

Eligibility of TREATgermany registry patients for systemic treatment for atopic dermatitis according to the German S3 guideline's checklist criteria



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Introduction & Objectives: Referring to the German S3 guideline's¹ checklist for the indication for systemic therapy (ST) in patients with atopic dermatitis (AD) two research questions were posed: 1. How many patients without ST at enrollment in the registry satisfy the checklist criteria and subsequently receive ST? 2. How many patients receive ST without satisfying the checklist criteria?

Methods: Data from the TREATgermany registry (up to 12/2024) was used, including information on 2,369 adults from 71 study centers. For 1,480 patients who did not receive ST for AD at inclusion in the registry the documentation was sufficient to apply the S3 guideline's checklist criteria. Logistic models were used to further investigate potential factors influencing the decision for or against prescribing a ST.

Results: 1,048 (70.8%) out of 1480 patients without ST satisfied the checklist criteria at enrollment, and 432 patients (29.2%) did not. Of the 1,048 patients fulfilling the checklist criteria, 768 patients (73.3%) started systemic therapy, whereas 280 patients (26.7%) did not. Here, the models indicate that females had a lower chance of starting ST (odds ratio (OR)=0.58). The group of those who did not meet the checklist criteria is divided into 247 patients (57.2%) who started on a ST and 185 patients (42.8%) who did not. The more recent the enrollment in the registry (ranging from 2016 to 2024) the higher were the chances for receiving ST. Furthermore, there appears to be a role for physician (study center) preferences (ORs ranging from 0.3 to 14.5) affecting the decision to prescribe a ST.

Conclusions: TREATgermany data reflect that the physician's indication for ST in adults with AD increased since 2016 and, for the majority of patients, is consistent with the German S3 guideline's criteria for ST for AD. Nevertheless, there is a need for more-in-depth analysis to identify the reasons why a subgroup, predominantly females, does not receive ST, even though the checklist criteria are met.

¹S3-Leitlinie „Atopische Dermatitis“ (AWMF-Registernr. 013-027) (2023) verfügbar unter: <https://register.awmf.org/de/leitlinien/detail/013-027>

Grouping TREATgermany patients at registry inclusion according to S3 guideline's checklist criteria

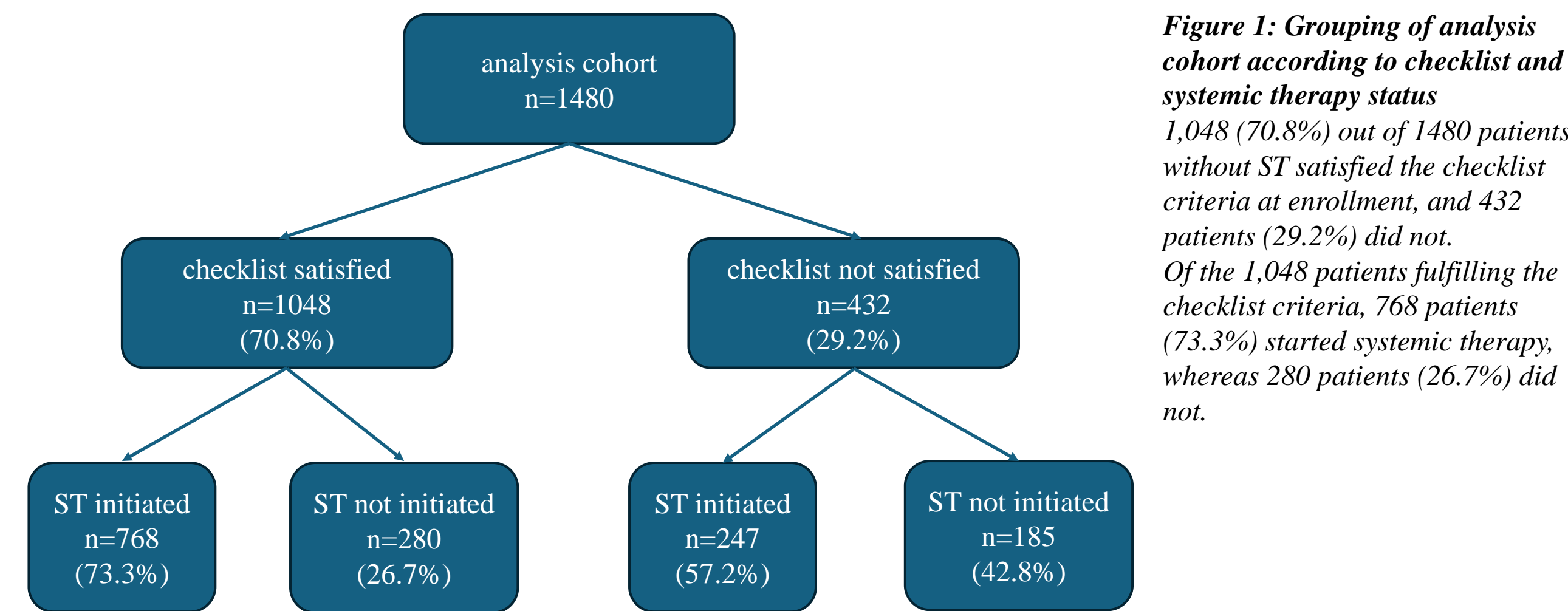


Figure 1: Grouping of analysis cohort according to checklist and systemic therapy status
1,048 (70.8%) out of 1480 patients without ST satisfied the checklist criteria at enrollment, and 432 patients (29.2%) did not. Of the 1,048 patients fulfilling the checklist criteria, 768 patients (73.3%) started systemic therapy, whereas 280 patients (26.7%) did not.

Table 1: Baseline characteristics of AD patients within the TREATgermany registry at ST initiation.

	Total	Checklist satisfied	Checklist satisfied & therapy start	Checklist not satisfied	Checklist not satisfied & therapy start	Checklist not satisfied & no therapy start
N	1480	1048	768	432	247	185
Sex (female)	692 (46.8%)	517 (49.3%)	366 (47.7%)	151 (53.9%)	99 (40.5%)	76 (41.1%)
Age, mean ± SD	38.9 ± 15.0	38.8 ± 14.8	38.6 ± 14.7	39.5 ± 15.0	39.0 ± 15.4	40.1 ± 15.8
Age of AD onset						
before school age	1062 (72.8%)	755 (73.3%)	568 (75.2%)	187 (68.2%)	308 (71.6%)	176 (71.8%)
during school age	190 (13.0%)	131 (12.7%)	96 (12.7%)	35 (12.8%)	59 (13.8%)	28 (15.2%)
during adulthood	206 (14.1%)	143 (13.9%)	91 (12.1%)	52 (19.0%)	63 (14.7%)	25 (13.6%)
Allergic comorbidities	862 (58.6%)	625 (60.0%)	462 (60.4%)	163 (59.1%)	237 (55.0%)	135 (54.9%)
Currently smoker	353 (23.9%)	257 (24.6%)	184 (24.0%)	73 (26.3%)	96 (22.3%)	61 (24.8%)
Type of study centre (practice)	585 (39.5%)	392 (37.4%)	304 (39.6%)	88 (31.4%)	193 (44.7%)	126 (51.0%)
Year of enrolment, mean ± SD	2020.5 ± 2.4	2020.5 ± 2.4	2021.1 ± 2.1	2018.6 ± 2.1	2020.4 ± 2.4	2021.5 ± 2.0
High level of suffering (PGA ≥ 4)	749 (50.7%)	608 (58.2%)	481 (62.9%)	127 (45.5%)	141 (32.6%)	108 (43.7%)

Larger recruiting sites and operationalization of checklist criteria

Study centre	Checklist satisfied			Checklist not satisfied		
	Checklist satisfied	Checklist satisfied & therapy start	Checklist satisfied & no therapy start	Checklist not satisfied	Checklist not satisfied & therapy start	Checklist not satisfied & no therapy start
centre #1	61 (5.8%)	50 (6.5%)	11 (3.9%)	21 (4.9%)	17 (6.9%)	4 (2.2%)
centre #2	81 (7.7%)	32 (4.2%)	49 (17.5%)	46 (10.6%)	10 (4.0%)	36 (19.5%)
centre #3	52 (5.0%)	51 (6.6%)	1 (0.4%)	21 (4.9%)	20 (8.1%)	1 (0.5%)
centre #4	123 (11.7%)	89 (11.6%)	34 (12.1%)	48 (11.1%)	22 (8.9%)	26 (14.1%)
centre #5	108 (10.3%)	83 (10.8%)	25 (8.9%)	29 (6.7%)	6 (2.4%)	23 (12.4%)
other study centres	623 (59.4%)	463 (60.3%)	160 (57.1%)	212 (49.1%)	138 (55.9%)	74 (40.0%)

Table 2: Distribution of AD patients within the TREATgermany registry between large centers and all other centers. "Large" was defined as centers with more than four percent of the total number of patients in the respective subsample.

Domain	Checklist criterion	Operationalization based on TREATgermany variables
A	Physician global assessment (PGA) ≥ 3	Investigator's Global Assessment (IGA) ≥ 3 (range: 0: healed; 5: very severe)
A	EASI ≥ 15	EASI ≥ 15
A	SCORAD ≥ 40 / oSCORAD ≥ 20	oSCORAD ≥ 20
A	Treatment-refractory affection of BSA of >10%	How many of your own hands (including fingers) do you need to cover all affected skin areas? (referring to the last 3 days) (range: 0-100)
A	Treatment-refractory eczema in sensitive/visible areas	Are there currently eczematous changes in the following body areas? - Face; hands; genital area; neck/neckline
A	High frequency of relapses (>10/year) with current treatment (flares)	How often have you experienced atopic dermatitis flares in the past 12 months? (0: none; 1: several times a year; 2: monthly; 3: constantly affected)
B	DLQI ≥ 10	DLQI ≥ 10
B	Pruritus ≥ 6 (NRS)	Pruritus ≥ 6 (NRS) POEM sleep item ≥ 2
B	Relevant sleep disturbance at night due to eczema/pruritus	(In how many nights during the past week was your sleep disturbed due to your eczema? (0: not at all; 1: 1-2 days; 2: 3-4 days; 3: 5-6 days; 4: every day)
C	No satisfactory response to topical therapy in accordance with guidelines	Topical therapy within the last 12 months: glucocorticoids class 2, 3, or 4 with a frequency of at least 2 days per week; phototherapy; pimecrolimus; tacrolimus
C	No expectation of success with topical measures alone	
C	Patient has already received one indicated systemic therapy without success	

Table 3: S3 guideline's checklist criteria used for operationalization based on variables documented in TREATgermany.

Modelling of potential factors influencing prescription of ST

Models for subgroup: checklist satisfied (odds ratios for nominally stat. signif. terms)

	Model 1	Model 2	Model 3
Female	0.580***	0.592***	0.566***
Age group 18-29 years	-	-	-
Age group 30-44 years	1.098	1.149	1.106
Age group 45-59 years	1.019	1.028	0.936
Age group 60 or more years	2.309***	2.203***	2.188**
Age of AD onset since infancy	-	-	-
Age of AD onset before school age	1.379	1.402	1.416
Age of AD onset during school age	0.663*	0.664*	0.693
Age of AD onset during adulthood	0.510*	0.514*	0.560*
Year of enrolment	1.853***	1.840***	1.876***
High level of suffering (PGA ≥ 4)	-	1.904***	1.739***
Other study centres	-	-	-
Study centre #1	-	4.437***	-
Study centre #2	-	0.282**	-
Study centre #3	-	14.473***	-
Study centre #4	-	1.048	-
Study centre #5	-	1.868	-
Observations	1,012	1,012	1,012
Pseudo R-squared	0.240	0.253	0.300

Table 4: Factors associated with receiving systemic therapy among patients who fulfill the checklist criteria The models indicate that females had a lower chance of starting ST (odds ratio (OR)=0.57). Being 60 years or older increases the odds of starting ST, as does a later year of enrolment and a high level of suffering. Onset of AD in adulthood decreases the odds of starting ST.

Models for subgroup: checklist not satisfied (odds ratios for nominally stat. signif. terms)

	Model 1	Model 2	Model 3
Age group 18-29 years	-	-	-
Age group 30-44 years	2.187**	2.228**	2.170**
Age group 45-59 years	1.656	1.697	1.150
Age group 60 or more years	3.403***	3.984***	3.633**
Year of enrolment	1.747***	1.741***	1.812***
High level of suffering (PGA ≥ 4)	-	3.359***	3.611***
Other study centres	-	-	-
Study centre #1	-	12.785***	-
Study centre #2	-	0.235***	-
Study centre #3	-	11.212**	-
Study centre #4	-	0.422*	-
Study centre #5	-	1.296	-
Study centre #6	-	1.831	-
Study centre #7	-	0.207***	-
Observations	425	425	425
Pseudo R-squared	0.247	0.280	0.383

Table 5: Factors associated with receiving systemic therapy among patients who do not fulfill the checklist criteria. Results (i.e., nominal significance and direction of effect) are largely similar to the subgroup satisfying the checklist. However, the odds for females are no longer different compared to males. Having a PGA ≥ 4 leads to numerically greater odds in favor of ST compared to the subgroup, who satisfies the checklist.

Logistic models

Dependent variable: Prob(systemic therapy = yes)

Model 1: independent variables: sex, age group, age of AD onset, year of enrolment in registry, education, BMI >= 25, allergic comorbidities, hypertension, current smoker, practice (versus clinic)

Model 2: independent variables: addition of indicator for high level of suffering (patient global assessment >= 4).

Model 3: independent variables: addition of larger centers and all other smaller centers lumped into one (as reference category).

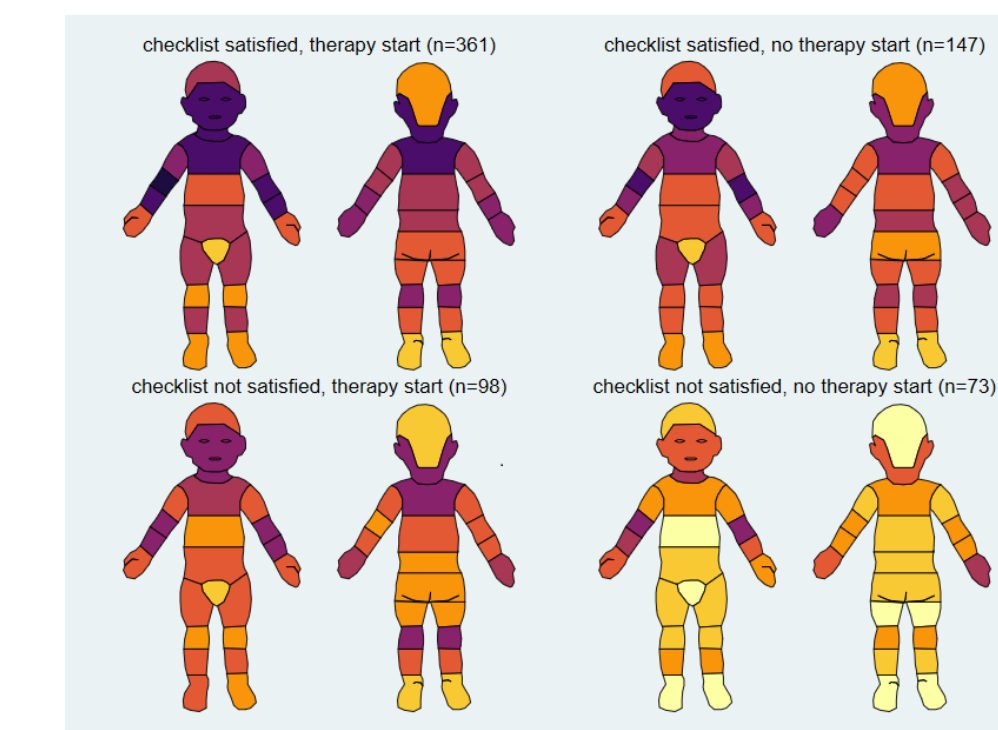
Further take-aways:

The more recent the enrollment in the registry (ranging from 2016 to 2024) the higher were the chances for receiving ST.

Furthermore, there appears to be a role for physician (study center) preferences (ORs ranging from 0.2 to 14.5) affecting the decision to prescribe a ST. Some larger centers have "consistently" higher odds (e.g., center #3) or lower odds (e.g., center #2) compared to the reference group of centers for prescribing ST regardless of checklist status.

Affected body areas at registry inclusion in patients without ST (females vs. males)

Females



Males

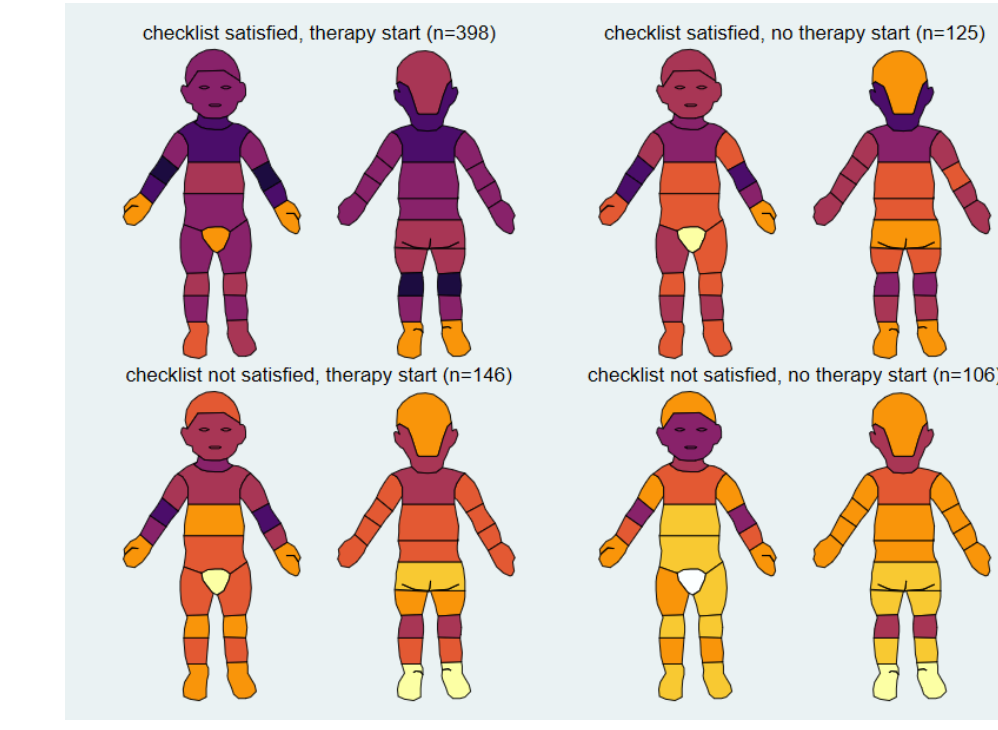


Figure 2: We found lower odds for females of receiving ST compared to men when the checklist is satisfied (see Table 4).

However, by considering body areas affected by atopic dermatitis we do not find compelling evidence that females are "disadvantaged twice". We do not observe substantial differences in body surface areas affected by AD.

Acknowledgements

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Conclusion

TREATgermany data reflect that the physician's indication for ST in adults with AD increased since 2016 and, for the majority of patients, is consistent with the German S3 guideline's criteria for the indication for systemic therapy in adults with AD. Nevertheless, there is a need for more-in-depth analysis to identify the reasons why specific subgroups, e.g., females, are less likely to receive ST, even though the checklist criteria are met.