



# Early and late onset psoriasis

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**Early and late onset psoriasis: a cross-sectional clinical and immunocytochemical investigation**

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**What's already known about this topic?**

- Late onset psoriasis (LOP), presenting after 40 years of age, has distinct genetic differences to early onset psoriasis (EOP), which presents at or before 40 years of age.
- LOP is specifically associated with distinct polymorphisms at the interleukin (IL)-1B gene and an impairment of epidermal Langerhans' cells (LCs) mobilization in response to IL-1 $\beta$  has been demonstrated in the uninvolved skin of EOP but not LOP.

**What does this study add?**

- We have shown differences in the T-cell infiltration in lesional skin between the two subtypes of psoriasis, demonstrating a higher CD4+/CD8+ ratio in the involved epidermis of LOP patients in comparison to EOP patients.
- We have provided evidence to suggest differences in the heritability of LOP as compared to EOP; while we have shown that LOP is more strongly associated with type 2 diabetes and autoimmune thyroiditis as compared to EOP. LOP patients were also more likely to be anxious compared with EOP patients.
- This paper provides further evidence for the hypothesis that LOP and EOP are two distinct conditions.

**Abstract**

**Background:**

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There is accumulating evidence that early onset psoriasis (EOP; presenting at or before 40 years of age) and late onset psoriasis (LOP; presenting after 40 years of age) are different diseases.

### **Objectives and Methods:**

We aimed to identify potential differences between EOP and LOP by assessing immunocytochemistry involved (PP) and uninvolved (PN) skin (n=31) and demographics, psoriasis phenotype and psychological parameters (n=340) in a cross-sectional study. We categorized patients who developed psoriasis before age 40y in the EOP group, whilst those whose psoriasis occurred after age 50y were included in the LOP group.

### **Results:**

Immunocytochemistry revealed (17 EOP; 14 LOP) a greater lymphocytic infiltrate in PP skin of EOP than LOP (p=0.03), with a higher epidermal CD4<sup>+</sup>/CD8<sup>+</sup> ratio in LOP (1.3) compared to EOP (0.5; p=0.002). In 340 psoriasis patients (278 EOP; 62 LOP), we found a lower association with a positive 1<sup>st</sup> or 2<sup>nd</sup> degree family history of psoriasis (35.6% vs 62%; OR 0.33, 95% CI 0.18-0.59) and lower likelihood of having parents with EOP (OR=0.093, 95% CI 0.012-0.74) in LOP compared with EOP. EOP patients were more likely to have received biologic therapy (13.3%, EOP vs 3.5% LOP; P=0.042), whilst LOP patients had a higher likelihood of having type 2 diabetes (adjusted OR 3.43, 95%CI 1.004-11.691) and autoimmune thyroiditis (adjusted OR 5.05, 95%CI 1.62-15.7). LOP patients also had greater anxiety than EOP (mean HADS-A score LOP 8±5; EOP 5±5, p=0.006).

### **Conclusions:**

Our findings provide further evidence for the difference between EOP and LOP.

### **Introduction**

Psoriasis is a common, chronic, inflammatory skin condition affecting approximately 2% of the Caucasian population, with a highly variable clinical presentation and a significant long-term psychological and societal impact <sup>1</sup>. Current putative immunopathogenesis of psoriasis involves the dysregulation of cutaneous innate and adaptive immune responses, with T-cells having a primary role in the initiation and maintenance of the inflammatory process.

Henseler and Christophers (1985) described two distinct subtypes of chronic plaque psoriasis; early onset psoriasis (EOP), which presents before 40 years of age and accounts for 75% of patients and late onset psoriasis (LOP) which first presents after the age of 40 years (25% of patients). Patients with EOP were reported as more likely than those with LOP to: suffer from severe psoriasis; require systemic treatment; have a family history of the disease and; be positive for the HLA-Cw\*06:02 allele <sup>2,3</sup>. Certain clinical phenotypes, such as guttate and erythrodermic psoriasis, are more frequent in EOP, whilst LOP is more likely to be limited to the scalp and nails <sup>4,5</sup>. Our group has demonstrated that EOP and LOP have distinct genetic and immunopathogenic characteristics. We showed that only LOP is specifically associated with distinct polymorphisms at the interleukin (IL)-1B gene <sup>6</sup>, and also showed an impairment of epidermal Langerhans' cells (LCs) mobilization in response to IL-1 $\beta$  in the uninvolved skin of EOP but not LOP <sup>7</sup>.

Despite the above, the distinctions between EOP and LOP have not been fully delineated. We carried out a comprehensive analysis of immunohistologic, demographic, phenotypic and psychosocial parameters in EOP and LOP patients.

## **Materials and Methods**

The studies were conducted at Salford Royal NHS Foundation Trust (SRFT), Manchester, UK, between 2010 and 2012. All contemporary patients provided informed consent and completed a detailed questionnaire covering key demographic and medical history, with a physical examination and full skin assessment performed by the study physician (ET).

Patients were included in the immunocytochemical study if they were Caucasian aged at least 50 years; had a diagnosis of plaque psoriasis by a consultant dermatologist or GP for at least six months; had psoriasis on unexposed skin to the sun; and agreed to have an appropriate drug wash out period if they were on phototherapy, topical treatments or systemic therapy (2 weeks for topical treatments, 4 weeks for systemic therapies and phototherapy, 12 weeks for biological agents). The exclusion criteria included patients who had received lithium, anti-malarials, intramuscular gold within four weeks of the study visit; diagnosed with HIV, hepatitis B or hepatitis C; had uncontrolled comorbid disease; had other

inflammatory skin conditions; unwilling to undergo injection of local anaesthetic; participating in other studies using investigational agents or procedures; or donating a skin sample which is positive to Periodic acid Schiff (PAS) staining. Patients who developed psoriasis before age 40y were classified as EOP, whilst those whose psoriasis occurred after age 50y were included in the LOP group.

Each volunteer provided four, 6mm, skin biopsies (2,PP; 2,PN), taken from sun-protected buttock or hip under 1% lidocaine local anesthesia, were processed and stained with H&E. A Leica Bond-Max fully automated staining system (Leica Microsystems, UK) was used to stain the sections stained with T-cell markers, including CD1a, CD8 (DAKO Denmark), and CD3, CD4 (Leica Microsystems, UK). Six sections per biopsy were examined across the whole of the epidermis and dermis, per x200 magnification field. Positive epidermal cells were presented in counts, whilst the dermal infiltrate was assessed using a 0-3 semi-quantitative scale depending on the severity of the inflammation from 0, none to 3, most severe.

Epidermal cell counts and epidermal CD4+/CD8+ ratio were presented as mean values  $\pm$  SD and comparison between groups was carried out with independent samples t-test. The second level of analysis accounted for *a priori* potential confounding variables; including gender, disease duration, PASI and clinical phenotype; using a linear regression model. Dermal cell counts were presented as frequencies and compared for trends using chi square.

The clinical study was an observational cross-sectional study with contemporary and retrospective patients. Patients were included in the contemporary group if they were aged 18 years or above; had a diagnosis of psoriasis by a consultant dermatologist or GP; and had their first sign or symptom of psoriasis  $\leq$  12 months before diagnosis. The retrospective group comprised of patients with psoriasis who have attended the weekly psoriasis clinic between the years of 2005-2010, at SRFT. Patients were categorised in two different groups (EOP and LOP) using the same criteria as the above study. A set of psychometric questionnaires, including HADS, PSWQ, BDI-II and DLQI, was completed by the patients in the contemporary group. Regarding PSWQ, a score between 45 and 55 was set as a reference of moderate raised anxiety (within variable clinical presentation), while a score of 65 and above was a definite diagnosis for generalised anxiety disorder (GAD).<sup>8,9</sup>

Patients in the retrospective group represented newly referred patients to the Psoriasis clinic, at SRFT. A proforma similar to the study questionnaire of the contemporary group was completed for all the patients, including demographic, clinical information and DLQI.

Family history of psoriasis was assessed in two different ways in the contemporary group: a) patients were asked whether they had a positive family of psoriasis in their 1st (parents, siblings and offspring) or 2nd degree (aunts, uncles, grandparents, grandchildren, nieces, nephews, or half-sibling) relatives. This information was extracted from the proformas for the retrospective group; however detailed information regarding the age of onset of the family members was not available in this data.

The assessment of clinical severity was made using the PASI. Clinical phenotype was defined by the following criteria in the contemporary group only: small thin plaques defined by plaque size  $\leq 3$ cm, induration  $\leq 0.75$ mm; small thick plaques defined by plaque size  $\leq 3$ cm and induration  $> 0.75$ mm; large thin plaques by plaque size  $> 3$ cm and induration  $\leq 0.75$ mm; large thick plaques by plaque size  $> 3$ cm and induration  $> 0.75$ mm. Continuous numerical variables were presented as mean values  $\pm$  SD. Chi-square ( $\chi^2$ ) and Fischer's exact test were used to detect trends between categorical variables and independent samples; independent samples t-test was used to identify any significant differences in the means of continuous numerical data. Binary logistic regression was employed to control for *a priori* potential confounders and detect risk factors. As by definition all LOP patients were over 50 years old, analysis on a restricted cohort comparing patients over 50 years old in the EOP group against the LOP group was performed for associated comorbidities and psychosocial morbidity, in order to age-match the two groups.

IBM SPSS statistics 20.0 software (SPSS Inc., Armonk, NY: IBM Corp U.S.A) was used to perform the statistical analysis in both studies. Ethical approval was obtained by the Salford and Trafford Research Ethics Committee (Ref: 05/Q1404/249) for the immunocytochemistry study and obtained from the North West 10 Ethics committee (Ref: 10/H1011/68) for the clinical study.

## Results

### Immunocytochemistry

The immunocytochemical study recruited 17 EOP patients (mean age, 58.7 S.D.  $\pm 7.7$  years; mean age of onset,  $29 \pm 15.4$  years), and 14, age-matched LOP subjects (mean age,  $65.5 \pm 7$  years; mean age of onset of  $56.4 \pm 7.5$  years). The clinical and demographic data for the two groups are listed in supplementary table 1.

In the involved skin (PP), there was a significantly higher epidermal influx of CD4<sup>+</sup> cells in LOP (mean epidermal CD4<sup>+</sup> count: EOP,  $6.7 \pm 4.6$ ; LOP,  $15.1 \pm 6.2$ ;  $p < 0.001$ ) with no significant difference in the number of epidermal CD8<sup>+</sup> cells between the subtypes (mean epidermal CD8<sup>+</sup> count: EOP,  $19.1 \pm 11.1$ ; LOP,  $15.8 \pm 7.8$ ;  $p = 0.35$ ; Figure 1). This resulted in a significantly higher epidermal CD4:CD8 ratio in LOP compared to EOP (mean CD4:CD8 ratio: EOP,  $0.5 \pm 0.5$ ; LOP,  $1.3 \pm 0.8$ ;  $p = 0.002$ ). A multivariate linear regression model adjusted for gender, disease duration, PASI and clinical phenotype also found a significant difference in the mean epidermal CD4<sup>+</sup> count between psoriasis subtypes (Coefficient 11.26,  $p = 0.003$ , 95%CI 4.20-18.31). There was a trend towards a greater epidermal CD3<sup>+</sup> inflammatory infiltrate in LOP (mean epidermal CD3<sup>+</sup>: EOP,  $31.7 \pm 17.5$ ; LOP  $42.8 \pm 13.3$ ;  $p = 0.061$ ) but no significant difference in mean epidermal CD1a<sup>+</sup> cells between EOP and LOP (EOP  $11.1 \pm 5.2$ ; LOP  $13.3 \pm 6.2$ ;  $p = 0.30$ ).

The PP dermis demonstrated a moderate to severe lymphocytic infiltration. There were more CD4<sup>+</sup> cells in LOP than EOP ( $\chi^2$ ,  $p = 0.049$ ); with no observed difference in CD1a<sup>+</sup> cells between EOP and LOP ( $\chi^2$ ,  $p = 0.79$ ). CD3<sup>+</sup> cells were increased, but not significantly so, in the dermis of LOP compared to EOP ( $\chi^2$ ,  $p = 0.067$ ). There were no observed differences between epidermis or dermis of uninvolved skin (PN) in EOP and LOP.

### Clinical characteristics

The clinical study recruited 340 psoriasis patients (108 recruited at time of consent and 232 retrospectively), 278 EOP (mean age of onset of  $20.6 \pm 9.9$  years), and 62 LOP (mean age of onset of  $55.4 \pm 7$  years). Other demographic data are presented in table 1. The vast majority of subjects (96%) were Caucasian. There was no statistical difference in clinical severity or impact on quality of life between

EOP and LOP patients (PASI ,EOP 8.3±6.4; LOP 7±5.4, p=0.23; DLQI, EOP 8±8; LOP 8±7, p=0.098).

Adjusting for patient gender and the presence of affected parents, those with affected first degree relatives (adjusted OR 2.41, 95%CI 1.22-4.78), second degree relatives (adjusted OR 3.38, 95%CI 1.23-7.34), and both affected first and second degree relatives (adjusted OR 8.32, 95%CI 1.90-36.52) were more likely to have EOP as compared to patients with no family history of psoriasis (Table 2). Of the contemporary patients who had data collected on the age of onset of psoriasis in their parents (n=107), patients with EOP parents (19 out of the 22 EOP patients with positive family history, had an EOP parent, and 1 out of 5 LOP patients with positive family history, had an EOP parent) were more likely to develop EOP (EOP 26%, LOP 3.1%; adjusted OR 10.34, 95%CI 1.32-81.83, Table 2). 12 EOP and 3 LOP patients had an affected mother with psoriasis, while 10 EOP and 2 LOP patients had an affected father, and the gender of affected parents was not associated with the type of psoriasis of the subjects (p=0.65).

In the clinical study, chronic plaque psoriasis was the most prevalent phenotype in both groups (86.7%, EOP; 88.1%, LOP; Table 3). There was a trend towards a difference between the plaque phenotype between the groups in that LOP patients demonstrated a higher prevalence of large thin plaques (47.8% vs 29.5%, p=0.115) while EOP patients demonstrated higher prevalence of small thick plaques (9.8% vs 0%, p=0.316) although these differences did not achieve statistical significance. Guttate psoriasis (4.9%), erythrodermic (1.9%) and pustular psoriasis (0.8%) occurred in EOP alone. The prevalence of nail psoriasis, assessed in the contemporary group, was similar in the two groups (36.8% EOP; 25% LOP, p=0.21).

Psoriasis flares following upper respiratory tract infections (URTIs) were more frequent in the EOP group (28.3%, EOP; 16.1% LOP; p=0.049). EOP patients were more likely to require biologic therapy (15.9%, EOP; 3.3% LOP, p=0.01) while LOP patients were more likely to have received phototherapy (13.3%, LOP; 1.8%, EOP patients; p<0.001; Table 4).

### **Associated comorbidities**

Psoriatic arthritis occurred equally in both groups (25.3%, EOP; 23% LOP). A significantly higher proportion of patients with LOP had type 2 diabetes (T2DM), compared to EOP (9% EOP; 37.7% LOP;  $p=0.001$ ). This difference remained significant after a restriction of age 50 or above was applied to both cohorts (15.8% EOP, 37.7% LOP;  $p=0.001$ ). A multivariate logistic regression model adjusted for ischemic heart disease, hypertension, dyslipidemia, central obesity, disease duration and psoriasis severity for this restricted cohort demonstrated a three-fold higher likelihood of finding T2DM in LOP patients as compared to EOP patients (adjusted OR 3.43, 95%CI 1.004-11.691). Similarly, a higher proportion of patients with LOP had autoimmune thyroiditis (AIT); 4% EOP; 16.7% LOP;  $p=0.002$ ), with the difference remaining significant with the restricted cohort (3.6% EOP, 16.7% LOP,  $p=0.005$ ), and a multivariate logistic regression model adjusted for gender, dyslipidemia, disease duration, smoking status (smokers versus non-smokers) and psoriasis severity for the restricted cohort finding a five-fold higher likelihood of AIT in LOP patients (adjusted OR 5.1, 95%CI 1.63-15.9). Crohn disease was only seen in EOP patients (1.4% of EOP).

### **Psychological morbidity**

Patients from both groups had a similar Dermatology Life Quality Index score (DLQI); mean DLQI for EOP  $7.4\pm 7.1$ ; LOP,  $7.8\pm 7.1$ ;  $p=0.7$ ). In the contemporary group data ( $n=106$ ), patients with LOP ( $n=31$ ) had similar levels of anxiety to the EOP patients ( $n=75$ ) based upon the Anxiety subscale of the Hospital Anxiety and Depression scale (HADS; EOP  $6\pm 5$ ; LOP,  $8\pm 5$ ,  $p=0.068$ ). However, in the age restricted cohort ( $\geq 50$  years,  $n=62$ , EOP 32, LOP 30) there was a significant difference between the HADS-A score for the two groups (EOP  $5\pm 5$ ; LOP,  $8\pm 5$ ,  $p=0.006$ ). The Penn State Worry Questionnaire (PSWQ) scores were elevated in LOP and close to the diagnostic cut off of 45 for a diagnosis of excessive worry, although there was no significant difference between the two groups (mean PSWQ for EOP= $43\pm 14$  vs  $46\pm 15$  for LOP). There was no significant difference in the prevalence of possible depression between EOP and LOP group members either (13.7% EOP; 15.5% LOP;  $p=0.720$ ). Data from the second subscale of HADS, the HADS-Depression (HADS-D), were below the cut-off point of 8 in both groups (mean HADS-D for EOP  $4\pm 4$  vs  $5\pm 4$  for LOP,  $p=0.26$ ). Patients who scored  $\geq 8$  in the HADS-D (EOP 44; LOP

14) were asked to complete a Beck Depression Inventory-II (BDI-II), which showed no significant difference between groups (LOP 14±12; EOP 13 ±11; p=0.67).

## Discussion

### Immuno-immunocytochemical findings

We have demonstrated that there are distinct immunoimmunocytochemical differences between the involved skin of LOP and EOP. LOP is characterized by a greater cutaneous inflammatory infiltrate and there are significant differences in the distribution of T-cell subtypes in EOP and LOP. The PP epidermis of LOP contained twice as many CD4+ cells and consequently a higher CD4:CD8 ratio (EOP, 0.05; LOP, 1.3), whilst CD4+ cells were also more plentiful in the PP dermis of LOP as compared to EOP. As there was no significant difference in the number of mean epidermal CD1a+ cells between EOP and LOP, with histiocytic cells rarely seen in the epidermis with the exception of Langerhans cells, it is likely that the majority of CD4+ cells in the epidermis represent lymphocytes.

Recently, research into the psoriasis immunogenetics has revealed significant associations between LOP and the IL-1B-511\*1/1 homozygous genotype, a polymorphic variation of the gene encoding for IL-1 $\beta$  (IL1B gene) and that LOP, and not EOP, is specifically associated with distinct polymorphisms at IL-1B gene<sup>6</sup> (rs16944 and rs2853550;). In addition, there is an impairment of epidermal LCs mobilization in response to IL-1 $\beta$  in the PN skin of EOP but not in LOP<sup>7</sup>. To our knowledge, this is the first study to examine immunoimmunocytochemical differences between the involved and uninvolved skin in EOP and LOP.

Lymphocytes play a key role in the pathogenesis of psoriasis; they induce pathological immune reactions and alter the epidermal homeostasis of PP skin, which in turn leads to the activation of keratinocytes and other immune cells. Influx of CD4<sup>+</sup> T-cells may play a crucial role in the development and maintenance of the inflammatory process in LOP and may in part be a reflection of the non-association of this sub-type of psoriasis with *HLA-Cw\*0602*, unlike EOP which is strongly associated. This finding is underscored by the

understanding that MHC class I is more likely to be linked to the function of CD8 T-cells than to CD4 T-cells <sup>10</sup>.

### **Clinical findings**

In line with previous studies <sup>3,4,11,12</sup>, we confirmed that EOP is a familial form of psoriasis; 62% of EOP patients had family history of psoriasis versus 35.6% of LOP subjects. Having an affected EOP parent was strongly associated with having EOP. This is the first study to detect the association between the age of onset of affected parents and EOP/LOP status in their offspring, and further supports the notion that the age of onset of psoriasis has a strong genetic background.

We found that small thick plaque, guttate, pustular and erythrodermic psoriasis were confined to EOP patients. This is partially congruent with previous research that demonstrated significant associations of EOP with guttate and eruptive psoriasis <sup>5,13</sup>. It is important to note, however, that the sample size of the EOP group is more than four times the size of the LOP group. There is the possibility that these findings could be down to sample size and chance rather than representing a genuine association. Thus, larger studies are needed to interrogate these findings. Nail involvement was present in 88.9% of patients. Contrary to other reports which connect nail psoriasis to either EOP <sup>11</sup> or LOP <sup>14</sup>, both groups had similar occurrence of nail changes.

In line with recent reports <sup>15,16</sup>, EOP patients were more likely to be receiving biologic therapies, whilst LOP patients were more likely to be treated with phototherapy. Our observation that LOP patients had a higher prevalence of thin-plaque psoriasis (either small or large plaque) could act as a source of channelling bias towards phototherapy in this subset as this form has been shown to be more responsive to phototherapy <sup>17,18</sup>.

Our study is the first to extensively explore links between psoriasis comorbidities and the two subtypes of psoriasis. We showed that psoriatic arthritis occurred equally in both disease subsets. In keeping with other research groups, we also found an association of T2DM with LOP after accounting for relevant

potential confounders, including history of ischaemic heart disease, hypertension, dyslipidaemia, central obesity, disease duration and disease severity<sup>19,20</sup>. We demonstrated that LOP patients were approximately 2.5 times more likely to have T2DM compared to EOP patients (OR 2.6, 95% CI 1.001-6.538).

To our knowledge, this is the first study to show an association between AIT and LOP. We showed that LOP patients were 5 times more likely to have AIT than EOP patients. It is unclear from the literature regarding the overall association of AIT with psoriasis – one study found a higher prevalence of AIT in PsA patients as compared to controls<sup>21</sup>, while another study looking at psoriasis patients without PsA did not find an association of AIT with psoriasis<sup>22</sup>. It should be noted that the mean age of the patients with psoriasis in the latter study was 40.5, and therefore this study is unlikely to have included many patients with LOP.

There is strong evidence that psoriasis has a profound psychosocial impact on the daily life of patients<sup>23-25</sup>. It is also well established that anxiety increases with age in psoriasis patients<sup>26</sup>. After controlling for age by stratification, we showed that for patients aged 50 years or above, LOP patients were clinically more anxious than those with EOP, which is contrary to other reports<sup>27,28</sup>.

Limitations to the histologic study include a gender imbalance between study groups, with 80% of EOP patients being male, whereas for the LOP group the male to female ratio was equal. Unsurprisingly, LOP patients had a shorter duration of disease compared to EOP (supplementary data, Table 4), and therefore disease duration cannot be ruled out as a confounder or an intermediate variable accounting for some of our findings. Our study population consisted mainly of Caucasians, hence limiting generalisability to other psoriasis populations. Certain data from the clinical study could be influenced by recall bias. There was also limited information on the *HLA-Cw\*0602* profile of the study patients; thus it remains for a more thorough assessment to be performed of any association between epidermal T-cell phenotypes and HLA status. The sample size for the immunocytochemical study was small and this is reflected in the wide 95% confidence intervals reported.

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## Summary

Our results suggest that an infiltration of epidermal CD4<sup>+</sup> T-cells and the consequent increase in the ratio of epidermal CD4<sup>+</sup>/CD8<sup>+</sup> in the LOP group is a differentiating factor between the two subtypes of psoriasis. There were differences between the demographic and clinical features of EOP and LOP, with a stronger association with family history of psoriasis found in EOP patients, and higher levels of anxiety and stronger associations with T2DM and AIT found in LOP patients. The data add further weight to the hypothesis that EOP and LOP are two distinct subtypes of psoriasis with a difference in immunocytochemical, immunological and demographic background; heritability; clinical phenotypical features and; the experience of anxiety in the sub-group older than 50 years. This in turn should be taken into account when managing the two conditions.

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#### Figure legends

**Figure 1** Box-plot comparing mean epidermal CD4<sup>+</sup>, CD8<sup>+</sup>, CD3<sup>+</sup> and CD1a<sup>+</sup> cell counts in involved skin of early-onset psoriasis (EOP; n=17) and late onset psoriasis (LOP; n=14) patients, presenting the median and the interquartile range. P= p-value for t-test comparing difference in the mean values. There is an increased CD4:CD8 ratio in the PP epidermis of LOP compared to EOP.

Demographics	Frequencies (%) and Mean $\pm$ SD			
	Total cohort (N=340)		Restricted cohort	
	EOP (N=278)	LOP (N=62)	EOP (N=139)	LOP (N=62)
Ethnicity				
White	268 (96%)	58 (94%)	133 (96%)	58 (94%)
Other	10 (4%)	4 (6%)	6 (4%)	4 (6%)
Gender				
Male	148 (53%)	30 (48%)	77 (55%)	30 (48%)
Female	130 (47%)	32 (52%)	62 (45%)	32 (52%)
Age of onset	20.6 $\pm$ 9.9	55.4 $\pm$ 7	24.23 $\pm$ 9.95	55.48 $\pm$ 7.13
Age during study (mean $\pm$ standard deviation)	46.56 $\pm$ 14.53	65.46 $\pm$ 8.62	61.31 $\pm$ 8.38	67.65 $\pm$ 9.06
Disease duration (mean $\pm$ standard deviation)	28.9 $\pm$ 14	12.6 $\pm$ 7.8	36.98 $\pm$ 12.88	12.77 $\pm$ 7.56
Body Mass Index (kg/m <sup>2</sup> )	29.48 $\pm$ 6.8	30.62 $\pm$ 6.66	30.19 $\pm$ 6.51	30.70 $\pm$ 6.59
Waist circumference	97.43 $\pm$ 16.61	104.63 $\pm$ 14.9	100.42 $\pm$ 17.15	104.63 $\pm$ 14.9

**Table 1** Demographic characteristics of the clinical cohort.

EOP – Early-Onset Psoriasis; LOP – Late-Onset Psoriasis

Inheritance Pattern	EOP (%)	LOP (%)	OR	Adj. OR	P	95% CI
No family history of psoriasis <sup>1</sup>	105 (38%)	38 (64.4%)	-	-	-	-
Affected parent(s) with EOP <sup>†</sup>	19 (26%)	1 (3.1%)	0.10	<b>10.34</b>	<b>0.025*</b>	<b>1.32-81.83</b>
Affected parents with LOP <sup>†</sup>	3 (4.1%)	4 (12.5%)	3.5	0.29	0.16	0.49-1.67
1 <sup>st</sup> degree affected relatives	88 (31.9%)	14 (23.7%)	0.44	<b>2.41</b>	<b>0.011*</b>	<b>1.22-4.78</b>
2 <sup>nd</sup> degree affected relatives	42 (15.2%)	5 (8.5%)	0.33	<b>3.38</b>	<b>0.018*</b>	<b>1.23-7.34</b>
Both 1 <sup>st</sup> and 2 <sup>nd</sup> degree affected relatives	41 (14.9%)	2 (3.4%)	0.14	<b>8.32</b>	<b>0.005*</b>	<b>1.90-36.52</b>

**Table 2** Familial predisposition of psoriasis between early-onset (EOP; n=276, missing=2) and late-onset psoriasis (LOP; n=59, missing=3) patients. Odds ratio (OR) for LOP – univariate logistic regression; Adjusted (Adj.) OR for LOP –logistic regression, co-variables included gender, gender of affected parents; <sup>1</sup>Reference category; <sup>†</sup>only taken from contemporary group, n=107; \* represents statistically significant ORs; CI=confidence interval

Clinical phenotype	EOP(n=264, *n=61)	LOP (n=59, *n=23)	X <sup>2</sup> p value
<b>Plaque psoriasis</b>	229 (86.7%)	52 (88.1%)	0.562
<b>Large Thick*</b>	24 (39.3%)	6 (26.1%)	0.207
<b>Large Thin*</b>	18 (29.5%)	11 (47.8%)	0.115
<b>Small Thick*</b>	6 (9.8%)	0 (0%)	0.316
<b>Small Thin*</b>	13 (21.3%)	6 (26.1%)	0.641
<b>Guttate</b>	13 (4.9%)	0 (0%)	0.082
<b>Intertriginous</b>	7 (2.1%)	1 (1.7%)	1.000
<b>Palmoplantar</b>	4 (1.5%)	2 (3.4%)	0.302
<b>Pustular</b>	2 (0.8%)	0 (0%)	0.503
<b>Seborrhoeic</b>	1 (0.4%)	1 (1.7%)	0.332
<b>Erythrodermic</b>	5 (1.9%)	0 (0%)	0.287

**Table 3** Distribution of clinical phenotypes of psoriasis between early onset (EOP) and late onset psoriasis (LOP) groups. To detect significant differences, when the expected count of cells was 0, the test of independent proportions was used. When the expected count of cells was >0 but <5, the Fisher's exact test was used. \*analysis only includes patient from contemporary group (n=84).

Psoriasis Therapies	Current Treatment		
	EOP n=271	LOP n=60	$\chi^2$ (p value)
Missing data	7 (2.5%)	2 (3.2%)	/
No treatment	6 (2.2%)	1 (1.7%)	1.000
Topical treatment	145 (53.5%)	38 (63.3%)	0.166
Phototherapy	<b>5 (1.8%)</b>	<b>8 (13.3%)</b>	<b>&lt;0.001*</b>
Systemics	65 (24%)	11 (18.3%)	0.346
Biologics	<b>43 (15.9%)</b>	<b>2 (3.3%)</b>	<b>0.010*</b>
Systemics and Biologics	7 (2.6%)	0 (0%)	0.358

**Table 4** The use of treatments for psoriasis between early onset (EOP) and late onset psoriasis (LOP) patients (n=331).

