

# Psoriasis/Psoriatic Arthritis Patients' Long-term Treatment Patterns and Adherence to Systemic Treatments Monitoring Recommendations

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**Limited information exists regarding treatment of patients with psoriasis/psoriatic arthritis in primary care. The aim of this study is to assess treatment patterns, adherence, persistence, and compliance in newly diagnosed patients with psoriasis/psoriatic arthritis from 2012 to 2018 in Stockholm, Sweden. In addition, laboratory monitoring before initiation of treatment and at recommended intervals was quantified for patients prescribed methotrexate or biologics. A total of 51,639 individuals were included, with 39% initiating treatment with topical corticosteroids and <5% receiving systemic treatment within 6 months post-diagnosis. During a median (interquartile range) follow-up of 7 (4–8) years, 18% of patients received systemic treatments at some point. Overall, 5-year persistence rates were 32%, 45% and 19% for methotrexate, biologics, and other systemic treatments, respectively. Pre-initiation laboratory tests, as recommended by guidelines, were performed in approximately 70% and 62% of methotrexate and biologics users, respectively. Follow-up monitoring at recommended time intervals occurred in 14–20% and 31–33% of patients prescribed methotrexate and biologics, respectively. These findings highlight gaps in the pharmacological care of patients with psoriasis/psoriatic arthritis, including suboptimal adherence/persistence and inadequate laboratory monitoring.**

*Key words:* adherence; persistence; treatment patterns; guideline concordance; monitoring.

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Psoriasis (PsO) is a chronic, inflammatory disease that affects 2–4% of the worldwide population (1), with one-third of patients developing psoriatic arthritis (PsA) within an average of 7–10 years after onset (2), resulting in additional social, work, and healthcare-related impact (3). During recent decades, there has been increased awareness of PsO in society, Swedish national and international consensus treatment guidelines have been established, and significant changes in treatment

## SIGNIFICANCE

This study explored treatment patterns and persistence among newly diagnosed patients with psoriasis/psoriatic arthritis (PsO/PsA). Importantly the study included patients diagnosed in primary care, enabling a more comprehensive coverage of the psoriasis population. Swedish treatment guidelines include laboratory monitoring recommendations for systemic treatment. However, the degree to which monitoring guidelines are implemented is unclear. The study highlights several shortcomings in the management of patients with psoriasis, including insufficient monitoring and inadequate treatment compliance. These findings call for both further study regarding the low compliance with monitoring recommendations and improvement in the management of patients with psoriasis to ensure better patient outcomes.

options have been launched. Despite this, reports from several countries suggest undertreatment of patients with PsO (4, 5).

Treatment recommendations are based on disease severity, its impact on quality of life, and the localization of PsO lesions. Guideline-indicated therapeutic options include topical therapies and phototherapy for mild-moderate psoriasis and systemic therapies for more severe cases. These may include oral treatments, such as methotrexate (MTX) or biologics, but the choice of a systemic drug requires consideration of cost-effectiveness, patient satisfaction, comorbidities, and compliance (6, 7).

Studies evaluating treatment patterns and compliance with systemic treatments in PsO have often been short-term (8–10), including both prevalent and incident PsO patients (8–10) or representing only dermatology-specialized practices (8, 11, 12). As a result, there is little information on long-term treatment patterns including non-dermatology/rheumatology specialist care, which may comprise a large proportion of patients with PsO.

European and Swedish treatment guidelines recommend close monitoring for laboratory abnormalities in patients with PsO initiating systemic therapies, in order to detect and avoid possible side-effects (13). However, much of the supporting data is extrapolated from non-dermatological conditions. The extent to which monitoring recommendations are followed in routine practice

in general, and in Sweden in particular, has not been well characterized.

The aims of this study were to evaluate treatment patterns, treatment compliance, and persistence among newly diagnosed patients with PsO/PsA in the region of Stockholm, Sweden, including primary care. Finally, the study assessed the agreement between laboratory monitoring of PsO/PsA patients in routine care and guideline recommendations.

## MATERIALS AND METHODS

### Data source

This study is based on data from the Stockholm Creatinine Measurements (SCREAM) project in Stockholm, Sweden, that collects laboratory test results and healthcare utilization data (including primary and subsidized healthcare) from residents in the region between 2006 and 2021 (14).

### Study population

The study included individuals with a first-recorded diagnosis of PsO/PsA from Jan 2006 to Dec 2018. Patients with inflammatory comorbidities treated with systemic treatments that coincide with those of PsO/PsA were excluded (Table S1 and Fig. S1). Patients with PsA were not excluded (15). Patients with only PsO index-diagnoses are referred to as "PsO patients", while patients with both PsO and PsA or PsA-only index-diagnoses are referred to as "PsO+PsA/PsA patients". The index date was defined as the date of the first-encountered diagnosis of PsO/PsA and it varied across analyses (further details on the index dates are shown in Fig. S1). Patients were followed until death, emigration from the region, or study-end (31 December 2019).

### Psoriasis/psoriatic arthritis treatment

This study evaluated the use of phototherapy and various pharmacological medications, including topical treatments, non-biologic systemic drugs, and systemic biologics, used to manage PsO/PsA (details and definitions are shown in Table SII) [AQ2]. Systemic drugs were categorized into 3 groups: MTX, biologics, and other systemic treatments (i.e. all oral conventional DMARDs and newer small molecules drugs used in PsO/PsA except MTX). The utilization of these drugs was determined using data from the Swedish National Prescribed Drug Register (16), as well as recorded infusions or phototherapy procedures in the Region Stockholm healthcare utilization database (17).

### Outcome measures

**Treatment patterns.** The study assessed the proportion of patients initiating treatment and the type of treatment after receiving a diagnosis of PsO/PsA. Median time to treatment initiation per pharmacological treatment was reported. Changes in treatment were quantified for prevalent users, who were already using the treatments at the time of diagnosis. Time-trends in treatment patterns were evaluated by calendar year. Prevalent medication users were identified using filled prescriptions in the 6 months previous to the index date.

**Treatment discontinuation, re-initiation, switch, enrichment, and adherence.** Among patients who initiated systemic treatments during observation this study evaluated: treatment discontinuation (also called non-persistence). This was identified as a gap of at least 90 days in medication supply after the previous drug

fill. If patients had a supply of the same drug available from a prior prescription, it was added to the supply of the following prescription. Re-initiation was a new recorded fill of the same systemic treatment, which was identified as discontinuation. Treatment switch was defined as filling a drug prescription that was different from any previous treatment before and within the time gap defining persistency of the earlier drug. Switching from oral MTX to subcutaneous MTX therapy and between different biologics was identified as persistence. Treatment enrichment was filling an additional medication class while continuing therapy of another medication class.

Treatment adherence was assessed using the proportion of days covered (PDC) method. This involved calculating the number of days the patient was covered by medication during a given observation period (6 months or yearly intervals) divided by the length of the same period in days. Patients were categorized based on their adherence level: highly adherent (PDC  $\geq$  80%), moderately adherent (PDC 20–79%), and poorly adherent (PDC < 20%) (18).

**Concordance with guidelines for laboratory monitoring.** Among new users of MTX or biologics, this study assessed whether laboratory monitoring for adverse effects was consistent with the guidelines. Patients on combination therapy were excluded. The study analysed whether patients underwent testing for kidney, liver, and haematological levels at the recommended intervals in the Swedish guidelines (19). Creatinine, alanine aminotransferase or aspartate aminotransferase, haemoglobin, and complete and differential blood counts were evaluated. Laboratory measurements before treatment initiation were ascertained 60 days before or within 2 days after the index date. Post-initiation monitoring for MTX was recommended at 1, 3, 5 and 7 weeks, and every 6 months thereafter. For biologics, testing was recommended after 12 weeks and annually thereafter. Patients were censored at the date of their first treatment discontinuation, switch, or enrichment with a different systemic agent.

### Study covariates

Study covariates, including demographics, comorbid conditions, estimated glomerular filtration rate (eGFR), baseline laboratory tests, care setting department (dermatology/rheumatology/other), and medications were collected from issued clinical diagnoses and filled prescriptions in the 6 months previous to the index date (see Tables SII and SIII for details and definitions).

### Statistical analysis

The baseline characteristics were assessed using descriptive statistics. Continuous variables were summarized using means and standard deviations (SD) or medians and interquartile ranges (IQR), while categorical variables were presented using absolute and relative frequencies. The median time to first treatment initiation for each pharmacological drug was reported.

Persistence and adherence analyses were performed on patients with  $\geq$  1 year of follow-up. Each treatment episode of individual pharmacological treatments was analysed separately. Consequently, patients could be included in more than 1 treatment class. Kaplan–Meier curves were generated to present the probability of persistence, restart, switching, and enrichment at specific time-points. Median times to events were estimated using the Kaplan–Meier function.

The proportion of patients who had pre-initiation and follow-up laboratory tests at recommended intervals was reported. Multivariable logistic regression was used to identify predictors of failure to perform short-term ( $\leq$  6 months) and long-term (> 6–12 months) guideline-recommended monitoring.

Where indicated, paediatric patients (< 18 years old) were analysed separately from adults. Missing laboratory tests, which were

not ordered by the attending physician, were hence assumed to not be missing at random and categorized as "missing". The statistical analyses were performed using R, version 4.0.

## RESULTS

### Population characteristics

The study identified 51,639 patients with newly diagnosed PsO/PsA (Fig. S2 shows exclusions), with a mean age of 48.2 years and 49% males (Table I). Only 2,782 (5.4%) had PsO+PsA/PsA at index, while 5.5% of the cohort received an additional diagnosis of PsO+PsA/PsA during follow-up. Of the total cohort, 6.4% ( $n=3,318$ ) were paediatric patients (<18 years old).

### Treatment initiation patterns and changes over time

During a median (IQR) follow-up of 80 (45–100) months (~7 (4–8) years), 1.6% of patients ( $n=828$ ) died, while 3.7% ( $n=1,933$ ) were censored due to emigration from the Stockholm region. Patients with PsO+PsA/PsA were more likely to start treatment with a systemic agent (59%), primarily MTX (45%) and biologics (30%) compared with patients with PsO (9.3% MTX and 4.1% biologics) (Fig. S3).

**First-line of treatment.** Overall, 48% of patients received treatment within 6 months from diagnosis, and 76% initiated treatment throughout the entire follow-up (Fig. 1). Topical corticosteroids (39%) and phototherapy (4%) were the most common first-line treatments. A smaller proportion of patients began with systemic treatments, such as MTX (2.5%), biologics (0.5%), and other systemic treatments (<0.5%) (Fig. 1). Patients with PsO+PsA/PsA were more likely to start treatment directly with a systemic agent (37%), primarily MTX (24%) and biologics (6.4%), compared with patients with PsO (2.1%). Fig. S3 presents these treatment patterns by diagnosis (PsO or PsO+PsA/PsA) and age (paediatric or adult).

**Initiation of systemic treatments.** Eighteen percent of patients in the cohort initiated systemic treatments during follow-up, with MTX being the most common (11%), followed by biologics (5.5%) (Fig. 1). Trends showed a stable proportion of patients with PsO initiating MTX, but a progressive increase in biologic use (from 5% in 2006 to 15% in 2019, Fig. S4). The proportion of patients receiving biologics as first-choice systemic treatment was larger in patients with PsO+PsA/PsA (from 8% in 2005 to 40% in 2019) (Fig. S4b, left panel). There were no clear trends in paediatric patients (Fig. S4c, right panel). Patients with PsA+PsO/PsA initiated MTX and biologics earlier after diagnosis than patients with

**Table I. Baseline characteristics of patients receiving a new diagnosis of psoriasis/psoriatic arthritis (PsO/PsA) in Stockholm, Sweden, during 2006–2019, overall and by age strata**

	Children (<18 years) N = 3,318	Adults (≥18 years) N = 48,321	Overall N = 51,639
Age, years; mean [SD]	11.3 [4.5]	50.8 [17.4]	48.2 [19.4]
Age categories, n (%)			
< 18 years	3,318 (100)	0 (0)	3,318 (6.4)
18–44 years	0 (0%)	18,603 (38)	18,603 (3)
45–64 years	0 (0%)	17,849 (37)	17,849 (35)
65+ years	0 (0%)	11,869 (25)	11,869 (23)
Sex, n (%)			
Male	1,609 (48)	23,942 (50)	25,551 (49)
Female	1,709 (52)	24,379 (50)	26,088 (51)
eGFR, mL/min/1.73m <sup>2</sup> ; mean [SD]	143.9 [24.0]	89.6 [20.2]	90.7 [21.7]
eGFR categories, n (%)			
≥ 60 mL/min/1.73 m <sup>2</sup>	584 (18)	25,734 (53)	26,319 (48)
30–59 mL/min/1.73 m <sup>2</sup>	0 (0)	1,913 (4.0)	1,913 (3.7)
< 30 mL/min/1.73 m <sup>2</sup>	1 (<0.1)	218 (0.4)	219 (0.4)
Missing	2,733 (82)	20,455 (42)	23,188 (45)
Index diagnosis, n (%)			
PsO+PsA/PsA	136 (4.1)	2,646 (5.5)	2,782 (5.4)
PsO	3,182 (96)	45,675 (95)	48,857 (95)
Additional diagnosis of PsO+PsA/PsA during follow-up, n (%)	87 (2.6)	2,736 (5.7)	2,823 (5.5)
Comorbid conditions, n (%)			
Hypertension	3 (<0.1)	10,866 (22)	10,869 (21)
Diabetes mellitus	23 (0.7)	3,573 (7.4)	3,596 (7.0)
Myocardial infarction	0 (0)	957 (2.0)	957 (1.9)
Peripheral arterial disease	3 (<0.1)	864 (1.8)	867 (1.7)
Cerebrovascular disease	2 (<0.1)	1,371 (2.8)	1,373 (2.7)
Heart failure	2 (<0.1)	1,184 (2.5)	1,186 (2.3)
Atrial fibrillation	0 (0)	1,688 (3.5)	1,688 (3.3)
Liver disease	2 (<0.1)	410 (0.8)	412 (0.8)
Melanoma	0 (0)	1,086 (2.2)	1,086 (2.1)
Relevant treatments for PsO/PsA, n (%)			
Prevalent use of:	610 (18)	14,180 (29)	14,790 (29)
Topical corticosteroids	592 (18)	13,443 (28)	14,035 (27)
Topical calcineurin inhibitors	23 (0.7)	310 (0.6)	333 (0.6)
Biologics	3 (<0.1)	209 (0.4)	212 (0.4)
Anti-TNF-α inhibitors	3 (<0.1)	196 (0.4)	199 (0.4)
Interleukin inhibitors	0 (0)	17 (<0.1)	17 (<0.1)
Methotrexate	16 (0.5)	726 (1.5)	742 (1.4)
Other systemic treatments	135 (4.1)	3,256 (6.7)	3,391 (6.6)
Sulfasalazine	1 (<0.1)	137 (0.3)	138 (0.3)
Alitretinoin	0 (0)	140 (0.3)	140 (0.3)
Leflunomide	0 (0)	11 (<0.1)	11 (<0.1)
Apremilast	0 (0)	20 (<0.1)	20 (<0.1)
Dimethyl fumarate	0 (0)	4 (<0.1)	4 (<0.1)
Cyclosporine	1 (<0.1)	23 (<0.1)	24 (<0.1)
Other ongoing medications, n (%)			
RASi	3 (<0.1)	7,262 (15)	7,265 (14)
Diuretic	2 (<0.1)	3,521 (7.3)	3,523 (6.8)
Beta-blocker	7 (0.2)	6,035 (12)	6,042 (12)
Lipid-lowering	0 (0)	5,149 (11)	5,149 (10.0)
Anti-diabetics	18 (0.5)	2,535 (5.2)	2,553 (4.9)
Systemic glucocorticoids	71 (2.1)	1,964 (4.1)	2,035 (3.9)
NSAIDs	145 (4.4)	6,605 (14)	6,750 (13)
Laboratory determinations, n (%)			
C-reactive protein			
< 1 mg/dL	291 (8.8)	4,555 (9.4)	4,846 (9.4)
≥ 1–< 3 mg/dL	529 (16)	11,796 (24)	12,325 (24)
≥ 3–< 10 mg/dL	500 (15)	10,800 (22)	10,035 (19)
≥ 10 mg/dL	304 (9)	9,731 (20)	10,035 (19)
Missing	1,694 (51)	11,439 (24)	13,133 (25)
Haemoglobin			
< 10 g/dL	15 (0.8)	1,369 (2.8)	1,384 (2.7)
>= 10 g/dL	1,831 (42.3)	38,882 (80)	40,713 (79)
Missing	1,472 (44)	13,121 (27.1)	9,542 (18)
AST, n (%)			
Normal level (< 100 IU/L)	1,312 (40)	31,445 (65)	32,757 (63)
Mild elevation (100–249 IU/L)	10 (0.3)	521 (1.1)	531 (1.0)
Moderate elevation (250–2000 IU/L)	1 (<0.1)	142 (0.3)	143 (0.3)
Large elevation (> 2000 IU/L)	1 (<0.1)	52 (0.1)	53 (0.1)
Missing	1,994 (60)	16,161 (33)	18,155 (35)
ALT, n (%)			
Normal level (< 100 IU/L)	1,546 (47)	36,709 (76)	38,255 (74)
Mild elevation (100–249 IU/L)	23 (0.7)	613 (1.3)	636 (1.2)
Moderate elevation (250–2,000 IU/L)	2 (<0.1)	111 (0.2)	113 (0.2)
Large elevation (> 2,000 IU/L)	2 (<0.1)	45 (<0.1)	47 (<0.1)
Missing	1,745 (53)	10,843 (22)	12,588 (24)

RASi: renin-angiotensin system inhibitors; NSAIDs: non-steroidal anti-inflammatory drugs; AST: aspartate aminotransferase; ALT: alanine aminotransferase; SD: standard deviation.

PsO (median time for MTX 13 respectively 27 months, and for biologics 13 respectively 55 months) (Fig. S5). *Treatments pattern over time.* Fig. S6 shows the patterns of medication use over the years since diagnosis. Patients with PsO showed a gradual increase in systemic treatment, with a larger increase in biologics than MTX (Fig. S6a), especially among paediatric patients (Fig. S6c). In contrast, patients with PsO+PsA/PsA had high and constant use of systemic treatments since the early years after diagnosis (Fig. S6b).

*Persistence, re-initiation, switching, enrichment, and adherence with systemic treatments.* A total of 6,345 patients who started systemic treatments and had at least 1 year of follow-up were included (Fig. S2 and Table SIV). Most patients started MTX (64%), followed by other systemic treatments (26%) and biologics (10%). These patients were followed for a median (IQR) of 65 (35–103) months (~5 (3–9) years). Overall, 5-year persistence rates were 32%, 45%, and 19% for MTX, biologics, and other systemic treatments, respectively (Table II). Patients on biologics demonstrated relatively longer persistence, with a median of 52 months without interruptions, while persistence was lower for MTX (24 months) and lowest for other systemic treatments (10 months) (Fig. S7a). Across all therapies, persistence decreased with time (Table II). Biologics had significantly lower switching rates compared with MTX or other systemic drugs (Fig. S7b). Re-initiation rates significantly differed between the 3 groups, and the mean time from discontinuation to restart was 13 months for MTX, 18 months for biologics, and 46

months for other systemic treatments (Table II and Fig. S7c). Discontinuation and re-initiation of treatment were more common than treatment switch for all 3 categories of treatments. Adherence rates for biologics and MTX were highest during the first few months, but decreased gradually over time (Fig. 2 and Fig. S8).

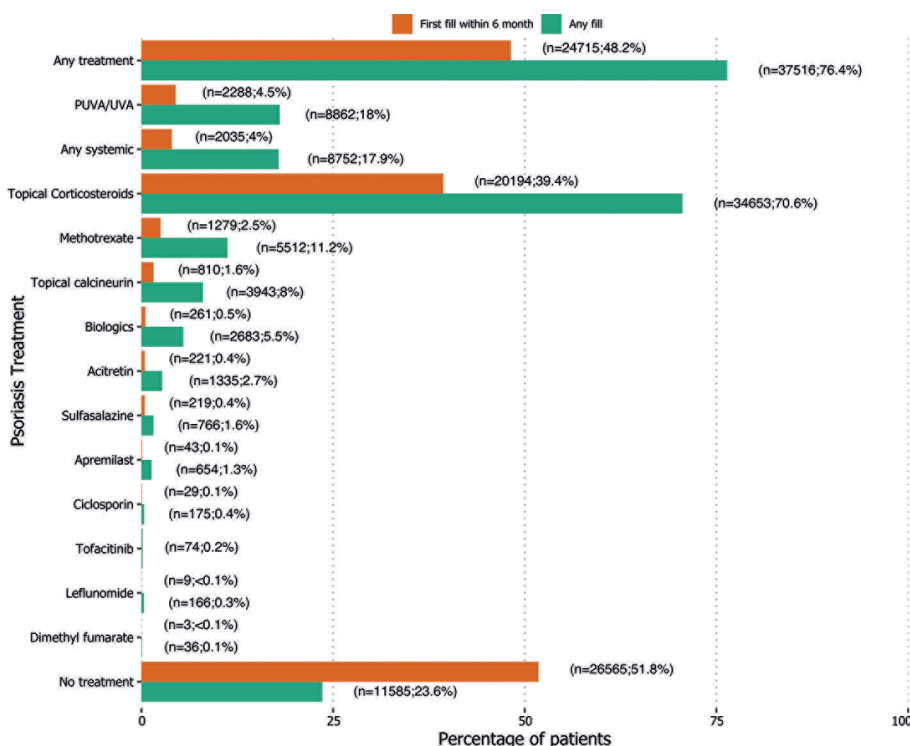
#### Concordance with laboratory monitoring guidelines

Laboratory monitoring compliance was evaluated in patients who initiated MTX or biologics as monotherapy. Their baseline characteristics are shown in Table SV.

Among MTX users, 26–29% did not have evidence of testing for creatinine, liver function, or haematological parameters prior to treatment. The proportion of patients compliant with laboratory monitoring according to the guidelines during the first year was low and decreased with time (Fig. 3). The lowest rate of laboratory monitoring was identified for renal function. Approximately 80% of patients did not receive consistent guideline-compliant monitoring during the entire follow-up of use (Fig. 3).

Among users of biologics, 38% did not have liver function, complete and differential blood counts, and haemoglobin levels checked before starting the treatment (Fig. 3). The proportion of patients who underwent recommended monitoring during the follow-up was low, with over 60% not receiving consistent guideline-compliant monitoring.

On multivariable analyses (Fig. 4, right panel), few of the hypothesized predictors demonstrated a definite association with the likelihood of non-monitoring. In general,

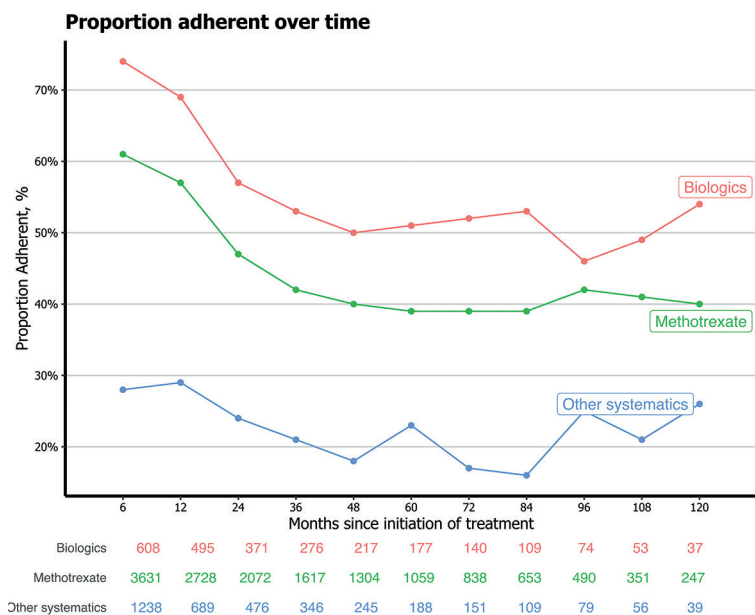


**Fig. 1. First line of medication filled within 6 months from psoriasis/psoriatic arthritis diagnosis (orange bars) or at any time post-diagnosis (green bars).** The denominator is the total number of patients with follow-up available at each period: N=51,280 at 6 months; N=49,101 at all post-index.

**Table II. Time and survival rate from initiation of systemic treatments to first detected treatment discontinuation, switch, enrichment or restart**

	Methotrexate N = 4,113			Biologics <sup>a</sup> N = 625			Other systemics <sup>b</sup> N = 1,643		
	n at risk	n event	Survival rate (%)	n at risk	n event	Survival rate (%)	n at risk	n event	Survival rate (%)
<b>Treatment persistence</b>									
3 months	3,886	636	84.3	581	52	91.6	1,053	407	73.8
6 months	2,995	164	79.9	527	41	84.8	762	142	62.2
12 months	2,159	561	63.7	433	62	74.2	449	168	45.9
24 months	1,223	409	49.5	259	54	62.9	208	104	32.6
60 months	372	315	31.9	72	41	45.6	44	60	19.0
120 months	67	66	23.4	9	9	37.2	4	9	13.0
Median months to non-persistence (95% CI)	24 (22–26)			52 (42–65)			10 (9–12)		
<b>Treatment switch</b>									
3 months	3,743	110	97.2	522	5	99.2	1,019	110	92.0
6 months	2,775	40	95.8	455	2	98.8	711	40	87.6
12 months	1,912	71	92.9	355	2	98.3	409	34	81.8
24 months	995	52	89.4	206	3	97.3	173	12	78.1
60 months	269	24	85.6	52	0	97.3	30	2	77.0
120 months	42	5	83.3	6	0	97.3	1	0	77.0
Median months to switch (95% CI)	NR (NR–NR)			NR (NR–NR)			NR (NR–NR)		
<b>Treatment enrichment</b>									
3 months	3,505	280	92.5	443	52	89.9	958	172	86.9
6 months	2,600	150	87.5	390	17	86.1	668	68	79.5
12 months	1,784	191	79.9	308	16	82.1	385	50	71.9
24 months	925	171	70.0	178	13	77.8	164	42	61.3
60 months	253	129	54.4	44	8	72.0	30	17	47.8
120 months	40	34	41.0	6	1	69.4	1	5	27.8
Median months to enrichment (95% CI)	74 (62–92)			NR (NR–NR)			47 (41–73)		
<b>Treatment restart (among discontinuers)</b>									
3 months	2,162	214	90.1	256	24	90.6	914	96	89.5
6 months	1,458	617	61.6	178	66	64.8	637	217	65.8
12 months	1,109	245	50.2	144	26	54.7	527	84	56.6
24 months	836	125	44.1	102	19	46.8	418	29	53.2
60 months	438	75	39.1	43	12	39.2	226	27	48.7
120 months	119	28	35.8	9	3	34.0	58	7	46.4
Median months to restart (95% CI)	13 (11–17)			18 (12–37)			46 (50–NR)		

Kaplan–Meier function was >0.5 for the duration of the study, thus median times or CI to switch could not be estimated.  
<sup>a</sup>Consists of 188 adalimumab, 7 certolizumab pegol, 328 etanercept, 19 infliximab, 1 ixekizumab, 33 secukinumab and 49 ustekinumab treatment episodes. <sup>b</sup>Consists of 898 acitretin, 186 apremilast, 75 cyclosporine, 11 dimethyl fumarate, 26 leflunomide, 446 sulfasalazine, and 1 Tofacitinib treatment episodes.  
 NR: not reached; 95% CI: 95% confidence interval.

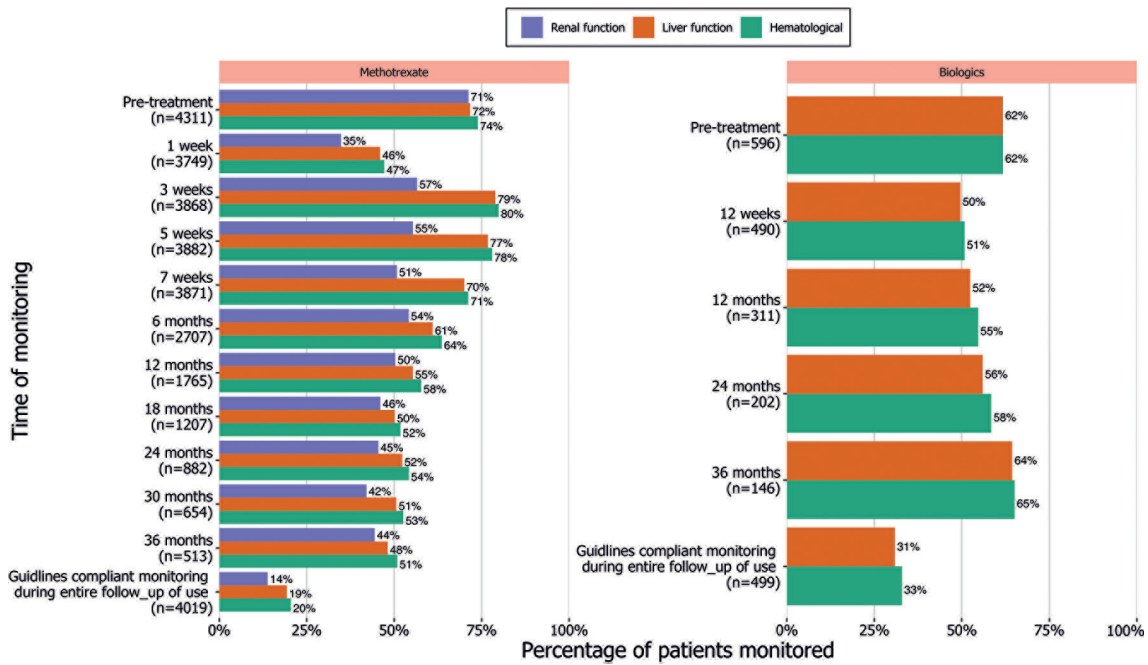


**Fig. 2. Adherence rate methotrexate, biologics, or other systemic treatments.** Adherent patients are defined as those with a proportion of days covered of 80% or higher.

patients who received MTX treatment in non-hospital departments, those with PsO, and those without laboratory values in their medical records were more likely to be non-monitored. For biologics, patients with eGFR <60 mL/min/1.73 m<sup>2</sup> and a history of liver disease were more likely to be monitored.

## DISCUSSION

This study of newly diagnosed patients with PsO/PsA from the Stockholm region, including data from primary care centres, made some key observations. Firstly, most patients were treated with topical treatments, and approximately 18% received systemic treatments, with MTX being the most common. Secondly, treatment adherence and persistence were found to be suboptimal across all systemic treatments, with a gradual decline over longer treatment durations. Among these treatments, biologics exhibited a relatively higher persistence and adherence rate.

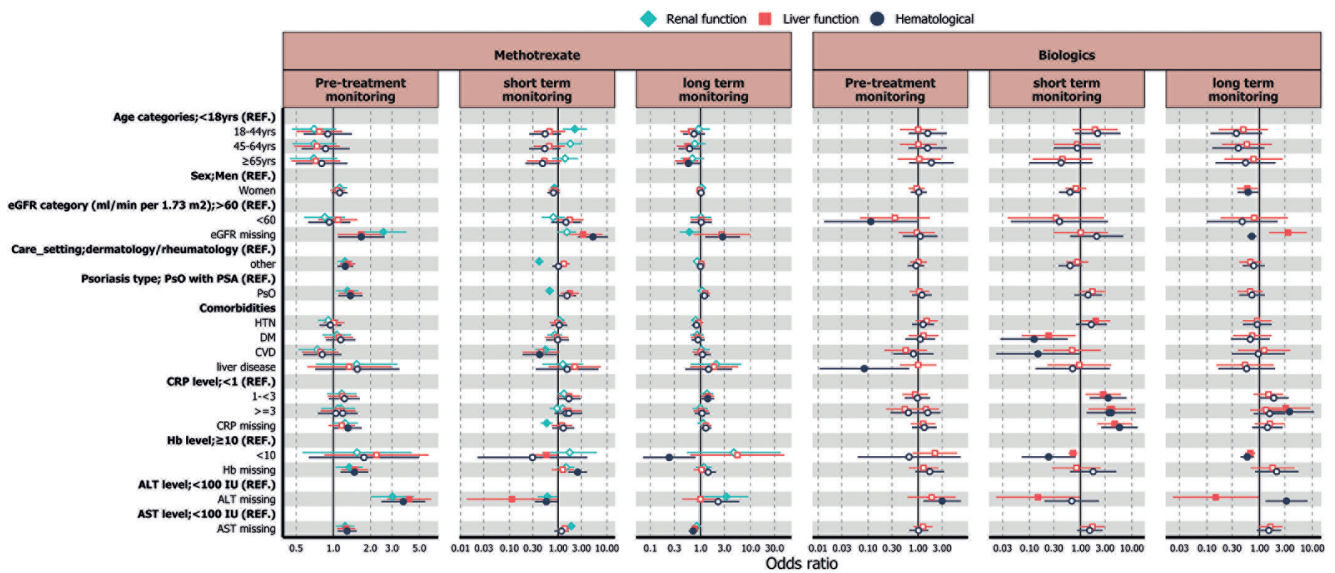


**Fig. 3. Proportion of patients undergoing laboratory tests at the intervals recommended by national guidelines.** The x-axis represents the percentage of patients monitored. The y-axis represents the guideline recommended intervals/time of monitoring.

Thirdly, the laboratory monitoring was also suboptimal and did not follow the national guidelines.

The study found that 27% of patients with PsO and 17% of patients with PsO+PsA did not receive any pharmacological treatment. There is a lack of information on disease severity, but higher rates of untreated patients have previously been reported in other studies from dermatology clinics in Europe and North America, where up to 40% of patients with moderate to severe PsO remained untreated (5, 20, 21). The current study might reflect the real-world population more comprehensively by including those patients with milder disease managed

in primary care. The inclusion of these milder cases could also explain the large proportion of patients managed solely with topical corticosteroids (19) in the current study. The study shows that 18% of patients received systemic treatment, primarily MTX. The use of MTX has been stable over time, while the use of biologics has increased slowly, which is consistent with trends in other countries (22–25). This pattern is expected, as MTX has been the recommended first-line systemic treatment for PsO in Sweden until 2019 when TNF- $\alpha$  was added as first-line systemic treatment. Since 2019, Swedish guidelines recommend methotrexate as the preferred first-line



**Fig. 4. Predictors of laboratory non-monitoring.** Short-term and long-term monitoring was defined as  $\leq 3$  months and  $> 3$ –12 months post-treatment initiation follow-up window. Significant estimates are shown as solid circles.

systemic treatment agent or directly biologics (adalimumab) if the patient has severe localized psoriasis (19).

The current study also evaluated the quality of pharmacological management for patients with PsO/PsA. Although prescribing relevant medications is crucial, it is ineffective if patients do not adhere to or persist with the treatment. In general, inadequate adherence and persistence rates were observed for all systemic treatments. It is not possible to elucidate the cause of the low rates of adherence and persistence from observational studies such as this. However, this highlights the need for improved patient-clinician interaction, support programmes, and discussion of risk/benefits/efficacy of treatments, all of which have been shown to improve adherence and persistence (26–28). Furthermore, existing literature suggests that biologics, including interleukin inhibitors, have been associated with higher adherence and persistence rates (6, 29, 30). However, it is worth noting that the current study was unable to analyse individual biologic subclasses separately due to the recent introduction of interleukin inhibitors (IL12/23i and IL17i) in the Swedish healthcare system. Consequently, it has not been possible to provide specific insights regarding the persistence rates of these subclasses within the current study dataset.

A novel and important finding pertains to the observed suboptimal rates of laboratory monitoring, in disagreement with guideline recommendations (19, 32). Pre-evaluation of renal, liver, and haematological parameters were lacking in 30–40% of patients newly started on MTX or biologics, and only 20–30% of patients underwent the recommended annual monitoring. During long-term therapy, 50% of patients did not undergo annual monitoring. Other studies from different regions of the world have suggested suboptimal monitoring to be common, with rates as low as 42% reported in a German study (32) of patients initiating MTX, and <65% in a UK cohort (33) from general practitioners. A French study reported that approximately 65% of patients starting MTX underwent pre-initiation monitoring and <50% during follow-up and that more frequent monitoring led to earlier discontinuation of MTX therapy (34). Factors that may contribute to suboptimal monitoring include patient awareness of the need for monitoring, physician knowledge of monitoring guidelines, and time and resource constraints. In addition, physicians may perceive certain treatments, particularly novel biologics, as safe, based on results from randomized controlled trials and real-world registry studies. As a result, they may perceive less need for laboratory monitoring than the current guidelines recommend. The current study analysis shows that diagnosis and prescriber characteristics were factors affecting laboratory monitoring. Suboptimal monitoring was more common in patients with PsO compared with those with PsO+PsA, among patients managed in non-hospital departments and among those with no prior laboratory test information. Further research is needed

to understand the reasons for non-compliance with these recommendations.

The strengths of this study include a contemporary population with long follow-up and completeness of care settings, making it less susceptible to biases from the fragmentation of care. Sweden's universal healthcare system also minimizes selection bias from access to healthcare. However, the current study has limitations. First, there is a lack of information on disease severity or patient treatment satisfaction measures. Secondly, the study used treatment episodes instead of individual patients, which may impact outcomes by rapid cycling of treatment within 1 class or needing augmentation soon after treatment begins. Furthermore, treatments were dispensed at the pharmacy, but it is not known if they were taken as recommended. Finally, these results represent clinical practice in Stockholm during a defined period, and caution should be used when extrapolating these findings to other regions, countries, or health systems. However, literature suggests that similar practice gaps may exist elsewhere.

In conclusion, this study identifies gaps in the care of patients with PsO/PsA that warrant correction, involving suboptimal adherence/persistence for all systemic treatments, and especially, inadequate laboratory monitoring.

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The Regional Ethical Review Board in Stockholm approved the study (approval number: EPN 2017/793-31).

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