BJD
British Journal of Dermatology

Treatment persistence in paediatric and adolescent patients with psoriasis followed into young adulthood. From topical to systemic treatment: a prospective, longitudinal, observational cohort study of 448 patients*

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Linked Comment: Salman. *Br J Dermatol* 2021; **184**:387–388.

Summary

Background Although solely topical treatment often suffices, patients with psoriasis may require more intensive treatment (phototherapy and/or systemic treatments) to control their disease. However, in paediatric, adolescent and young adult patients, little is known about persistence of topical treatment and time until switch to systemic treatment.

Objectives To determine the median time from psoriasis onset until (i) discontinuation of solely topical agents and (ii) switch to systemic treatment, and to identify patient characteristics associated with switching to systemic treatments.

Methods Data were extracted from the Child-CAPTURE registry, a prospective, observational cohort of patients with paediatric-onset psoriasis followed into young adulthood from 2008 to 2018. Data prior to inclusion in the registry were collected retrospectively. Median times were determined through Kaplan–Meier survival analyses. Cox regression analysis was used to identify patient characteristics associated with switch to systemic treatment.

Results Of 448 patients, 62·3% stayed on solely topical treatment until data lock; 14·3% switched from topicals to phototherapy, but not to systemic treatment; and 23·4% switched to systemic treatment. The median time from psoriasis onset until discontinuation of solely topical treatment was 7·3 years, and until switch to systemics was 10·8 years. Higher Psoriasis Area and Severity Index and (Children's) Dermatology Life Quality Index > 5 were independently associated with switching to systemic treatment.

Conclusions In a population of paediatric and adolescent patients with mild-to-severe psoriasis, one-third needed more intensive treatment than solely topical therapy to control their disease. We consider the median time until switching to systemics to be long.

What is already known about this topic?

- Psoriasis in the majority of paediatric and adolescent patients can be adequately managed with solely topical treatment. However, some patients require a switch to more intensive treatment in order to control their disease.
- Little is known about persistence of topical treatment and time until switch to systemic treatment.

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Accepted for publication
3 June 2020

Funding sources
This study was supported by a grant from Eli Lilly and Company, who were involved in the study design and who reviewed the study's protocol and manuscript. Eli Lilly and Company had no involvement in the conduct of the study; collection, management, analysis and interpretation of the data; preparation and approval of the manuscript; or decision to submit the manuscript for publication. Fees were paid directly to the independent research fund of the Department of Dermatology of Radboud University Medical Centre, Nijmegen.

Conflicts of interest
F.M.B. has carried out clinical trials for *AbbVie*, Janssen, LEO Pharma, Lilly, Pfizer and Celgene. I.M.G.J.B. has carried out clinical trials for *AbbVie*, LEO Pharma and Pfizer. R.C. and M.K. are paid employees of IQVIA BV; IQVIA has received consulting fees from Eli Lilly & Co. for research carried out in this work. J.M.M.G. has no conflicts of interest. E.M.G.J. de J. has received research grants for the independent research fund of the Department of Dermatology of the Radboud University Medical Centre Nijmegen, from *AbbVie*, Pfizer, Novartis, Janssen and LEO Pharma, and has acted as a consultant and/or paid speaker for and/or participated in research sponsored by companies that manufacture drugs used for the treatment of psoriasis including *AbbVie*, Janssen Pharmaceutica, Novartis, Lilly, Celgene, LEO

Pharma, UCB and Almirall. All funding is not personal but goes to the independent research fund of the Department of Dermatology of Radboud University Medical Centre Nijmegen. M.M.B.S. has received grants from or has been involved in clinical trials for AbbVie, Celgene, Eli Lilly, Janssen, LEO Pharma and Pfizer; and has served as a consultant for AbbVie, Eli Lilly, Janssen, LEO Pharma and Pfizer; fees were paid directly to the institution.

**Plain language summary available online*

DOI 10.1111/bjd.19301

What does this study add?

- In 448 paediatric patients with mild-to-severe psoriasis, 62·3% persisted on solely topical treatment, 14·3% switched to phototherapy, but not to systemics, and 23·4% switched to systemic treatment at data lock (total median follow-up 4·2 years, interquartile range 1·8–7·5).
- The median time from psoriasis onset until discontinuation of solely topical treatment was 7·3 years, and until switch to systemic treatment 10·8 years.
- Higher Psoriasis Area and Severity Index and (Children's) Dermatology Life Quality Index > 5 at switch were independent characteristics associated with switching to systemic treatment.

Several treatment modalities for the management of psoriasis exist.[1,2] Topical treatments, consisting of topical corticosteroids, vitamin D analogues and calcineurin inhibitors, are generally considered to be the first choice of treatment.[2,3] Dithranol is a topical treatment often applied in a daycare setting as short-contact therapy, and it has been shown to be safe and effective in the treatment of moderate-to-severe psoriasis.[4,5] Short-contact dithranol therapy is usually given as a daily application in increasing concentrations and application time (from 15 to 45 min) until the skin is clear or almost clear (average duration 2 months).[4,6] In the Netherlands, the majority of paediatric patients are treated with dithranol as a second-line topical treatment before commencing phototherapy or systemic treatment.[1,7] Although solely topical treatment is sufficient for many patients with psoriasis, some patients may require more intensive treatment to control their disease, such as phototherapy or systemic therapy. Apart from a possible lack of efficacy of topical treatments, adherence to topicals is often low in patients with psoriasis, which consequently limits treatment effect, leading to insufficient disease control.[8,9] Yet, especially in paediatric patients with psoriasis, systemic therapies are commonly reserved for more severe or refractory psoriasis due to potential adverse events and/or frequent monitoring.

As systemic treatment options for patients with psoriasis are expanding, and as more data regarding the safety of systemic treatments are becoming available, a point of discussion is whether we should initiate more effective treatment earlier on. This is especially true for children, adolescents and young adults with psoriasis. As these young patients with psoriasis might have a substantial cumulative life course impairment by inadequately controlled psoriasis, they might benefit most from early and effective intervention.[10–13] It is therefore important to gain insight into how long solely topical treatments currently suffice and the duration until the start of systemic treatments in this patient group. Data on this subject are scarce, with only a few retrospective treatment pattern studies assessing these durations in adult patients with psoriasis.[14–17] Most of these studies were based on retrospective administrative databases, which have the advantage of complete coverage of the psoriasis population, but might not always accurately reflect the treatment use of patients.[14,15,17] Furthermore, due to the retrospective nature of these studies, they were unable to address the influence of psoriasis severity or the association with patient characteristics on the switch to systemic treatments.[14–17] Moreover, to the best of our knowledge, no previous study has examined the time to topical discontinuation and switch to systemics in paediatric, adolescent and young adult patients with psoriasis.

With this prospective, longitudinal, observational, single-centre, daily clinical practice cohort study of young patients with psoriasis, we therefore aim to give insight into treatment persistence, taking into account psoriasis severity and patient characteristics. The following objectives were formulated. Firstly, to describe the proportions of patients who persisted on solely topical treatment, switched to phototherapy but not to systemics, or switched to systemic treatment at data lock. Secondly, to determine the median time from psoriasis onset until (i) discontinuation of solely topical treatment and (ii) switch to systemic treatment, both for all patients and split for patients with moderate-to-severe vs. mild psoriasis at first visit. Additionally, we sought to identify patient characteristics associated with switching to systemic treatment.

Patients and methods

Registry and data collection

Data for this prospective, single-centre cohort study were extracted from the Child-CAPTURE (Continuous Assessment of Psoriasis Treatment Use Registry), a prospective, longitudinal, observational, daily clinical practice cohort of paediatric-onset patients with psoriasis. This ongoing cohort includes all patients with a diagnosis of psoriasis aged < 18 years at first visit, who attended the outpatient clinic of the Department of Dermatology at the Radboud University Medical Centre between September 2008 and May 2018 (data lock). Patients included in the registry who reach the age of 18 years are followed as young adults. Patients are referred by general practitioners and dermatologists from all over the Netherlands.

This study was reviewed by the ethics committee of the region of Arnhem-Nijmegen (file number CMO: 2012/383) and was deemed to not fall within the remit of the Medical Research Involving Human Subjects Act. Written informed consent was obtained from the parents or guardians and/or from the participating patients according to applicable rules.

Treatment characteristics

Treatment characteristics were collected prospectively from the moment of inclusion in the registry. Characteristics of treatments used prior to inclusion and the date of psoriasis onset (self-reported by parents and/or patients) were collected retrospectively at the first visit. For all treatments, the type of treatment (i.e. solely topical, daycare dithranol, phototherapy and systemic treatment) and the date of treatment start or switch were recorded. A treatment switch was defined as occurring when a patient switched to or added on a different type of treatment. Regarding solely topical treatment, intermittent use of topical treatment (e.g. temporary discontinuation due to disease improvement, but restart after a psoriasis flare) was considered as continuous use of topical treatment and was not recorded as a treatment stop or switch. All patients were treated according to daily clinical care. Treatment decisions were made by the treating physician according to the Dutch evidence- and consensus-based guideline on psoriasis.[1,7,18] Patients were categorized according to treatment patterns as follows: (i) patients who stayed on solely topical treatment until data lock; (ii) patients who switched from solely topical treatment to ultraviolet B phototherapy, but not to a systemic treatment; and (iii) patients who switched to systemic treatment.

Patient characteristics

The following baseline patient characteristics were collected: sex, date of psoriasis onset and family history of psoriasis. At every visit, patient and psoriasis characteristics, including age, length and weight, psoriasis location, psoriasis severity and impact of psoriasis on quality of life were collected prospectively using a standard case report form. Psoriasis severity was measured through the Psoriasis Area and Severity Index (PASI, range 0–72) and body surface area. The impact of psoriasis on quality of life was measured with the Children's Dermatology Life Quality Index (CDLQI, range 0–30) if a patient was < 16 years old and/or the Dermatology Life Quality Index (DLQI, range 0–30) if a patient was ≥ 16 years old.[19,20]

Statistical analysis

Patient characteristics

Clinical and demographic data were presented as a mean $\pm$ SD in case of normally distributed continuous variables, as a median with interquartile range in case of non-normally distributed continuous variables, and as a number (%) for categorical variables. Patient and disease characteristics were presented for (i) all patients; (ii) patients who stayed on solely topicals until data lock; (iii) patients who switched to phototherapy, but not to a systemic treatment; and (iv) patients who switched to systemic treatment during follow-up.

Median-time analyses

To determine the median time from psoriasis onset until (i) discontinuation of solely topical treatment and (ii) switch to first systemic treatment, Kaplan–Meier survival analyses were performed. For purpose of visualization, the median time until switch to first systemic treatment was displayed as a one-minus-survival curve. In addition, to account for the use of dithranol as a second-line topical treatment in this study, a sensitivity analysis was performed. In this sensitivity analysis the median time until topical treatment discontinuation was recalculated with dithranol considered as a next step after topical treatment (together with phototherapy and systemic treatment). Patients were censored when lost to follow-up or if no event had occurred at the moment of data lock. Subanalyses were performed split for patients with mild psoriasis, defined as PASI < 5 at the first visit, and moderate-to-severe psoriasis, defined as PASI ≥ 5 at the first visit. Log-rank tests were performed to compare Kaplan–Meier curves.

Patient characteristics associated with switching to systemic treatment

A Cox proportional hazards regression model was used to examine the association between patient characteristics and switch to systemic treatment. For this analysis only prospectively collected data were used, and therefore patients with a history of systemic treatment before inclusion in the registry were excluded. The following patient characteristics were included in the analyses: sex, first-degree family history of psoriasis, body mass index at the moment of switch, age at switch, PASI at switch, body surface area at switch, CDLQI or DLQI > 5 at switch and presence of psoriasis on either the scalp, face or nails at switch. All variables were tested with univariable analyses and were incorporated into the multivariable analysis when the P-value was $< 0{\cdot}2$. Final determinants were selected through backward selection. Hazard ratios (HRs) with 95% confidence interval (CIs) for the determinants were calculated.

As this study follows patients from childhood into young adulthood, both CDLQI and DLQI were used during follow-up. Because these scores cannot be combined into one score, a cutoff of either CDLQI > 5 or DLQI > 5 was used for analysis.[21] Body mass index was categorized into thinness, normal weight and overweight/obesity based on the extended international (International Obesity Task Force) body mass index cutoffs reported by Cole and Lobstein.[22] Missing data were excluded from analyses.

SAS (SAS for XP PRO, release 9·4 TS2 M3; SAS Institute Inc., Cary, NC, USA) and SPSS version 25 (IBM, Armonk, NY,

USA) were used to perform analyses. For all statistical tests, P-values < 0·05 were considered significant.

Results

Treatment pattern and patient characteristics

The treatment pattern of all children and adolescents, and if applicable young adults, is shown in Figure 1. Of the 448 patients, 279 (62·3%) stayed on solely topical treatment (including dithranol) during follow-up, 64 (14·3%) switched from topical to phototherapy, but not to systemic treatment, and 105 (23·4%) had eventually switched to systemic treatment at the moment of data lock. The patients' characteristics at the first visit are presented in Tables 1 and 2. Less than half of the patients were male (42·9%), and the overall mean ± SD age at psoriasis onset was 8·4 ± 4·0 years. The mean age at the last follow-up visit was 13·5 ± 4·8 years (range 2·0–24·4). The total median follow-up time was 4·2 years (interquartile range 1·8–7·5) and the mean follow-up time was 5·2 ± 4·0 years. Regarding patients who switched to systemic treatment, 70 (66·7%) switched to methotrexate and 22 (21·0%) to fumaric acid esters as first systemic treatment.

Median-time analyses

Median time until discontinuation of solely topical treatment

Figure 2(a) shows the Kaplan–Meier curve for the median time from psoriasis onset until discontinuation of topical treatment and subsequent switch to phototherapy or systemics (whichever initiated first). In total 169 patients switched from solely topical treatment. The overall median time from psoriasis onset until discontinuation of solely topical treatment was 7·3 years (95% CI 5·2–9·4), with a switching rate of 13·8% after 1 year, increasing to 27·4% after 3 years. The median time from psoriasis onset until discontinuation of solely topical treatment was significantly shorter for patients with moderate-to-severe psoriasis at the first visit at our department (5·8 years, 95% CI 4·9–6·7) than for patients with mild psoriasis at the first visit (11·2 years, 95% CI 8·6–13·9, P < 0·001). A sensitivity analysis in which dithranol was regarded as a more intensive treatment together with phototherapy and systemic treatment revealed a shorter median time (3·9 years, 95% CI 3·3–4·5) from psoriasis onset until discontinuation of solely topical treatment (including only topical corticosteroids, vitamin D analogues and/or calcineurin inhibitors) (Figure S1; see Supporting Information).

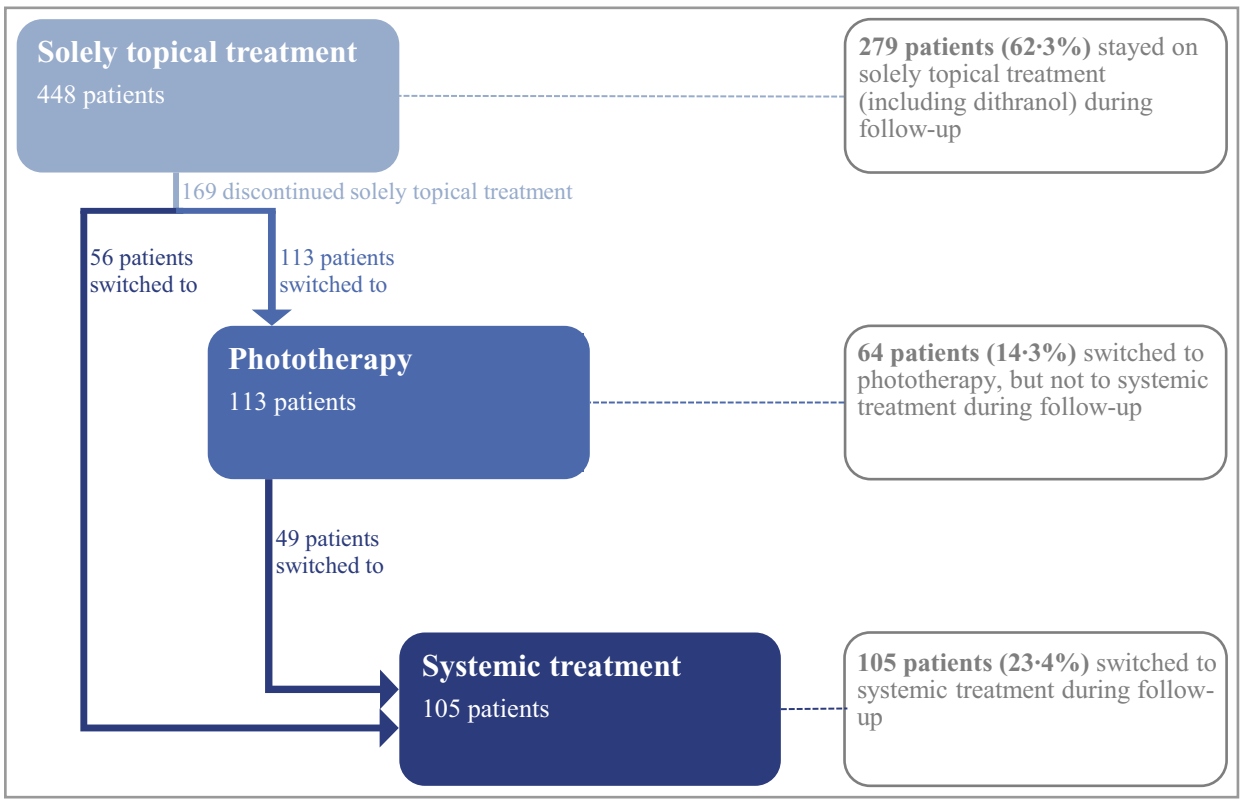

Figure 1 Treatment pattern in paediatric and adolescent patients with psoriasis followed into young adulthood. In total 448 patients initiated solely topical treatment after psoriasis onset. During follow-up 169 patients discontinued solely topical treatment and switched to a more intensive treatment: 113 patients to phototherapy and 56 to systemic treatment. Of the 113 patients who switched to phototherapy, 49 further switched to systemic treatment, giving a total of 105 patients who switched to systemic treatment during follow-up.

Table 1 Demographic and follow-up characteristics of patients with paediatric-onset psoriasis

Variable	All patients (n = 448)	Patients on solely topicals during FU (n = 279, 62·3%)	Patients who switched to phototherapy but not to systemics (n = 64, 14·3%)	Patients who switched to systemics during FU (n = 105, 23·4%)
Sex male, n (%)	192 (42·9)	120 (43·0)	27 (42·2)	45 (42·9)
First-degree family history, n (%)	141 (31·5)	86 (30·8)	16 (25·0)	39 (37·1)
Age (years)				
At psoriasis onset, mean ± SD [range]	8·4 ± 4·0 [0·0–17·6]	7·7 ± 3·7 [0·0–16·6]	9·4 ± 3·8 [0·5–15·9]	9·4 ± 4·3 [0·5–17·6]
At switch to systemic, mean ± SD [range]	–	–	–	14·2 ± 3·3 [6·5–21·5]
At last follow-up visit, mean ± SD [range]	13·5 ± 4·8 [2·0–24·4]	11·7 ± 4·4 [2·0–24·4]	14·7 ± 3·5 [6·4–22·8]	17·5 ± 3·5 [7·4–24·4]
0 to < 6, n (%)	25 (5·6)	25 (9·0)	0	0
6 to < 12, n (%)	151 (33·7)	130 (46·6)	14 (21·9)	7 (6·7)
12 to < 18, n (%)	183 (40·8)	94 (33·7)	38 (59·4)	51 (48·6)
≥ 18, n (%)	89 (19·9)	30 (10·8)	12 (18·8)	47 (19·9)
Psoriasis location at first visit,[a] n (%)				
Scalp	349 (77·9)	217 (77·8)	48 (75·0)	84 (80·0)
Face	66 (14·7)	49 (17·6)	5 (7·8)	12 (11·4)
Inverse	171 (38·2)	111 (39·8)	23 (35·9)	37 (35·2)
Nails	78 (17·4)	38 (13·6)	12 (18·8)	28 (26·7)
Disease duration at first visit, median (IQR) [range]	1·7 (0·8–4·4) [0·0–14·1]	1·3 (0·7–3·4) [0·0–14·1]	2·5 (1·3–5·0) [0·0–13·3]	3·0 (1·2–6·4) [0·0–12·5]
Follow-up time (years),[b] median (IQR) [range]	4·2 (1·8–7·5) [0·0–19·1]	3·2 (1·3–6·0) [0·0–18·2]	4·5 (2·2–8·1) [0·2–14·4]	7·7 (4·8–11·4) [0·6–19·1]
Follow-up time (years),[b] mean ± SD [range]	5·2 ± 4·0 [0·0–19·1]	4·1 ± 3·4 [0·0–18·2]	5·4 ± 3·7 [0·2–14·4]	8·1 ± 4·3 [0·6–19·1]
Follow-up status at data lock, n (%)				
Active	294 (65·6)	174 (62·4)	39 (60·9)	81 (77·1)
Referred back to general practitioner or dermatologist	37 (8·3)	20 (7·2)	4 (6·3)	13 (12·4)
Lost to follow-up	117 (26·1)	85 (30·5)	21 (32·8)	11 (10·5)

FU, follow-up; IQR, interquartile range. [a]More than one location of psoriasis can be reported in the same patient. [b]Follow-up time includes retrospective data.

Median time until switch to systemic treatment

Figure 2(b) shows the Kaplan–Meier curve for the median time from psoriasis onset until switch to first systemic treatment. In total 105 patients switched to systemic treatment during follow-up. The overall median time until switch to first systemic treatment was 10·8 years (95% CI 9·8–11·9). In the first year after psoriasis onset 3·4% switched to systemic treatment, increasing to 12·0% after 3 years. The median time until first systemic treatment was shorter for patients with moderate-to-severe psoriasis than for patients with mild psoriasis at the first visit ($P = 0·001$).

Patient characteristics associated with switching to systemic treatment

For this analysis, 22 patients who started systemic treatment prior to inclusion in the registry were excluded, as the disease and patient characteristics at the moment of switch were unavailable. Univariable Cox regression analysis of 426 patients identified that higher PASI, higher body surface area, facial psoriasis, scalp psoriasis, nail psoriasis and CDLQI or DLQI > 5 at the moment of switch were associated with switching to systemic treatment (Table S1; see Supporting Information). Sex, family history, age at switch and body mass index at switch were not associated with switching to systemic treatment. Multivariable Cox regression analysis showed that higher PASI (HR 1·26, 95% CI 1·13–1·42) and CDLQI or DLQI > 5 (HR 4·50, 95% CI 2·58–7·84) were independently associated with switching to systemic treatment (Table 3).

Discussion

In this prospective, longitudinal, observational cohort study of 448 paediatric and adolescent patients with psoriasis who were followed into young adulthood, 279 (62·3%) stayed on solely topical treatment until data lock, 64 (14·3%) switched to phototherapy but not to systemics and 105 (23·4%)

Table 2 Psoriasis outcome measures and treatments of patients with paediatric-onset psoriasis

Variable	All patients (n = 448)	Patients on solely topicals during FU (n = 279, 62·3%)	Patients who switched to phototherapy but not to systemics (n = 64, 14·3%)	Patients who switched to systemics during FU (n = 105, 23·4%)
Psoriasis severity at first visit, n (%)				
Mild (PASI < 5)	191 (42·6)	140 (50·2)	22 (35·5)	29 (27·6)
Moderate to severe (PASI ≥ 5)	255 (56·9)	139 (49·8)	40 (64·5)	76 (72·4)
PASI (0–72), median (IQR) [range]				
At first visit	5·6 (3·4–8·3) [0·0–42·4]	4·9 (3·0–7·8) [0–31·9]	6·2 (4·3–9·7) [0·4–29·0]	7·0 (4·6–9·5) [0·3–42·4]
At switch to systemic (n = 80)	–	–	–	8·4 (6·2–11·1) [0·4–42·4]
BSA, median (IQR) [range]				
At first visit	5·3 (2·5–11·0) [0·0–76·0]	4·5 (2·0–9·4) [0·0–72·0]	6·2 (2·9–14·0) [0·2–59·5]	8·0 (3·5–15·2) [0·1–76·0]
At switch to systemic (n = 79)	–	–	–	9·8 (6·0–16·5) [0·1–72·0]
CDLQI[a] (0–30), median (IQR) [range]				
At first visit (n = 409)	7 (5·0–11·0) [0–29]	7 (4·0–11·0) [0–25] (n = 261)	7·5 (5·0–12·0) [0–29] (n = 58)	8 (6·0–12·3) [0–22] (n = 90)
At switch to systemic (n = 52)	–	–	–	11 (6·0–15·0) [1–24]
DLQI[b] (0–30), median (IQR) [range]				
At first visit (n = 32)	8 (6·0–11·8) [1–24]	7·5 (4·3–11·8) [1–15] (n = 12)	9 (6·0–15·0) [6–16] (n = 5)	9 (6·0–11·0) [1–24] (n = 15)
At switch to systemic (n = 26)	–	–	–	9 (4·8–16·0) [2–22]
BMI[c] at first visit, n (%) (n = 398)				
Thinness	60 (15·1)	39 (15·9)	10 (18·9)	11 (11·1)
Normal weight	256 (64·3)	165 (67·1)	29 (54·7)	62 (62·6)
Overweight or obesity	82 (20·6)	42 (17·1)	14 (26·4)	26 (26·3)
BMI[c] at switch to systemic, n (%) (n = 74)				
Thinness	–	–	–	8 (10·8)
Normal weight	–	–	–	49 (66·7)
Overweight or obesity	–	–	–	17 (23·0)
Psoriatic arthritis at first visit, n (%)	2 (0·4)	0	0	2 (1·9)
First systemic treatment, n (%)				
Methotrexate	–	–	–	70 (66·7)
Fumaric acid esters	–	–	–	22 (21·0)
Ciclosporin	–	–	–	7 (6·7)
Retinoids	–	–	–	6 (5·7)

BMI, body mass index (in kg m^{-2}); BSA, body surface area; CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; FU, follow-up; IQR, interquartile range; PASI, Psoriasis Area and Severity Index. [a]For patients < 16 years old. [b]For patients ≥ 16 years old. [c]Cutoffs for overweight/obese were based on the extended International Obesity Task Force BMI cutoffs for thinness, overweight and obesity by Cole and Lobstein.[22]

eventually switched to systemic treatment during follow-up. The median time from psoriasis onset until discontinuation of solely topical treatment was 7·3 years, and the median time until switch to systemic treatment was 10·8 years. Both higher PASI and a CDLQI or DLQI > 5 at the moment of switch were independent characteristics associated with switching to systemic treatment.

A median time of 7·3 years from psoriasis onset until discontinuation of solely topical treatment and subsequent switch to either phototherapy or systemic treatment seems rather long. However, the use of dithranol as a second-line treatment in our cohort should be taken into consideration. In accordance with the Dutch guidelines for paediatric psoriasis, many patients who do not respond to classical topical treatments (corticosteroids, vitamin D analogues, calcineurin inhibitors) are treated with dithranol before commencing phototherapy or systemic treatment.[1,4,23] As dithranol is a safe and effective therapy and is often given in rotation with other topical treatments, many children stay on topical treatments (including dithranol) for a considerable time.[4] However, we realize that this is not common practice in many other countries, where the availability or practicality of dithranol might be problematic. Indeed, as dithranol treatment is currently unavailable at our practice due to supply issues (not during the conduct of this study), our experience in daily practice is that phototherapy and/or systemic treatment is initiated earlier on. Therefore we carried out a sensitivity analysis in which dithranol was regarded as a more intensive treatment together with phototherapy and systemic treatment, which revealed a shorter median time until topical discontinuation of 3·9 years

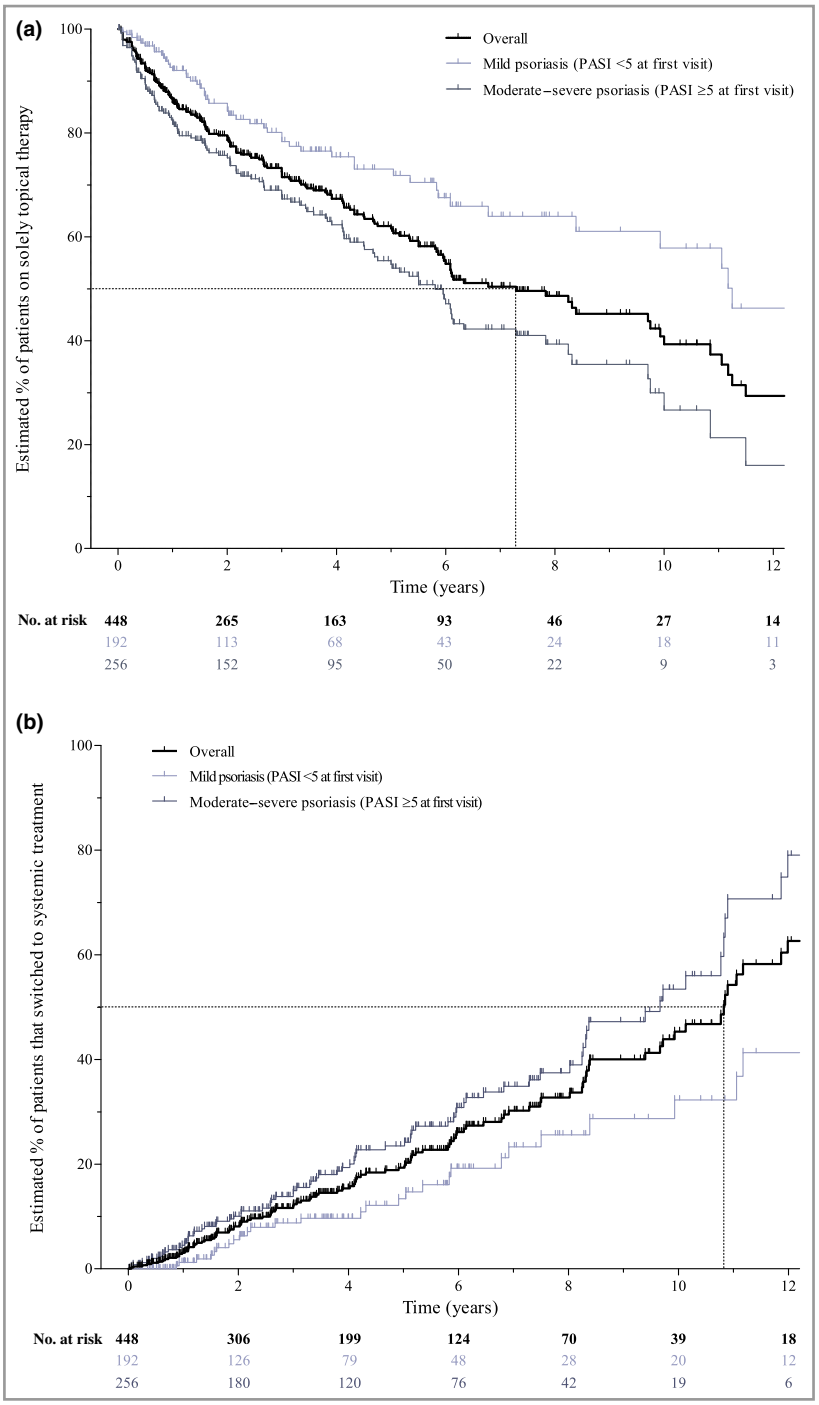

Figure 2 (a) Median time from psoriasis onset until discontinuation of solely topical therapy in paediatric and adolescent patients with psoriasis followed into young adulthood (n = 448). During follow-up 169 patients discontinued topical treatment and switched to a more intensive treatment. The median overall time until discontinuation of topical treatment was 7·3 years [95% confidence interval (CI) 5·2–9·4]. When split for psoriasis severity at first visit, the median time was 11·2 years (95% CI 8·6–13·9) for mild psoriasis and 5·8 years (95% CI 4·9–6·7) for moderate-to-severe psoriasis ($P < 0·001$). (b) Median time from psoriasis onset until switch to first systemic treatment in paediatric and adolescent patients followed into young adulthood (n = 448). During follow-up 105 patients switched to systemic treatment. The median overall time until switch to (first) systemic treatment was 10·8 years (95% CI 9·8–11·9). When split for psoriasis severity at first visit, the median time was 14·8 years (95% CI 8·0–21·6) for mild psoriasis and 9·7 years (95% CI 8·1–11·3) for moderate-to-severe psoriasis ($P = 0·001$). PASI, Psoriasis Area and Severity Index.

Table 3 Determinants associated with switch to first systemic treatment by multivariable Cox regression analysis (426 patients)

	Event = switch to first systemic treatment (80 events)	
Predictors	Hazard ratio (95% CI)	P-value
PASI at switch[a]	1·26 (1·13–1·42)	< 0·001
CDLQI or DLQI > 5 at switch	4·50 (2·58–7·84)	< 0·001

CDLQI, Children's Dermatology Life Quality Index; CI, confidence interval; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index. [a]Hazard ratio per 5 PASI points.

(Figure S1; see Supporting Information). Probably, this median time of 3·9 years until topical discontinuation is a better reflection of practices in which dithranol is not available. Indeed, the topical discontinuation rate after 3 years in our sensitivity analysis (43·6%) is comparable with the 3-year discontinuation rate in a retrospective administrative claims database study in the USA of 49·8%.[14]

The median time from onset of psoriasis to first systemic treatment was 10·8 years in all patients in our study and 9·7 years for patients with moderate-to-severe psoriasis at first visit. Van den Reek *et al.* found a slightly higher median time until conventional systemic treatment of 11·0 years in a study in which treatment patterns of adult patients with severe psoriasis using a biologic agent were assessed retrospectively.[16] However, this study included only patients with severe psoriasis, all of whom switched to systemic treatment, rather than the young patients in our cohort with a severity of psoriasis ranging from mild to severe. Moreover, the fact that 76·6% of the patients in our study did not switch to systemics may have influenced the relatively long time until switch to systemic treatment, and again the use of dithranol should be taken into account. Nevertheless, as knowledge on the safety and efficacy of systemic treatments in paediatric patients with psoriasis is increasing,[24,25] daily practice will develop towards initiating systemic treatments earlier on. We consider the time until switch to systemic treatment to be long, and given the reassuring safety profile especially of biologics in (paediatric) psoriasis, our results indicate there is potential for earlier initiation of systemic treatments.

We found that a higher PASI and CDLQI or DLQI > 5 at switch were independently associated with switching to systemic treatment. The finding that a higher PASI was associated is not surprising and reflects treatment guidelines. The association with CDLQI or DLQI > 5 reflects the importance of quality of life in treatment decisions. Additionally, the finding that facial, scalp and nail psoriasis were associated with switching in the univariate analysis suggests that psoriasis in visible areas might also influence the decision to the start systemic treatment. Interestingly, although we expected older age to influence switching to systemic treatment, both the univariable and multivariable analyses showed that age was not associated.

This study was limited by the single-centre design. Although this study took place at a tertiary referral centre, still 42·6% of patients had mild psoriasis (PASI < 5) at their first visit. Moreover, patients were referred by both general practitioners and dermatologists from across the Netherlands. However, as the percentage of (paediatric) patients with mild psoriasis in the general Dutch population is unknown, it is uncertain whether our study population is fully representative of the general psoriasis population in terms of psoriasis severity. Our study is strengthened by the overall large number of patients (448), the relatively long follow-up time and the fact that almost all of the data in this study were collected prospectively. Although the median times to analyses were based partly on retrospectively collected data, this study included young patients with psoriasis with only a short disease duration before inclusion in the registry (median 1·7 years). We were therefore able to record precisely all data regarding previous treatments, so the median-time analyses were probably not influenced.

In conclusion, our results give insight into the persistence of solely topical treatment and time until switch to systemic treatments in a population of children and adolescents with mild-to-severe psoriasis who were followed into young adulthood. The median times of 7·3 years until topical treatment discontinuation and of 10·8 years until switch to systemic treatment seem long, although the use of dithranol in this cohort should be taken into consideration. In this era in which reassuring safety data on methotrexate and biologics in paediatric psoriasis are emerging,[24,25] the question rises whether more effective systemic treatment should be initiated earlier on. In particular, young patients with psoriasis might benefit most from earlier intervention in terms of limiting life course impairment by uncontrolled psoriasis. This study adds to our knowledge of current prescribing patterns to further enhance the discussion about early intervention in this important subgroup of patients with psoriasis.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Figure S1 Median time from psoriasis onset until discontinuation of solely topical therapy and switch to a more intensive treatment, including dithranol treatment, in paediatric and adolescent patients with psoriasis followed into young adulthood.

Table S1 Determinants associated with switch to first systemic treatment by univariable Cox regression analysis.

Powerpoint S1 Journal Club Slide Set.

Video S1 Author video.