as plus one. Actual transfer is between these two visits. For patients in transition, visit number is varying from minus three to plus three, in paediatric patients from minus four to minus one, in adults from plus one to plus four. Dropout was defined as not attending the clinic at 2 consecutive visits.

Statistical analysis

Demographic and clinical data of the transition, paediatric and adult groups were presented as medians and interquartile range (IQR) as data were not normally distributed. Differences between the groups were tested using non-parametric tests (chi square, Mann-Whitney and Kruskal-Wallis where appropriate). Median disease activity, measured by JADAS27 and DAS28 was calculated at each time point during follow-up and stratified for each patient group. Results are presented as boxplots. Within the transition group, median disease activity at the time points before and after transition were compared using the paired Mann-Whitney test. To answer the question whether the course of disease activity over time varies in relation to transition, repeated measurement analysis was done with DAS28 as dependent and time-point to transfer as independent variable. In a second multivariate model, potentially confounders gender, disease subtype, use of MTX and biologicals as well as the patient groups were added to the model. Since DAS28 was not normally distributed, the Blom-transformation was used. Similar analysis with JADAS27 as an dependent variable were performed. JADAS27 could not be entered as continuous variable as it could not be normalised, therefore linear mixed model analysis was performed with JADAS as a dichotomised variable, remission yes or no (JADAS27 ≤1.0 *vs.* >1.0). Calculations were based on observed data and no imputation of missing data was performed.

Since dropout rate was 22% in the transition group, additional sensitivity

analyses were performed assuming the worst case scenario (all dropouts had active disease; JADAS27 >1.0) and a best case scenario (all dropouts were in JADAS27-remission; JADAS27 ≤1.0). Demographic and clinical data of patients continuing in care and those who dropped out were presented as medians (IQR) as data were not normally distributed. Differences were tested using non-parametric tests. Subsequently, multilevel logistic regression analysis was performed to evaluate the strongest association with dropout, entering those covariates with a $p<0.20$.

All statistical tests were 2-sided with a p-value less than 0.05 considered statistically significant. SPSS software, v. 21.0 was used to manage and analyse data.

Results

In total, 215 patients were invited to participate, 39 patients were not included (not willing n=14, lack of time n=6, other diagnosis n=11, unable to read n=5, unknown=3). Baseline variables of 176 included patients are shown in Table I. During follow-up, 64 patients were transferred from paediatric to adult care. Patients were evenly distributed over the patient groups. As age was a selection criteria, expected significant differences in age and disease duration were seen. Other demographic variables as gender, JIA subtype, presence of ANA, RF and HLAB27, percentage of uveitis and DMARD use were not statistically different between the groups (Table I).

Disease activity

Disease activity during follow-up is shown in Figure 1. Although DAS28 showed a tendency to decrease, this was not seen in JADAS27 (Fig. 1). Longitudinal disease activity in the transition group was comparable to the paediatric and adult group (p=0.29 for DAS28; p=0.32 for JADAS27-remission).

Transfer was not associated with a change in disease activity, as DAS28 and JADAS27 one visit before and after transfer were not significantly different (median difference in JADAS27 is 0.20, IQR 9.43; p-value 0.57 and median difference in DAS28 is 0,11 IQR 3.43, p-value 0.63). The course of disease activity over time was not related to transition, as repeated measurement analysis for JADAS27-remission revealed an odds of 0.87 (95% CI 0.70–1.09; p=0.24) and for DAS28 an estimate -0.60 (SE 0.05; p=0.23). In addition, using a multivariate model, location of treatment (paediatric, transition or adult patient group) was also not associated with disease activity over time (JADAS27-remission odds-ratio 1.4, 95% CI 0.74–2.48, p=0.32; DAS28 estimate 0.09, SE 0.08, p=0.26; Supplementary Table I). Higher JADAS27 (no remission) was associated with MTX-use; DAS28 was associated with MTX-use, biological-use and female gender (results in Supplementary Table I). In additional sensitivity analyses results were similar for both worst and best scenarios; odds-ratio for JADAS27-remission for location of treatment changes from 0.32 to 0.28 in worst case and to 0.38 in best case scenario. JADAS27-remission was also associated with MTX-use in worst and best case scenario (Supplementary Table II).

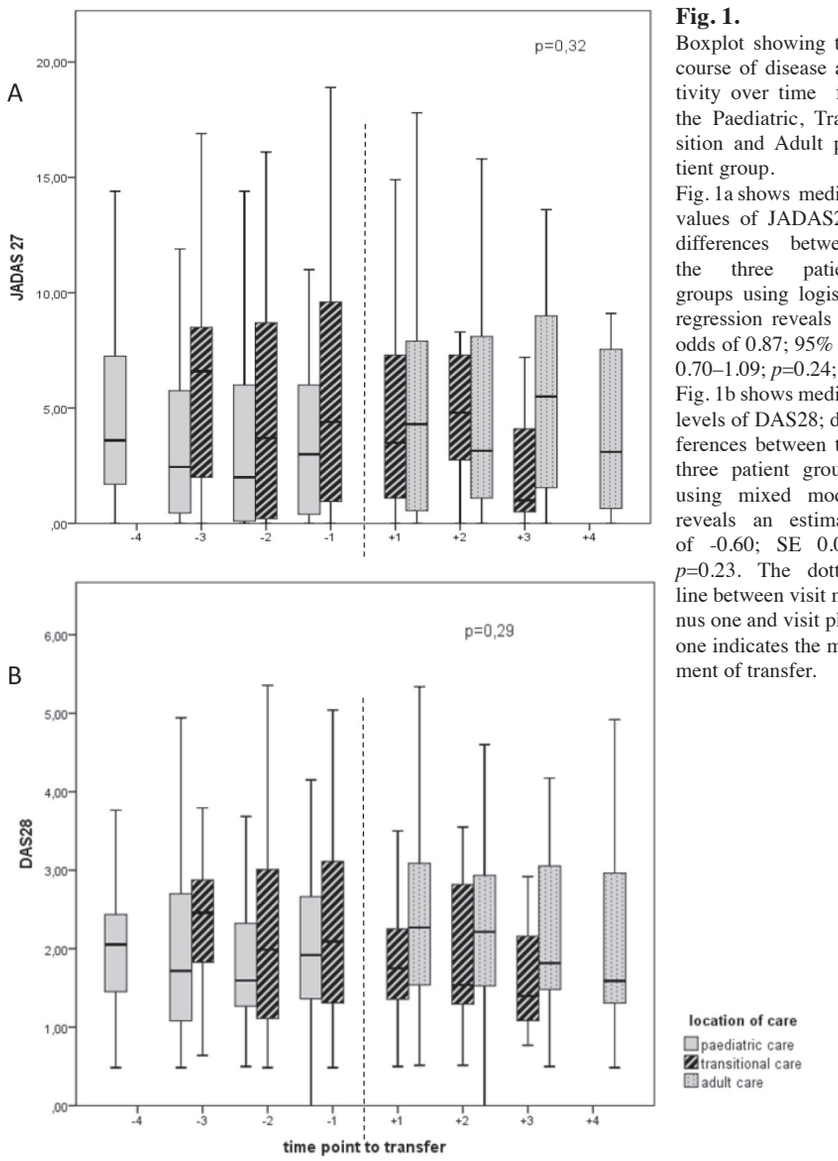

Fig. 1.
Boxplot showing the course of disease activity over time for the Paediatric, Transition and Adult patient group.
Fig. 1a shows median values of JADAS27; differences between the three patient groups using logistic regression reveals an odds of 0.87; 95% CI 0.70–1.09; p=0.24;
Fig. 1b shows median levels of DAS28; differences between the three patient groups using mixed model reveals an estimate of -0.60; SE 0.05; p=0.23. The dotted line between visit minus one and visit plus one indicates the moment of transfer.

Dropout

A significant higher number of patients were classified as dropout in the transition group (22%; n=14) compared to the paediatric (3%; n=2) and adult group (10%; n=5; p=0.01). Table II presents the differences between patients who continue outpatient care and those who dropout. Eleven out of 14 patients

Table II. Demographic and disease specific variables of patients continuing in care and those who dropped out.

Median (IQR)[1] OR % (n)	Dropout transition (n=14)	Continuous transition (n=50)	*p*-value	All patients, dropout (n=21)	All patients, continuous (n=155)	*p*-value
Female gender	65% (9)	70% (35)	0.75	64% (9)	70% (35)	0.75
Subtype JIA			0.89			0.49
Systemic	14% (2)	12% (6)		19% (4)	12% (19)	
Oligoarthritis[2]	21% (3)	16 (8)		33% (7)	23% (36)	
Polyarthritis[3]	57% (8)	58% (29)		43% (9)	55% (85)	
Other[4]	7% (1)	14% (7)		5% (1)	10% (15)	
ANA + % (n)	43% (6)	62% (31)	0.23	48% (10)	57% (88)	0.24
RF + % (n)	0% (0)	13% (6)	0.33	5% (1)	10% (16)	0.38
HLAB27+ % (n)	13% (1)	29% (8)	0.65	10% (2)	13% (20)	0.35
Disease activity baseline	n=10	n=40		n=15	n=114	
JADAS27	1.7 (5.0)	4.5 (7.1)	0.12	1.4 (5.0)	4.1 (6.6)	**0.02***
DAS 28	1.8 (1.0)	2.4 (1.5)	0.22	1.6 (1.1)	2.2 (1.7)	0.15
Disease activity last known	n=8	n=20		n=11	n=78	
JADAS27	1.8 (5.5)	3.3 (6.1)	P=0.64	1.8 (6.8)	3.2 (6.1)	0.49
DAS28	2.1 (1.3)	1.5 (0.9)	P=0.53	2.2 (1.2)	1.6 (1.5)	0.33
Baseline						
MTX	29% (4)	74% (37)	**<0.01***	33% (7)	65% (100)	**0.01***
Biologicals	21% (3)	14% (7)	0.68	14% (3)	12% (18)	0.47
Last known						
MTX	23% (3)	56% (24)	0.12	25% (5)	49% (67)	**0.03***
Biologicals	23% (3)	40% (17)	0.35	20% (4)	33% (45)	0.44

[1]IQR: interquartile range. [2]oligoarthritis: oligo-persistent subtype of JIA. [3]polyarthritis: Oligo-extended and polyarticular subtype of JIA. [4]other: enthesitis related and psoriatic arthritis related subtype of JIA. *Significant at a *p*-level of <0.05.

in the transition group dropped out before transfer (p=<0.01), associated with this dropout was a lower use of MTX at baseline (p<0.01). Dropout in all patients was significantly associated with lower use of MTX at baseline (33% *vs*. 65%; p=0.01)) and at last visit before dropout (25% *vs*. 49%; p=0.03) and lower JADAS27 at baseline (1.4 *vs*. 4,1; p=0.02), DAS28 was not associated (p=0.15). Gender, disease subtype, and autoimmune antibodies were not related to dropout. Multilevel analysis revealed no significant combinations of predictors for dropout.

Discussion

In contrast to what is currently suggested, we found in this longitudinal study of JIA-patients transferred from paediatric to adult health care, that the process of transition is not associated with increased disease activity. Disease activity over time is comparable to patients treated at either paediatric or adult clinics. However, transition is a risk factor for dropout, as frequency of dropout is significantly higher in patients in transition compared to paediatric and adult care.

The lack of association between transition and increased disease activity was not expected, as retrospective studies evaluating adult outcomes of JIA patients after transition describe increased disease activity (9, 10). In a prospective study regarding JIA patients before and after transition, equal disease activity is described. However, all included patients in that study used biologics at study entry, while in our study only 16% used biologics at baseline (Table I) (16).

Process related barriers to successful transition which may lead to higher disease activity (2, 3) are expected of low influence in our study due to the active role of the transition-coordinator and the use of a collective electronic patient file in our hospital. Whether the role of the transition-coordinator indeed affects disease activity, needs to be studied in a case-control study.

Overall, disease activity is low, probably due to intensive treatment. In line with literature, other variables associated with increased disease activity in our study were the use of MTX and biologics, as well as female gender (17, 18). Results are consistent across all three patient groups. Our hypothesis (a higher disease activity after transfer) is not confirmed. According to disease activity, patients, parents and paediatric health-care givers can be reassured of transferring the paediatric JIA patient to adult care.

Reported general factors associated with dropout in JIA are low disease activity and low DMARD use (10, 16), which is also shown in our population. However, some patients (23%) used MTX or a biologic agent at their last known visit before dropout. A complication for JIA patients without medication is a high risk of relapse (50%) within the first two years after remission (19-21). This underlines the importance of an intensified well structured transition process, as a higher dropout is seen in transitional care. A speculated cause for higher dropout is a reluctance to leave services with known and trusted staff (3). This hypothesis is confirmed by the timing of dropout, 79% of dropout in our cohort is before transfer. Other causes, not investigated but described elsewhere, might be inadequate self-management and social support, and age-related factors, so called "adolescence behaviour": patients are not willing of being confronted with the consequences of the disease (22).

Although frequency of dropout is higher in transitional care (22%), frequency is low compared to other studies describing dropout after transfer (52%) (10). Hazel used the definition for dropout as not attending the adult clinic for the first visit or lost to follow-up at two years following transfer, we used a different definition. Using the definition of Hazel, a dropout is seen in 14% in the first visit after transfer and a dropout of 24% after 2 years of transfer (results not shown). Our transition-coordinator might as well play a role in preventing dropout, as no shows are always followed by a phone call or email to the patient. Patients participating in our study are actively followed even when logistic reasons (movement to another region) has led to transfer to other hospitals in the country in 10% percent (n=17) of the patients. This active approach has probably also led to lower dropout compared to other transition studies. To confirm this hypothesis a case-control study is needed.

Our study has some limitations. Due to missing values of ESR and/or VAS (Table I, Fig. 1) it was not possible to construct a disease activity score from all visits. However, using the active joint count score (13) with a lower percentage of missing values (10%), similar results were obtained (results not shown). The use of mixed models had the advantage that patients with missing data on single time-points were retained in the analyses. Higher dropout rates in the transition group compared to the paediatric and adult group might lead to different conclusions. Additional sensitivity analyses assuming a best and worst case scenario for disease activity reveals the same results leading to same conclusions. Despite trying several transformations, JADAS27 was not normally distributed. We therefore used in repeated measurement analysis JADAS27 state-of-remission, which is less commonly used in daily practice. Another limitation is that disease activity was obtained from the attending physician, which implies in transitional care two (different) observers for the same patient. However, we expect that different observers have little impact on outcome as no differences over time were seen in transitional care and results were comparable to paediatric and adult care. Additionally, DMARD prescription is uniformly distributed to all three groups. To assess the impact of transition on disease activity in the long term, a longer follow-up is required than the maximum of three years described in the present study.

We conclude that in this study the process of transition is not associated with increased disease activity, but has a high risk for dropout especially in those patients with low disease activity. More attention during transitional process should be payed to those patients with low disease activity.

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References

1. BLUM RW, GARELL D, HODGMAN CH *et al*.: Transition from child-centered to adult health-care systems for adolescents with chronic conditions. A position paper of the Society for Adolescent Medicine. *J Adolesc Health* 1993; 14: 570-6.
2. MCDONAGH JE: Transition of care from paediatric to adult rheumatology. *Arch Dis Child* 2007; 92: 802-7.
3. TUCKER LB, CABRAL DA: Transition of the adolescent patient with rheumatic disease: issues to consider. *Rheum Dis Clin North Am* 2007; 33: 661-72.
4. SHAW KL, SOUTHWOOD TR, MCDONAGH JE: Transitional care for adolescents with juvenile idiopathic arthritis: A Delphi study. *Rheumatology* 2004; 43: 1000-6.
5. ROBERTSON LP, MCDONAGH JE, SOUTHWOOD TR, SHAW KL: Growing up and moving on. A multicentre UK audit of the transfer of adolescents with juvenile idiopathic arthritis from paediatric to adult centred care. A*nn Rheum Dis* 2006; 65: 74-80.
6. ELEFTHERIOU D, ISENBERG DA, WEDDERBURN LR, IOANNOU Y: The coming of age of adolescent rheumatology. *Nat Rev Rheum* 2014; 10: 187-93.
7. HILDERSON D, EYCKMANS L, VAN DER ELST K, WESTHOVENS R, WOUTERS C, MOONS P: Transfer from paediatric rheumatology to the adult rheumatology setting: experiences and expectations of young adults with juvenile idiopathic arthritis. *Clin Rheumatol* 2013; 32: 575-83.
8. SHAW KL, SOUTHWOOD TR, MCDONAGH JE: Young people's satisfaction of transitional care in adolescent rheumatology in the UK. *Child Care Health Dev* 2007; 33: 368-79.
9. HERSH AO, PANG S, CURRAN ML, MILOJEVIC DS, VON SCHEVEN E: The challenges of transferring chronic illness patients to adult care: Reflections from pediatric and adult rheumatology at a US academic center. *Pediatr Rheumatol Online J* 2009; 7: 13.
10. HAZEL EM, ZHANG X, DUFFY CM, CAMPILLO S: High rates of unsuccessful transfer to adult care among young adults with juvenile idiopathic arthritis. *Pediatr Rheumatol Online J* 2010; 8: 2.
11. MINDEN K: Transition care programmes: a European perspective. 101136/annrheumdis-2016-eular6419 2016.
12. PETTY RE, SOUTHWOOD TR, MANNERS P *et al*.: International League of Associations for R. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. *J Rheumatol* 2004; 31: 390-2.
13. GIANNINI EH, RUPERTO N, RAVELLI A, LOVELL DJ, FELSON DT, MARTINI A: Preliminary definition of improvement in juvenile arthritis. *Arthritis Rheum* 1997; 40: 1202-9.
14. CONSOLARO A, RUPERTO N, PISTORIO A *et al*.; PAEDIATRIC RHEUMATOLOGY INTERNATIONAL TRIALS ORGANISATION: Development and initial validation of composite parent- and child-centered disease assessment indices for juvenile idiopathic arthritis. *Arthritis Care Res* (Hoboken) 2011; 63: 1262-70.
15. PREVOO ML, VAN 'T HOF MA, KUPER HH, VAN LEEUWEN MA, VAN DE PUTTE LB, VAN RIEL PL: Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum* 1995; 38: 44-8.
16. NIEWERTH M, MINDEN K, KLOTSCHE J, HORNEFF G: Therapy of juvenile idiopathic arthritis in early adulthood with biologics. Transition from pediatric to adult care. *Z Rheumatol* 2014; 73: 532-40.
17. ADIB N, SILMAN A, THOMSON W: Outcome following onset of juvenile idiopathic inflammatory arthritis: II. Predictors of outcome in juvenile arthritis. *Rheumatology* 2005; 44: 1002-7.
18. VAN DIJKHUIZEN EHP, WULFFRAAT NM: Early predictors of prognosis in juvenile idiopathic arthritis: A systematic literature review. *Ann Rheum Dis* 2015; 74: 1996-2005.
19. WALLACE CA, GIANNINI EH, SPALDING SJ *et al*.: Clinically inactive disease in a cohort of children with new-onset polyarticular juvenile idiopathic arthritis treated with early aggressive therapy: Time to achievement, total duration, and predictors. *J Rheumatol* 2014; 41: 1163-70.
20. FOELL D, WULFFRAAT N, WEDDERBURN LR *et al*.: Methotrexate withdrawal at 6 vs 12 months in juvenile idiopathic arthritis in remission a randomized clinical trial. *JAMA* 2010; 303: 1266-73.
21. IGLESIAS E, TORRENTE-SEGARRA V, BOU R *et al*.: Non-systemic juvenile idiopathic arthritis outcome after reaching clinical remission with anti-TNF-α therapy: A clinical practice observational study of patients who discontinued treatment. *Rheumatology Int* 2014; 34: 1053-7.
22. STINSON J, KOHUT SA, SPIEGEL L *et al*.: A systematic review of transition readiness and transfer satisfaction measures for adolescents with chronic illness. *Int J Adolesc Med Health* 2014; 26: 159-74.