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Healthcare situation and disparities of patients with alopecia areata – A mixed methods analysis

Running head: Healthcare situation and disparities of patients with alopecia areata

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Abstract

Objectives

Alopecia areata (AA) is a chronic immune-related disease with non-scarring hair loss. Treatment may reduce disease activity but cannot cure. In spite of being very burdensome and disfiguring, the German social act has categorized AA as a "lifestyle disease" and treatment is not covered by statutory health insurances (SHI). We aimed to characterise the healthcare situation of patients with AA in Germany, including potential inequalities, and to derive recommendations for action.

Design

This mixed-method study combined (1) semi-structured qualitative interviews with patients and dermatologists, analysed through qualitative content analysis and (2) claims data analyses of a large nationwide German SHI from 2016 to 2020. Both types of data were collected and analysed in parallel to enable integrated analysis. Consecutively, an expert panel derived recommendations for action.

Setting

Interviews were conducted online or via telephone.

Participants

Patients were recruited conveniently via a dermatological outpatient clinic, patient organisations and social media. Dermatologists were recruited from a nationwide network and the dermatological societies.

Primary and secondary outcome measures

Exploration of healthcare situation of adult persons with AA in Germany, investigating potential barriers to adequate care and identifying potential inequalities of access to care.

Results

We interviewed 20 patients (average age 40.7 years; 75.0% female) and 14 dermatologists (age 48.4 years, 50.0% female). SHI data included 4,692 persons with AA in 2020 (prevalence 0.23%; mean age 55.8 years; 76.2% female). The lack of reimbursement was criticised by both patients and dermatologists. Though 57.5% of patients received at least one drug prescription, mostly topical therapies, access to approved systemic drugs was very low. Drugs were prescribed mostly by general practitioners (41.1%) and dermatologists (32.8%). Some patients were sceptical regarding side effects of treatment and criticised exclusively symptomatic treatment. Patients reported an urge for information and exchange with others as well as

different ways of handling their disease, such as acceptance, and frustration or desperation. Patients living in urban areas received topical therapies more often than patients in rural areas. Furthermore, women were more likely to receive treatment than men. Recommendations for action include reimbursement of AA medication and developing a platform providing information on AA to physicians and patients.

Conclusions

Disease burden and frustration of patients with AA is high, mostly caused by limited treatment options and lack of reimbursement, limiting access to approved drugs such as JAK inhibitors. Through the mixed-method-design, we were able to combine patient experiences and quantitative data reflecting the reality of healthcare in Germany.

Strengths and Limitations of this study

- Limitations of the study stem from the methods applied: In the interviews, only German-speaking patients could participate and due to the nature of qualitative data, no quantitative assumptions can be made.
- Claims data analyses cover only services that are reimbursed by the statutory health insurance and data might be over- or underestimated due to insufficient or inadequate differential diagnoses, misclassifications, or coding behaviour of the practitioner.
- The major strength of this study is the mixed-methods design, in which the different methods compensated for their limitations.
- The mixed-methods approach allowed to generate and investigate additional research questions and enabled a comprehensive interpretation of the results.

  Overall, this study provides important new data on the healthcare of persons with AA. By including interviews with patients and dermatologists and linking these with quantitative data, we draw a wide picture on the current healthcare of patients with AA.

Funding statement

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Competing interests

TMJ, BH, KM, TK and KH have no conflict of interest.

CB has received speaker honoraria and/or research grants from Amgen/Celgene, AstraZeneca, Bauerfeind, Deutsche Gesellschaft für ME/CFS, Hartmann, Lilly, Mapi Group, medi, Pfizer, Sanofi, UCB, and Urgo.

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MA has served as a consultant, lecturer, researcher, and/or has received research grants from companies manufacturing drugs for alopecia areata, including AbbVie, Eli Lilly, Incyte and Pfizer.

Introduction

Alopecia areata (AA) is an inflammatory, immune-mediated disease leading to non-scarring hair loss. It is associated with other chronic inflammatory skin and autoimmune diseases.[1,2] Furthermore, AA can be triggered by numerous factors.[1] In patients with milder forms, around two thirds experience spontaneous remission.[2] However, an increased risk of recurrences remains. AA is characterised by a mostly high psychosocial burden. Since mostly visible body areas are affected, most patients experience or perceive stigmatisation, interpersonal strain and increased levels of psychosocial stress.[3,4]

Disease-halting drugs used for AA traditionally include topical glucocorticosteroids (TGCs) and calcineurin inhibitors (TCI), systemic glucocorticosteroids (SGCs) and immunosuppressants such as methotrexate and Janus kinase inhibitors (JAKi). With the JAKi baricitinib (since 2022) and ritlecitinib (since 2023) the first systemic drugs have been approved in Europe. Psychosocial support is indicated in many patients.[5,6] The first German therapy guideline for AA is expected to be available in 2026.[7]

The prevalence of AA is about 1.6% worldwide [8] and 0.2% in Germany.[9] Few studies have been conducted on the care of AA patients. The statutory health insurance (SHI) data from the USA

show that 44.2% of patients remained untreated after diagnosis[10]and that the male gender predicted fewer medical visits.[11] In the UK, access to care was influenced by gender, socioeconomic status, ethnicity, and urban residence.[12] Patients reported high out-of-pocket costs.[13]

In Germany, the German Social Act V includes a “lifestyle paragraph” excluding drugs from reimbursement by the SHI when they serve for improving hair growth. From the perspective of the Federal Joint Committee regulating details of healthcare in the SHI system, this applies to all forms of hair loss, including AA;[14] resulting, drugs for AA are generally not covered by the SHI. Hence, approved and evidence-based therapies such as JAK inhibitors are rarely used in patients with SHI status (constituting 89% of the German population)[15] but in markedly more patients who have private health insurance.

Thus, quality of care for AA in Germany is suboptimal and there seems to be an unmet need for adequate and equal treatment in this burdensome disease. This study being part of the project "Inequalities in access to medication for atopic dermatitis (AD) and AA in Germany: A mixed-methods study (AMEDA)" aimed to analyse the healthcare situation of adult persons with AA in Germany by a) investigating potential barriers to adequate care and b) identifying potential inequalities of access to care. Recommendations for action were to be derived from the results and addressed to the stakeholders in the German health system.

Design

The mixed-method study design combined qualitative interviews and data from a large nationwide German SHI. Both types of data were collected and analysed in parallel to enable integrated analysis: Interim results of all parts of the study were discussed by the project team, hence, patterns found in one study part could also be investigated in the other study part. The data were synthesized to an overall conclusion and from this, recommendations for action derived.

Qualitative analyses

Online or telephone interviews were conducted between June 2022 and April 2023. We used a semi-structured, pilot-tested interview guideline based on the research questions and

literature. If necessary, the guideline was adapted throughout the study to allow for integrating new aspects found in previous interviews and in the claims data analysis. The interviews were conducted by two female health scientists (M.Sc.) experienced in conducting qualitative interviews.

Patients were recruited conveniently via a dermatological outpatient clinic, patient organisations and social media. Dermatologists were recruited from a nationwide network and the dermatological societies, representing >95% of professionally working German dermatologists. The interviewers had no personal, professional or therapeutic relation with the interviewees, except for one dermatologist working at the same institute. Recruitment was stopped when further interviews added no additional content.

All interviews were recorded and transcribed verbatim, in the process of which the interviews were pseudonymised. Data were analysed with MAXQDA v. 24 (VERBI GmbH, Berlin, Berlin, Germany) using qualitative content analysis according to Kuckartz[16] taking a realist approach: Two researchers categorised the interviews and revised the main categories, if necessary. Based upon the categorised text passages, both researchers derived subcategories.

Claims data analyses

The analysis was based on an anonymised 40% sample (N=2,513,860; 58.0% women, average age 55.1 years in 2020) of all persons (aged at least 18 years) who were insured for at least one day with the DAK-Gesundheit (DAK-G) between 01/01/2016 and 31/12/2020.

Prevalent insured persons were considered to have AA (ICD-10 GM L63) if they had at least one confirmed outpatient or inpatient main or secondary diagnosis. Incident cases had to have a three-year diagnosis-free period in 2020.[9]

The utilisation of outpatient care for prevalent AA was determined based on all physician contacts.[17] AA-related drug prescriptions (coded by the Anatomical Therapeutic Chemical [ATC] definition system) and defined daily doses (DDD) or treatments (ambulatory doctors fee schedule [EBM]) were only recorded if an AA (Table S1) diagnosis was made in the same quarter.

In the sensitivity test, systemic antibiotics and their proportion of prescriptions in the total population were analysed to determine the population effect. The treatment history of AA patients was followed over four quarters using drug prescriptions. The proportion of outpatient psychotherapy (at least one prescription, Table S2) was compared between prevalent AA patients and other skin diseases (ICD-10 'L' diagnosis excluding L63).

Hospitalisation rates for full and partial inpatient stays with a principal diagnosis of AA were also recorded.

The administrative estimates of period prevalence and incidence (annual) were expressed as percentages with 95% confidence intervals (CI) and were standardised according to the German federal statistics institute DESTATIS as of 31 December for the observation year. Descriptive statistics and multivariate analysis methods were used according to the data level of variables. For comparative analyses, the data were adjusted for age, sex, and federal state using 1:3 nearest neighbour propensity score matching (PSM). Logistic regression was utilised to compute propensity scores (PS). Relative risks (RR) and 95% CI were calculated to assess differences between the comparison cohorts. The analyses were performed with SAS Version 9.4 German (SAS Institute, Cary, North Carolina, USA).

Development of recommendations for action

Based on the results of all study parts, an expert meeting was held with two dermatologists, two patient representatives and four scientists (researchers responsible for analyses of qualitative and claims data). Within the meeting, recommendations for action to reduce inequalities in the care of patients with AA were developed.

Results

Sample description and baseline characteristics

In the qualitative interviews (Table 1), 20 patients and 14 dermatologists participated (duration 20–85 minutes).

>>Insert Table 1<<

For each patient and dermatologist, distinct category systems were established through qualitative content analysis. Main categories in patient data were “healthcare” and “life with AA”. Main categories derived from dermatologist interview were: “healthcare stations”, “treatment” and “reasons for visits at dermatologist”. For the full category systems see Tables S3 and S4.

According to claims data, the standardised prevalence of AA in 2020 was 0.23% (N=4,692; mean age 55.8 years (standard deviation 19.0, median 57); 76.2% female) and incidence was 0.09% (N=1,565; 2019), corresponding to about 150,000 prevalent and 53,000 incident persons across Germany. The prevalence and incidence increased with age.

Treatments for AA

Following the claims data, 57.5% of the persons with AA received at least one drug prescription in 2020. Topical and systemic non-biological drugs were prescribed to 36.8% and 35.1%, respectively; among the topical drugs, 95.3% were TGCs (mostly class III and IV) and 11.1% received SGCs (Table 2). Less than 0.02% (n=9) used JAK inhibitors, namely tofacitinib and baricitinib (each 0.06%), ruxolitinib (0.04%) and upadacitinib (0.02%). Ultraviolet light (UV) therapy received 0.53% of the insured persons with AA in 2020 (0.78% in 2016) with selective phototherapy being the most common form of treatment. With 32.0% of insurees with AA receiving psychotherapeutic treatment, they were 19% (RR 1.19, CI 1.13-1.25) more likely to receive psychotherapy than persons with another skin disease (according to PSM).

>>Insert Table 2<<

The total prescription volume decreased continuously. The number of DDD dispensed fell from around 288,398 in 2016 to 233,264 in 2020. Only systemic biologics (i.e., Dupilumab) showed a slight increase from 1,206 DDDs in 2018 to 2,580 DDDs in 2020 (Figure 1).

>>Insert Figure 1<<

41.1% of the AA-related drugs were prescribed by general practitioners (GPs), 32.8% by dermatologists and 4.2% by internists. GPs prescribed antibiotics (65.6%), TGCs class I (63.4%), systemic antihistamines (53.4%), azathioprine (66.7%) and SGCs (50.4%) more often than dermatologists (Figure 2). Dermatologists prescribed the majority of biologics (i.e., Dupilumab; 75.0%). A total of 27.3% of insured persons with AA received a systemic antibiotic, compared to 21.7% of the general population (all insured persons without AA).

>>Insert Figure 2<<

In the qualitative data, patients reported the use of different **therapeutic options** including ***local***, ***systemic***, and ***further therapies*** or products. Some patients ***decided against therapy*** (Table 3, Q1.1), mostly due to experienced lack of improvement. Some reported the therapy was too time-consuming or was not likely to be successful (Q1.2). Female patients also reported ending treatment due to pregnancy.

Patients who received ***topical therapies*** reported different therapeutic success: in some patients, hair started growing again, while others did not see improvement.

Many reported wearing headgear (Q1.3), having permanent make-up, or using specific shampoos. Furthermore, patients reported lifestyle changes to improve hair growth.

For ***systemic therapies***, patients reported the use of immunosuppressants (Q1.4), oral or intralesional systemic corticosteroids, and (in few patients) JAKis and biologics through participation in a clinical study or as an off-label therapy. The patient with JAKi reported improvement of symptoms.

Most patients reported ***having tested various therapies and products***, including prescribed therapies and over-the-counter products or home remedies. They also mentioned ***critical aspects regarding therapy***: most patients were frustrated because of few therapeutic options. When receiving treatment, many felt lacking shared decision-making (Q1.5). Many reported scepticism towards medication and side effects. This scepticism includes a general scepticism not only against conventional medicine but also towards JAKi. Some patients criticised the exclusively symptomatic treatment and that no long-term improvement was achieved. Some wanted their practitioner to provide more information about the disease and therapy options (Q1.6). The most discussed aspects regarding therapy options were ***costs and external conditions***. Patients reported major differences in cost reimbursement between different SHIs and criticised that their insurance did not pay for the necessary equipment (e.g., wigs).

The dermatologists reported that they usually start treatment with ***local therapies***, mostly TGCs. Most dermatologists also mentioned therapies with diphenylcyclopropenone or platelet-rich plasma as treatment options; however, only few reported using these in practice. Also, both therapies could only be offered as privately paid treatments. Other local therapies were TCI and UV therapy.

Dermatologists also reported offering ***new therapies*** to patients, namely JAKi or immunomodulating therapies as off-label therapies. Study inclusion was reported as another possibility to offer persons with AA access to modern treatments (Q1.7). Regarding ***systemic therapies***, SGCs were described as a short-term, acute treatment. Dermatologists described JAKi as a very effective treatment (Q1.8), but as only a theoretical therapeutic option in Germany. As a treatment to "*simply stop this acute phase of the disease*" (dermatologist, male, 60–69 years), immunosuppressants such as ciclosporin and methotrexate, as well as minoxidil, were reported. Finally, dermatologists described that patients were often content with using ***wigs and other supportive devices*** (Q1.9), and some patients did not require or want any additional treatment.

Dermatologists also reported ***issues regarding the therapy***, notably the overall limited therapy options, especially for those working in office-based practice. The second major aspect was the lack of reimbursement by the health insurances (Q1.10). Further issues were recurrence after treatment end (Q1.11) and non-respondence to therapies.

Almost all dermatologists reported **spontaneous remission** in many patients with mild AA. They encouraged these patients to wait and document the symptoms (Q1.12).

An important aspect of AA treatment was **patient involvement**, which could be achieved through ***patient education*** (Q1.13) or by considering ***patient preferences***. Dermatologists reported overall high levels of ***adherence*** (Q1.14).

>>Insert Table 3<<

Life with AA

Patients reported their **symptoms** describing different severity of hair loss ranging from few bald spots to total hair loss; most had severe AA including some with a long disease history. Few patients had experienced a **spontaneous remission**. Some reported **co-morbidities**, including allergies, bronchial asthma, and other autoimmune diseases, or a **family history of AA**.

Few patients reported ***no obvious trigger***; most patients assumed their AA to be triggered by different factors such as ***stress***, for example through work (Table 4, Q2.1), private life or relationships. Few patients had experienced their first symptoms after an ***infection***. Several female patients reported changes in their symptoms (both increased and reduced) in relation

to ***physical or hormonal changes*** such as pregnancy, miscarriage, or breast feeding. Some patients experienced a ***seasonal influence*** on symptoms (Q2.2). Of these, all but one reported hair growth in spring/summer and hair loss in autumn/winter.

Information and exchange with other patients were very important for the participants, making use of social media, patient support groups or other ways of connecting with other patients. Some reported searching for new research results online. Few patients said they did not want or need exchange with other patients.

Patients have found different ways of **handling their disease**. Some patients reported having ***accepted the disease*** (Q2.3, Q2.4). Others talked about the ***mental burden***, ranging from "*of course, mentally you're not doing so great*" (patient, female, 57 years) to severe depression and suicidal thoughts. The ***visibility*** of the disease was a severe burden for many patients. They described ***resignation/frustration***, ***feeling uncomfortable*** and ***desperate***, or ***repressing*** thoughts about their AA.

Some patients described wanting to *understand the causes* of their disease and how to influence its progression (Q2.5); some ***hoped for a spontaneous remission***.

>>Insert Table 4<<

Patient pathways

In the qualitative interviews, for the initial examination of the AA, generally including blood tests, some patients visited a dermatologist while others first saw a GP. After this, the GP mostly was no longer a relevant provider for AA treatment. Visits at the dermatologist mostly happened as needed (Table 5, Q3.1), while some patients saw their dermatologist regularly for the monitoring of the disease/therapy progression. Some patients visited specific dermatologic consultations for hair loss. Pharmacies were only used by patients to pick up prescribed therapies (Q3.2). Most patients had made use of alternative options, including visits to homoeopaths or acupuncture therapy. Most of these patients reported no improvement in their symptoms and some mentioned the high costs of alternative providers; however, some appreciated that "*you are perceived quite differently. Of course, they have a completely different time register for you.*" (patient, female, 59 years). Some patients attained psychological care, mostly looking for help in handling their disease (Q3.3) but also hoping to reduce stress and improve the symptoms.

Most patients criticised a lack of empathy or felt like they were not taken seriously by the physician (Q3.4). However, some reported being taken seriously and appreciating the dermatologists' empathy and honesty (Q3.5). Some patients experienced a lack of competencies or expert knowledge (Q3.6) and therefore saw multiple different dermatologists. Patients mostly reported long waiting times until their appointment and difficulties finding good physicians.

>>Insert Table 5<<

Dermatologists reported that patients usually first visit GPs or dermatologists. GPs would usually do routine blood tests to exclude other diagnoses and then refer the patient to dermatologists. Patients with a long or complicated disease history are often referred to university clinics or specialised outpatient clinics (Q3.7). Inpatient clinic visits were reported to play a minor role. Furthermore, dermatologists reported that some patients used over-the-counter products from the pharmacy, for example shampoos against hair loss. Few mentioned suggesting the option of psychological support to patients.

Alternative medical options were mentioned by some dermatologists but reported that patients with AA generally make less use of these compared to other patient groups. Dermatologists also reported that information and exchange with other patients was important for many patients.

In 2019, 53.3% of the 1,565 patients with AA initially received prescriptions for AA. In the first quarter, 70.5% were treated by dermatologists and 31.5% by GPs, with 47.7% receiving prescriptions, falling to 39.6% in the third quarter. In the fourth quarter, the proportion of patients treated by GPs rose to 53.5%, while the proportion treated by dermatologists fell to 27.0% (Figure 3).

>>Insert Figure 3<<

The proportion of persons with AA having received systemic non-biologic drugs increased by age (Table 6). The user rate of topical treatment was significantly higher in women (26.2%; p<0.001) and those from urban areas (26.5%; p 0.002). Dermatologists prescribed topical and biological drugs more frequently (63.7%; 75.0%; each p<0.001), whereas GPs prescribed systemic non-biologics, especially GCs more frequently (60.3%; 48.1%; p<0.001).

>>Insert Table 6<<

Recommendations for action

In the expert meeting, recommendations for action to reduce barriers of access and/or inequalities in the healthcare of patients with AA were developed. The English translation on the recommendations for action can be found in S4. In the following, a summary is provided.

1. Evidence of poorer healthcare for patients with SHI

   To ensure that patients with SHI receive the same level of care as those with private health insurance, we recommend that the German legislation body (Bundestag) recognises AA as relevant autoimmune disease instead of classifying it as a lifestyle disease.

2. Evidence of regional differences in the quality of care

   The data show that dermatologists need more information on AA to provide adequate care. We recommend the development of a platform on AA that presents data on current scientific results; this platform could also be helpful for patients and might empower them by being well informed about their disease.

Discussion

This mixed-method study analysed the healthcare situation of adult persons with AA in Germany and investigated potential inequality, in particular regarding medication; from the study results, recommendations for action were derived.

Both the SHI data and the qualitative data reveal a large gap of healthcare for persons with AA in Germany. Concordantly they show that there is much less use of advanced therapies for AA as recommended. Baricitinib and ritlecitinib show efficacy in treatment[2] but have only been approved in 2022 and 2023 and, hence, after the time period represented by the claims data analysed for this study. At this time, these and other JAKis might have been only prescribed as off-label treatment. Our qualitative results confirm that prescribing advanced therapies still remains challenging due to the lack of reimbursement through the SHIs, which originates from the exclusion of drug treatments for AA by the Germans Social Act, which is

based on a false interpretation of the terms alopecia (hair loss) and "drugs improving hair growth" by the legislators. The intention was to exclude reimbursement of treatments for simple hair loss as caused by androgenetic alopecia, a common and harmless disease. The legal process by the German parliament failed to consider that alopecia areata is a distinct severe immune disease with a different pathogenesis, disease course, phenotype and disease burden. Being associated with a multitude of other immune-mediated diseases and autoimmune conditions, it needs stringent diagnostics and consequent treatment. The exclusion of such treatments thus violates the imperative of the German Social Act to provide support for persons with severe health conditions.

While expensive innovative drugs are not reimbursed, health insurances tend to pay for cheaper, often topical treatments. As in other dermatological diseases,[18] lower potency TGCs were mostly prescribed by GPs and higher potency TGCs by dermatologists. Additionally, in persons with AA, GPs might be hesitant to prescribe higher dosed medication due to limited research and experiences. While in the interviews GPs were often mentioned as first contact person but considered as not relevant in the treatment process, claims data showed that the number of patients contacting GPs increased over time. Throughout the observation period following the initial AA diagnosis, there was a notable decline in the prescription volume, from 48% in the first quarter to 40% in the third quarter. The results are in accordance with the findings from the US, which indicated that 44% of individuals with AA were not prescribed treatment in the year following diagnosis.[10] This corresponds to reports about resignation and ending treatment in case of lacking improvement. The participants emphasised their frustration with the lack of treatment options and sometimes inadequate knowledge by their healthcare provider. This may result from AA being a predominantly visual diagnosis. While patients expect to undergo more detailed examinations in the hope of finding triggers, once diagnosis has been confirmed, the patient is often left with regular monitoring, which might cause frustration.

Similar to previous findings,[19,20] patients reported high mental burden, often combined with lacking empathy and understanding by healthcare providers. Also, claims data show a higher probability to use psychotherapy compared to other skin diseases. Therefore, the mental health of people with AA should be considered and physicians should be made aware of this

issue. Psychological interventions might not only help patients to cope with their disease but also improve AA through reduced stress levels of patients.[21]

We found higher prevalence and higher therapy prescription in women. A possible reason is that women might be more sensitive to hair loss than men due to cultural factors. Furthermore, treatment prescription grows with age. Patients in urban areas receive more topical medication. This might confirm considerations in the qualitative interviews that dermatologists in rural areas often lack knowledge about AA treatment or are worried about reimbursement. Additionally, long travel distances might reduce the acceptance of therapies requiring regular physician visits. Surprisingly, a marked proportion of patients received prescription drugs attributable to AA though they are legally excluded from reimbursement. Two reasons may contribute to this: Low-cost drugs may not be queried by the payers and thus are tolerated in spite of the ban. Second, further diagnoses may have been used to hide the use of drugs for an indication not covered by the SHI. For example, patients with comorbid rheumatism might receive JAKis more often as in these indications advanced therapies is more likely to be remunerated. This might also explain why JAKis were not prescribed by dermatologists in our claims data set.

As part of this study, recommendations for action to reduce health disparities were developed. Firstly, the expert panel recommended to recognise AA as an autoimmune disease instead of classifying it as a lifestyle disease. Through this recognition, all patients will be able to receive adequately reimbursed care. This would reduce the patient burden and improve the healthcare situation significantly. Secondly, we the expert panel outlined the differences between urban and rural areas. Physicians should be better informed about AA, its treatment options and options for reimbursement and study inclusion; this should be done through an independent platform that informs about scientific results. The current development of treatment guidelines for AA will also help inform physicians better to enable providing adequate care for patients.

The major strength of our study is the mixed-methods design, which allowed us to generate additional research questions. Furthermore, the combination of the different results enabled a more comprehensive interpretation. Due to the nature of qualitative data, no quantitative

assumptions can be made and results are not generalizable to the wider public. In the interviews, only German-speaking participants could participate. Also, patients with only light symptoms are likely underrepresented in the qualitative data. Claims data cover all patients who have received healthcare covered by the SHI, and they allow for an objective quantification of the healthcare received. However, only services that are reimbursed by the SHIs are recorded. Therefore, data on privately paid services are not collected. In addition, the proportion of patients with AA could be over- or underestimated, for example, due to insufficient or inadequate differential diagnoses, misclassifications, or coding behaviour of the practitioner. To account for this, we used validity criteria such as confirmed outpatient diagnoses.

Overall, this study provides important new data on the healthcare of persons with AA. By including interviews with patients and dermatologists and linking these with quantitative data, we draw a wide picture on the current healthcare of patients with AA. We were also able to show that the treatment conditions need to be improved through the health insurance to provide adequate care to all patients. Lastly, the recommendations for action that we developed based on our study results aim to reduce disparities in healthcare.

Author's contribution

All authors had substantial contributions to the analysis or interpretation of data for this paper, revised it critically for important intellectual content, approved it finally and agreed to be accountable for this work in ensuring its integrity of interpretation of data.

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Ethics statement: The study has been approved by the Local Ethics Committee at the University Medical Center Hamburg-Eppendorf (LPEK-0427).

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Tables

Table 1: Characteristics of patients and dermatologists participating in the interviews

	Mean (Range) / n (%)	
	Patients (n=20)	**Dermatologists** (n=14)
Age (years)	40.7 (25–61)	48.4 (31–69)
Gender		
Female	15 (75.0)	7 (50.0)
Male	5 (25.0)	7 (50.0)
Education		
(Vocational) A-levels [12–13 years of education]	15 (75.0)	n.a.
10 years of education	3 (15.0)	n.a.
9 years of education	2 (10.0)	n.a.
Living/Practicing*		
Baden-Wuerttemberg	3 (15.0)	1 (7.1)
Bavaria	4 (20.0)	1 (7.1)
Berlin	1 (5.0)	0 (0)
Hamburg	1 (5.0)	1 (7.1)
Lower-Saxony	4 (20.0)	2 (14.3)
North Rhine-Westphalia	3 (15.0)	4 (28.6)
Rhineland-Palatine	1 (5.0)	4 (28.6)
Saxony	1 (5.0)	0 (0)
Saxony-Anhalt	0 (0.0)	1 (7.1)
Schleswig-Holstein	2 (10.)	1 (7.1)
Insurance		
Statutory	19 (95.0)	n.a.
Private	1 (5.0)	n.a.
Duration of AA symptoms (years)	16.3 (0.25–51)	n.a.
Missing hair		
Scalp	54% (0.0–100%)	n.a.
Face/body	62% (0.0–100%)	n.a.
Employment situation*		
Practice	n.a.	10 (71.4)
Clinic	n.a.	5 (35.7)
Experience as dermatologist (years)	n.a.	19.7 (7–37)

*multiple answers possible

Table 2: Alopecia Areata (AA) related prescriptions in prevalent insured persons with AA and at least one drug prescription in 2020

Drug group	Drug therapy	Patients with AA-diagnosis (N)	≥1 Rx (n)	≥1 Rx (%)	Total DDD	Mean Rx per patient	Mean DDD per patient
Total	**Any therapy**	**4,692**	**2,701**	**57.57**	**233,305.49**	**2.67**	**86.38**
Topicals	**Total**	**4,692**	**1,726**	**36.79**	**121,928.74**	**1.85**	**70.64**
	Antibiotics	1,726	124	7.18	1,117.01	1.18	9.01
	Antihistamines	1,726	2	0.12	30.00	1.00	15.00
	Corticosteroids, dermatological preparations	1,726	1,644	95.25	117,745.80	1.78	71.62
	- Group I	1,726	41	2.38	1,589.17	1.20	38.76
	- Group II	1,726	153	8.86	6,312.73	1.35	41.26
	- Group III	1,726	1,064	61.65	75,501.70	1.57	70.96
	- Group IV	1,726	454	26.30	26,499.54	1.50	58.37
	Corticosteroids, combinations with antiseptics	1,726	28	1.62	592.00	1.18	21.14
	Corticosteroids, combinations with antibiotics	1,726	117	6.78	1,947.33	1.28	16.64
	Corticosteroids, other combinations	1,726	97	5.62	5,303.32	1.40	54.67
	Pimecrolimus	1,726	51	2.95	1,602.50	1.39	31.42
	Tacrolimus	1,726	42	2.43	860.00	1.31	20.48
	Tars	1,726	4	0.23	573.44	1.00	143.36
Systemics	**Total**	**4,692**	**1,649**	**35.14**	**111,376.749**	**2.44**	**67.54**
Biologics	Total - Dupilumab	**4,692**	**8**	**0.17**	**2,579.56**	**4.50**	**322.45**
Non-biologics	Total	**4,692**	**1,644**	**35.04**	**108,797.189**	**2.42**	**66.18**
	Methotrexate	1,640	41	2.49	8,829.95	3.41	215.36
	Mycophenolic acid	1,640	7	0.43	1,437.50	3.43	205.36
	Alitretinoin	1,640	2	0.12	465.00	4.50	232.50
	syst. Antibiotics	1,640	1,283	78.04	21,484.73	1.74	16.75
	syst. Antihistamines	1,640	142	8.64	15,380.99	1.89	108.32
	Azathioprine	1,640	18	1.09	3,249.99	4.83	180.55
	Ciclosporin	1,640	4	0.24	530.00	8.50	132.50
JAKi	Janus kinase inhibitors*	**4,692**	**9**	**0.19**	**42.00**	**4.67**	**4.67**
	Tofacitinib	9	3	33.33	1,163.40	6.67	387.80
	Upadacitinib	9	1	11.11	120.00	2.00	120.00
	Baricitinib	9	3	33.33	735.00	3.00	245.00
	Ruxolitinib	9	2	22.22	317.34	5.50	158.67
GCS	Glucocorticosteroids*	**4,692**	**520**	**11.08**	**57,377.03**	**2.21**	**110.34**
	- Prednisolone depot	520	6	1.15	92.50	1.17	15.42
	- Triamcinolone depot	520	52	10.00	3,705.96	1.13	71.27

Multiple counting was possible; *Sub-type of non-biological treatment

Note: Rx=prescription; DDD=defined daily dose

Table 3: Quotes by patients and dermatologists referring to therapy options

Quote Number	Quote	Participant
Q1.1	"*No, except for taking zinc supplements, I don't do anything anymore. I let it [the hair] come and go.*"	Patient, female, 33 years
Q1.2	"*I would have had to go to [city 8] I think, every week or so [...] and that, um, I would not have managed in terms of time, to be honest. I then also heard, as soon as the treatment is finished, the hair will fall out again.*"	Patient, female, 57 years
Q1.3	"*The wig I got quite early, without the wig I would feel very stigmatized, because I have neither the strength nor the self-confidence to walk around without hair on my head.*"	Patient, female, 33 years
Q1.4	"*That worked well. I was symptom-free for a relatively long time. My hair stopped falling out. […] Then it abruptly stopped working*"	Patient, female, 28 years
Q1.5	"*So it was always said [by the dermatologist]: change of medication. Let's look for something new. I didn't have much say in the matter.*"	Patient, female, 28 years
Q1.6	"*I would have liked to have the possibilities, treatment options in more detail, in an overview, […] but instead we get something different [different information] from every dermatologist*"	Patient, male, 41 years
Q1.7	"*If the patient has a high level of suffering, I would send him to the university hospital, with the idea of getting into a study, because there is currently a lot happening. In our practice, we don't do too much, I have to say*"	Dermatologist, female, 30–39 years
Q1.8	"*And with baricitinib, regarding the experience so far, you really have a great therapy option, but with the restriction that it is not reimbursed*"	Dermatologist, male, 50–59 years
Q1.9	"*Sometimes the wig is so well made that you don't even see it. [...] And they [the patients] are really happy. With the wig, you have to say, a new phase begins for them*"	Dermatologist, female, 40–49 years
Q1.10	"*But these are patients who have been to other places [physicians] and who are simply hoping that you will prescribe them a systemic therapy that you may not be able to get from other doctors. […] I used to put a lot of work into asking the health insurance companies to cover it. […] The answer is always: Yes, you can prescribe it, but it is a lifestyle medication*"	Dermatologist, female, 40–49 years
Q1.11	"*But for the patient, I think it's an agony. It [the DCP therapy] is very tedious and almost always leads to a relapse when they stop taking it*"	Dermatologist, male, 60–69 years
Q1.12	"*Of course, we have a number of patients where there is a spontaneous remission, who do not come back into the practice*"	Dermatologist, female, 30–39 years
Q1.13	"*What is important, patients must be educated well that this disease runs in relapses. This means that once we have brought on a 'cure', we cannot guarantee that a relapse will not occur at some point [...]*"	Dermatologist, male, 40–49 years

Q1.14	*"But they are actually/ do what we recommend. [...] I always explain to them that theoretically you can also just wait. [...] But they are very willing to undergo therapy"*	Dermatologist, female, 40–49 years

Table 4: Quotes by patients referring to life with Alopecia Areata

Quote number	Quote	Participant
Q2.1	"*It started in 2015, a circular spot at the back of the head [...], I wanted to quit my job at the time and was afraid to tell my boss and I think that was the stress.*"	Patient, female, 32 years
Q2.2	"*With approaching winter [...] I already notice that the head hair is also thinner and not as good. [...] And in summer it grows again*."	Patient, female, 46 years
Q2.3	"*I'm feeling fine with it so far, in the sense that I have accepted it.*"	Patient, male, 41 years
Q2.4	"*For me in my everyday life this disease plays no role in this sense, [...] I am fine.*"	Patient, female, 25 years
Q2.5	"*What interests me now is whether I can influence it [...] by my actions, by my way of life, because although I have accepted it [...], I would like to understand it.*"	Patient, male, 41 years

Table 5: Quotes by patients and dermatologists referring to patient pathways and health care disparities

Quote number	Quote	Participant
Q3.1	"*I would say if I didn't need the prescription [for the wig], I wouldn't go there at all.*"	Patient, female, 59 years
Q3.2	"*I would say that pharmacists are not really educated about AA. I don't think they would suggest anything to you on their own.*"	Patient, female, 25 years
Q3.3	"*I started the therapy and that simply helps to focus on this stress management and partly also these fears that go along with it, to learn strategies.*"	Patient, female, 36 years
Q3.4	"*[…] to see the psychosocial side of this disease, that is not just your hair falling out, but what it does to the people and that would, I would just wish that […] that is also addressed and is also dealt with sensitively with those affected, that they feel taken seriously.*"	Patient, female, 25 years
Q3.5	"*He was very empathetic. He explained well that you really can't do much.*"	Patient, female, 28 years
Q3.6	"*The dermatologists were very overwhelmed here in the area.*"	Patient, female, 25 years
Q3.7	"*If this attempt has brought no success over weeks, months, then the dermatologist in private practice usually stops the treatment. [...] And that is actually when the normal topical steroid has failed, that the patient is then referred to us [a university hospital].*"	Dermatologist, male, 40–49 years

Table 6: Subgroup analyses of prescribed treatment groups (bold printed figure display significant differences) in prevalent adult persons with Alopecia Areata in 2020 (N=4,692)

Treatment	Topicals	Sys. Biologics	Sys. Non-biologics	Sys. GCS*
Age, p-value	**<0.001**	0.158	**<0.001**	**<0.001**
Up to 30, n(%)	**393 (7.9)**	2 (0.0)	**250 (5.0)**	**44 (0.9)**
> 30–45, n(%)	**377 (7.6)**	1 (0.0)	**285 (5.7)**	**64 (1.3)**
> 45–65, n(%)	**590 (11.9)**	5 (0.1)	**576 (11.6)**	**207 (4.2)**
> 65, n(%)	**499 (10.0)**	0 (0.0)	**611 (12.3)**	**215 (4.3)**
Gender, p-value	**<0.001**	0.471	**<0.001**	**<0.001**
Male, n(%)	**559 (11.2)**	4 (0.1)	**370 (7.4)**	**82 (1.6)**
Female , n(%)	**1,300 (26.2)**	4 (0.1)	**1,352 (27.2)**	**448 (9.0)**
Insurance district types, p-value	**0.002**	0.272	0.723	0.588
Urban, n(%)	**1,315 (26.5)**	4 (0.1)	1,176 (23.7)	365 (7.3)
Rural, n(%)	**543 (10.9)**	4 (0.1)	543 (10.9)	163 (3.3)
Specialist, p-value	**<0.001**	**<0.001**	**<0.001**	**<0.001**
None of both, n(%)	**131 (7.0)**	**2 (25.0)**	**523 (30.4)**	**187 (35.3)**
General practitioner, n(%)	**367 (19.7)**	**0 (0.0)**	**1,038 (60.3)**	**255 (48.1)**
Dermatologist, n(%)	**1,184 (63.7)**	**6 (75.0)**	**116 (6.7)**	**80 (15.1)**
Both n(%)	**177 (9.5)**	**0 (0.0)**	**45 (2.6)**	**8 (1.5)**

* Sub-type of non-biological

Figure legends

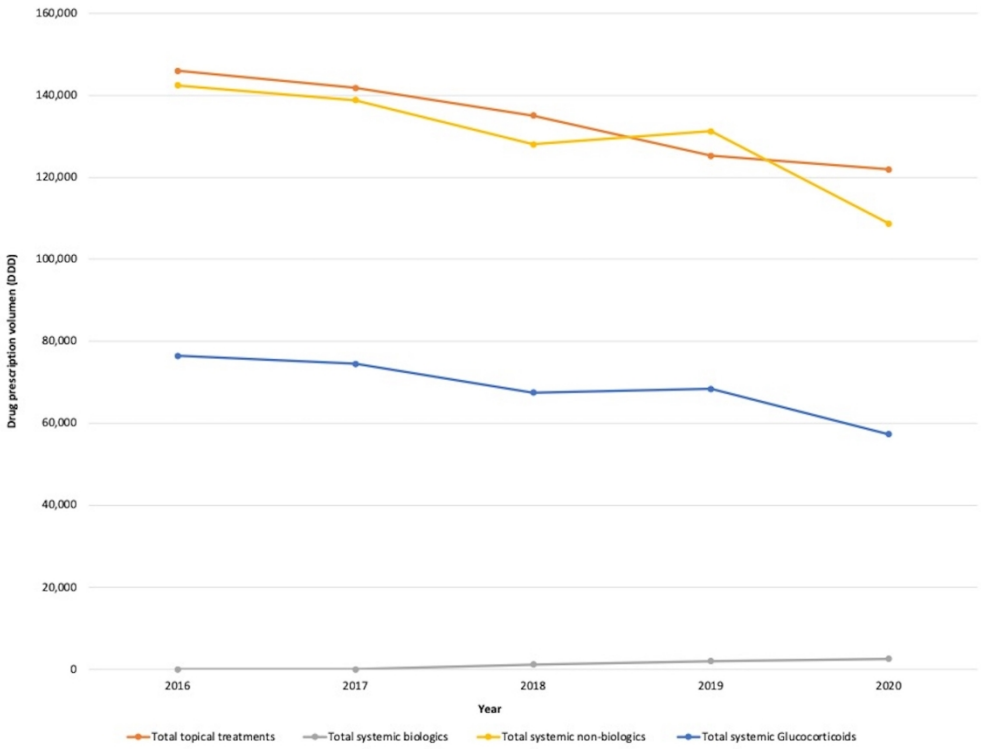
Figure 1: AA related drug prescription volume (defined daily doses [DDD]) in prevalent adult persons with AA and at least one prescription from 2016 to 2020 by drug group (2016 N= 3,337; 2017= 3,294; 2018 N= 3,321; 2019 N= 3,045; 2020 N= 2,699)

Figure 2: AA related topical prescriptions in prevalent adult persons with AA with at least one drug prescription by prescriber in 2020 (N= 1,726); Rx=prescription, multiple counting possible

Multiple counting; *Sub-type of non-biological drugs

Figure 3: Distribution of specialties treating incident adult persons with AA in 2019; person with at least one AA-related drug prescription were included (Quarter 1 N=803; Quarter 2 N=383; Quarter 3 N=342; Quarter 4 N=318), washout for incidence assessment 3 years

Note: The first observation quarter corresponded to the quarter in which the medication was prescribed



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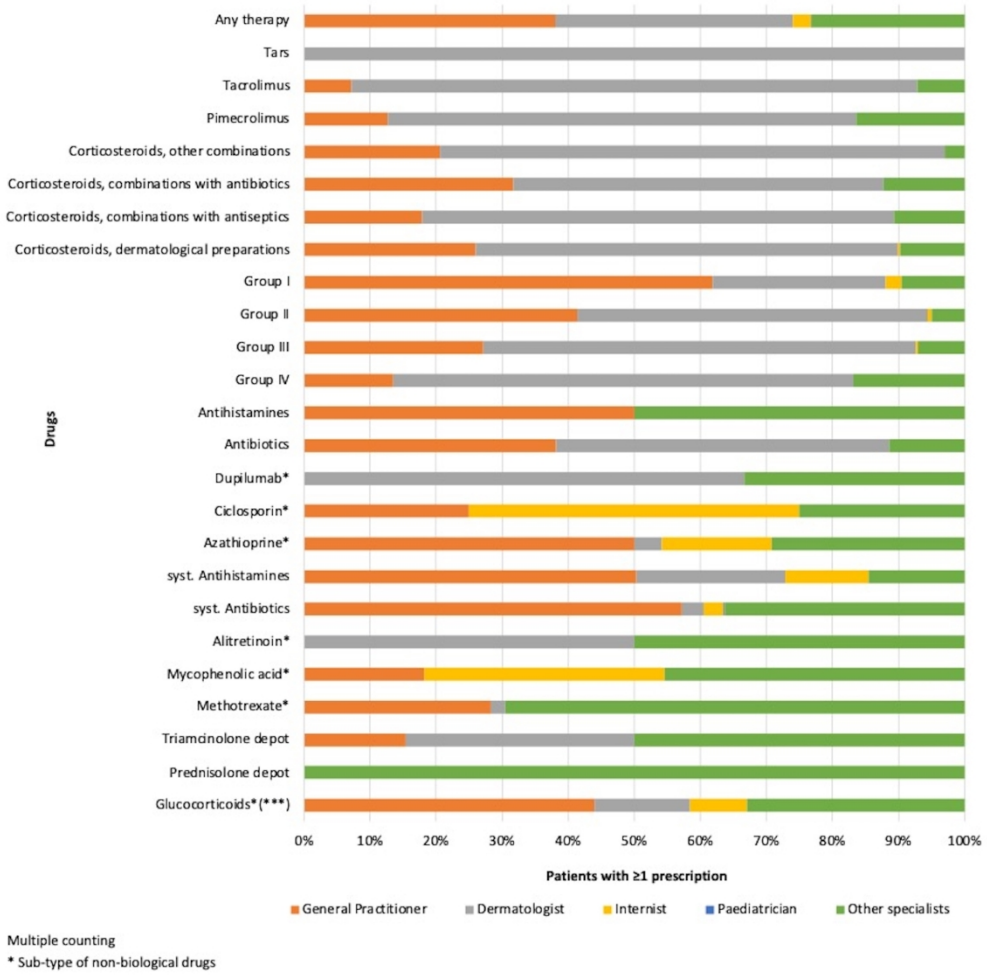

Multiple counting

* Sub-type of non-biological drugs

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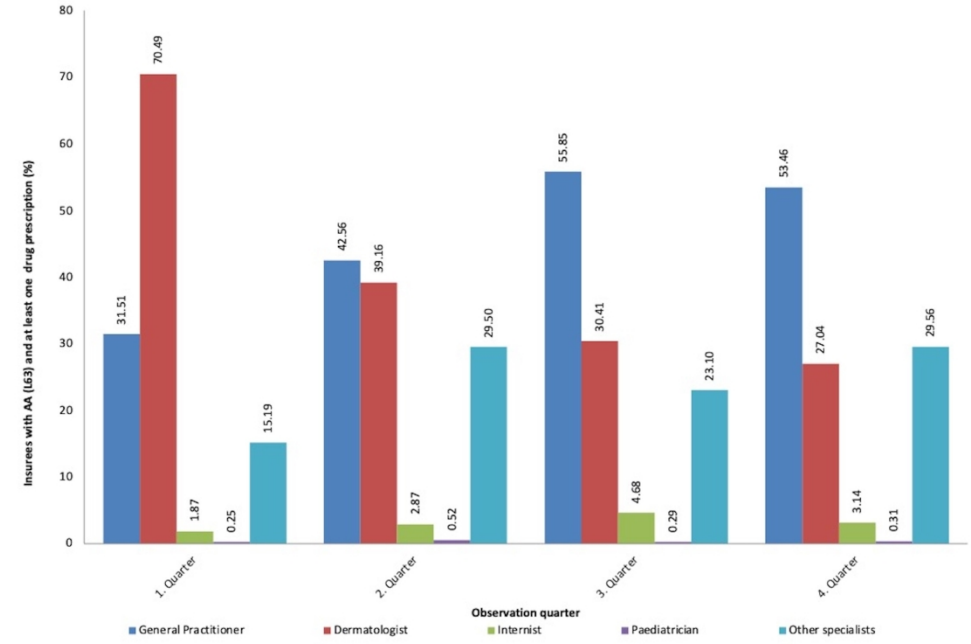

Note: The first observation quarter corresponded to the quarter in which the medication was prescribed

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Study plan

Inequalities in access to medication for atopic dermatitis and alopecia areata in Germany: A mixed-methods study (AMEDA)

Version: v1

Date: 17 February 2022

Principal investigator:

PD Dr. Christine Blome

Research Group Leader Patient-Reported Outcomes

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1 Synopsis

Study title	Inequalities in access to medication for atopic dermatitis and alopecia areata in Germany: A mixed-methods study
Financial support	Pfizer Inc. (Quality Improvement Grant RFP: Understanding healthcare disparities in Atopic Dermatitis and Alopecia Areata patients)
Objective	To describe and explain healthcare disparities in adult patients with atopic dermatitis (AD) and/or alopecia areata (AA) in Germany with a special focus on medication, and to deduce recommendations for action.
Target population	Adult patients diagnosed with AD or alopecia areata AA; dermatologists treating adult patients with AD or AA (in part 3)
Design	Mixed-methods study
Data basis	Part 1: claims data: nationwide data-on-file from the statutory health insurance DAK-G including 2.2 million insured people in 2016-2019; billing-relevant information from outpatient and inpatient care Part 2: survey data: nationwide data-on-file from the AtopicHealth study conducted in 2017-2019; patient- and clinician-reported data, such as patient characteristics, information on health care; patient-reported outcomes Part 3: qualitative study: in-depth interviews with patients with AD, patients with AA, and dermatologists using pilot-tested, semi-structured interview guidelines
Estimated number of participants	Part 1: claims data including approx. n=72,820 patient with AD and n=9,900 patients with AA Part 2: survey including n=1,291 patients with AD Part 3: qualitative sample including approx. n=25 patients with AD, n=25 patients with AA, n=20 dermatologists
Data analysis	Part 1: Prescription prevalence and health care utilization will be analyzed by medication, region and patient characteristics including co-morbidities, age, and gender; trends over time will be analyzed Part 2: Analysis of health care disparities by patient subgroups using appropriate descriptive and inferential statistical methods

	Part 3: Transcripts of interviews will be analyzed using qualitative content analysis Integration of study parts: The three study parts will be conducted in parallel. Interim findings and newly developed hypothesis from each study will be exchanged and discussed in the project team on a regular basis in order to determine which of these can also be investigated with the respective other data sources.
Study duration	February 2022 – July 2024
Quality assurance	The study will be conducted following the criteria for Good Scientific Practice by the German Research Foundation (Deutsche Forschungsgemeinschaft, DFG) as well as the Bylaws for Safeguarding Good Scientific Practice and Avoiding Scientific Misconduct at University Hamburg; claims data analysis will follow the Good Practice of Secondary Analysis. CVderm has been certified in accordance with DIN ISO 9001:2015 in the scope of the certification of the University Medical Center Hamburg-Eppendorf. In addition, CVderm follows its own standard operating procedures.
Ethics	The conduction of the study follows the legal requirements for data protection. The study has been approved by the Local Psychological Ethics Committee at the University Medical Center Hamburg-Eppendorf (LPEK-0427, 12 January 2022)

		03 May 2022
Principal investigator	PD Dr. Christine Blome University Medical Center Hamburg-Eppendorf IVDP Martinistr. 52 (CPW 3) D-20246 Hamburg	date
		03 May 2022
Sub-principal investigator	Kristina Hagenström, PhD University Medical Center Hamburg-Eppendorf IVDP Martinistr. 52 (Building 342) D-20246 Hamburg	date

Table of contents

2 Abbreviations

AA	Alopecia areata
AD	Atopic dermatitis
CVderm	German Center for Health Services Research in Dermatology
IVDP	Institute for Health Services Research in Dermatology and Nursing
UKE	University Medical Center Hamburg-Eppendorf

3 Responsibilities and addresses

3.1 Coordinating center and investigators

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4 Introduction

The need for improved health care for AD in Germany and the corresponding research gaps can be derived from a large body of previous research from our group, including the AtopicHealth study series (Langenbruch et al. 2014; Langenbruch et al. 2021). In summary, there is evidence of considerable patient burden and unmet patient needs (Augustin et al. 2020; Beikert et al. 2014; Steinke et al. 2014), high economic burden (Mohr et al. 2021), and significant comorbidity (Radtke et al. 2017; Zander et al. 2020). Quality of care often does not comply with guidelines (Werfel et al. 2016; Werfel et al. 2021; Hagenström et al. 2021; Steinke et al. 2018; Langenbruch et al. 2014) including insufficient access to prevention and education (Zyriax et al. 2021).

To ensure that this project does not duplicate existing work, we conducted a PubMed/Medline literature search in September 2021 using the following search term:

(Atopic dermatitis[TiAb] OR neuroderm*[TiAb] OR eczema[TiAb] OR alopecia areata[TiAb]) AND (healthcare[TiAb] OR (health AND care[TiAb]) OR medication[TiAb] OR prescription[TiAb])

There are limited studies addressing health disparities among patients with AD (Davis et al. 2021). For the US, it was found that resource utilization differed by age (Alexander et al. 2018; Singh & Silverberg 2019), AD severity (Drucker et al. 2018), and region (Wu et al. 2021). Two studies conducted in the UK and Denmark identified age, gender, ethnicity, socio-economic status, disease severity, co-morbidity with allergic rhinitis or asthma, smoking history, and urban setting as predictors of health care access (de Lusignan et al. 2020; Thyssen et al. 2020).

For Germany, we described the overall health care situation of patients with AD using 2019 claims data (Hagenström 2021). We found that only one-third of patients are treated by a specialist; that there is significant underuse especially of innovative drugs; and that women receive prescription drugs more often. Further studies described the situation of the overall AD population in Germany without differentiating by patient characteristics (Heratizadeh et al. 2020; Zietze et al. 2021) or are outdated (Schmitt et al. 2009 using data from 2003-2004).

Thus, there is a lack of knowledge on whether health care disparities found internationally also apply to German AD patients. Furthermore, both internationally and in Germany, reasons for disparities are not well understood.

For AA, literature on the health care situation is scarce, and we found none from Germany. A recent US claims data analysis showed that 44% of patients were not prescribed treatment in the year following AA diagnosis, but no analysis by patient subgroup was reported (Senna et al. 2021). An earlier US study showed male gender to be predictive of fewer physician visits (Farhangian et al. 2015); the

same was found for primary care visits in the UK (Harries et al. 2021). The latter study further identified gender, socio-economic status, ethnicity, and living in urban or deprived areas as predictors of health care access.

Not least given upcoming targeted treatments for both AD and AA, and the fact that quality of care is still suboptimal in Germany, it is crucial to understand health care disparities in these patients in order to enable improvement measures. This study will therefore build upon the methodology used successfully in our previous study on AD (Hagenström et al. 2021), extended by a detailed analysis of subgroups with inadequate access to high quality health care, and widening the analysis to a 4-year data set. The same analysis will be performed for patients with AA, which to our knowledge will be the first systematic analysis of the health care situation of this patient group in Germany. Claims data analysis will be integrated with survey (AD) and qualitative (AA and AD) data, enabling a broader perspective that also uncovers potential explanations of health care disparities.

5 Goals and objectives

This project aims to describe and explain healthcare disparities in adult patients with AD and/or AA in Germany with a special emphasis on medication, and to deduce recommendations for action.

Disparities associated with the following patient characteristics will be considered: age; gender; socio-economic status, including education and working situation; family situation; region of residence; disease severity and co-morbidities (insofar as associations with health care are not clinically substantiated, e.g., more potent medication for more severely affected patients).

Aspects of health care to be evaluated include: prescribed medication (type of medication; prescription frequency); treatment by dermatologists vs. other physicians with other specialties; number of physician consultations.

As found for other dermatological indications in Germany, as well as for AD and AA internationally, we hypothesize that access to health care and quality of care will be disparate, depending on several of the characteristics described above and/or interactions between these characteristics.

In using an innovative mixed-methods approach that combines large quantitative data bases with qualitative in-depth interviews, the study aims to both describe and explain group differences in health care and is thereby closely aligned with the RFP focus on understanding healthcare disparities. This understanding is fundamental for deriving suitable recommendations for action, which will be done as the last step of the project based on the integrated analysis of our data.

6 Study design

The study will use a mixed-methods design combining

- claims data (part 1)
- survey data on health care in AD (part 2)
- qualitative patient and physician interviews (part 3).

While part 1 and 2 focus on identifying healthcare disparities in AD and AA, part 3 aims to derive possible explanations.

The three study parts will be conducted in parallel to enable integrated analysis, with the different methodological approaches supplementing and enriching each other. Quantitative findings shall be addressed in the qualitative interviews in order to derive explanations, and analysis of the qualitative data will generate additional hypotheses to be tested with the quantitative data.

The three study parts are described in more detail in the following subheadings.

6.1 Part 1: Claims data

6.1.1 Objectives

To describe the care paths of adults with AD or AA, including prescription prevalence and health care utilization

6.1.2 Patients and data

Nationwide data-on-file from the statutory health insurance DAK-G including 2.2 million insured people in 2016-2019. Based on AD prevalence of 3.31% and AA prevalence of 0.58%, a sample of 72,820 patients with AD and 9,900 patients with AA can be assumed. The data set covers all billing-relevant information from outpatient and inpatient care, including all drugs prescribed for outpatients. Master data of the insured persons contain age and gender, district municipality code as well as start and end of the insured period (incl. reason for leaving).

6.1.3 Data management and statistical analysis

The data set contains de-identified health-insurance data. A linkage number allows to combine data from all service areas to analyse care paths of patients, mostly based on day-specific coding of medical services. Prescription prevalence and health care utilization will be analyzed by medication, federal state level and patient characteristics including co-morbidities, age, and gender. Trends over time will

be analyzed. More detailed information on data management and statistical analyses can be drawn from the statistical analysis plan for part 1.

6.2 Part 2: Survey data

6.2.1 Objectives

To describe the health care situation of adults with AD, including the analysis of health care disparities between patient subgroups.

6.2.2 Patients and data

Nationwide data-on-file from the AtopicHealth study conducted in 2017-2019 including 1,291 adult patients with AD and their treating physicians from 111 dermatological practices and ambulant clinics. Data includes patient characteristics (such as age, gender, family situation, working situation, school and professional education, region, disease severity (SCORAD), and comorbidities), information on health care (AD treatment, physician/clinic visits), and patient-reported outcome measurements (such as Dermatology Quality Life Index, and Patient Benefit Index).

6.2.3 Data management and statistical analysis

The data set of the AtopicHealth study is already available at the IVDP. Data will be prepared as needed (including calculation of scores, if not yet available, and grouping of variables). Analysis of healthcare disparities will be investigated through analysis by patient subgroup using the appropriate descriptive and inferential statistical method. More detailed information on data management and statistical analyses can be drawn from the statistical analysis plan for part 2.

6.3 Part 3: Qualitative Interview

6.3.1 Objectives

To explore patient journeys of adults with AD or AA and to explain healthcare disparities.

6.3.2 Participants and data

Patients will be recruited from the dermatological ambulant clinic at the UKE, from outpatient dermatologists, via patient organizations, and via social media. Dermatologists will be recruited from the broad networks of dermatologists available at the IVDP, including outpatient dermatologists and ambulant clinics, as well as dermatological associations. The final sample size cannot be determined beforehand due to the character of qualitative studies. Recruitment of patients will stop when interviews reveal no decisive added value and result in no further additional content. Based on

previous experiences, it is estimated that this will be reached after interviewing 50 participants (n=25 with AD, n=25 with AA) and 20 dermatologists.

In-depth interviews will be conducted using pilot-tested, semi-structured interview guidelines. The interview guideline will be based on the research question and existing literature. Throughout study conduct, the interview guideline will be adapted to allow for in-depth exploration of the findings from the quantitative study parts and for additional topics that may result from the respective previous interviews. The study team regularly reviews the current interviewing procedure, gives each other feedback on their interview guidance, and discusses preliminary findings.

6.3.3 Data management and qualitative analysis

All interviews will be audio-recorded and transcribed verbatim while clearing identifiers (e.g., names or places). Transcripts of the interviews will be analyzed using qualitative content analysis according to Kuckartz (2018) with regard to the research question.

Categorization will be conducted using the NVivo software.

6.4 Integration of study parts 1 to 3

All study parts will be conducted in parallel in a *convergent design*. Throughout the study conduct interim results of all study part will be discussed in the project team in a regular workshop, taking place bi-monthly after onset of the data analysis phase. This will allow for patterns and associations found in one study part to be explored also in the other study parts, if applicable. Thereby, quantitative results can be addressed and explored in the qualitative study part and qualitative findings can lead to additional quantitative analyses. Additionally, quantitative study parts can enrich each other as claims data analyses might evoke questions regarding additional clinician- and patient-reported outcomes, not captured in billing data, while analysis of AtopicHealth data may provoke longitudinal research questions. Accordingly, exchange between the study parts can lead to additional research questions, that might evoke amendments in the statistical analysis plans (quantitative parts) and changes in interview guidelines and sampling strategy (qualitative part). Qualitative and quantitative findings will be compared in terms of where they converge, diverge, or complement each other (Curry & Nunez-Smith, 2014, pp.229-258); if they diverge, it will be discussed whether this points at bias in one of the study parts or whether the findings can be reconciliated (i.e. plausible interpretations are sought).

6.5 Derivation of recommendations for action

The results of all study parts will be considered for derivation of recommendations for action. Results will be presented and discussed in an interdisciplinary expert group, including psychologists, health

scientists, statisticians, and physicians. Within this group, results will be analyzed with regard to political decisions and resource allocation as well as everyday clinical practice. From this, recommendations for action will be deduced.

6.6 Quality assurance

The study will be conducted following the criteria for Good Scientific Practice by the German Research Foundation (Deutsche Forschungsgemeinschaft, DFG) as well as the Bylaws for Safeguarding Good Scientific Practice and Avoiding Scientific Misconduct at University Hamburg; claims data analysis will follow the Good Practice of Secondary Analysis (Swart et al. 2015). The CVderm has been certified in accordance with DIN ISO 9001:2015 in the scope of the certification of the University Medical Center Hamburg-Eppendorf. In addition, the CVderm follows its own standard operating procedures.

6.7 Data protection and ethics

The conduction of the study follows the legal requirements for data protection.

Claims data will be processed only in a de-identified manner so that data cannot be linked to individuals. A linkage number allows to combine data from different service areas while keeping data de-identified.

Atopic Health data has been pseudonymized with the study team not being able to so link that data to the respective persons.

Qualitative data will be pseudonymized, that is, encrypted with a numerical code (only the qualitative study team is able to allocate personal data), and will only be analyzed in this pseudonymized way. Audio records will be transcribed without names, addresses or other information that allow identification of the participant. Personal data of the participant will be destroyed three years after data collection at the latest, and hence, data will be anonymized.

The study has been approved by the Local Ethics Committee at the University Medical Center Hamburg-Eppendorf (LPEK-0427, 12 January 2022).

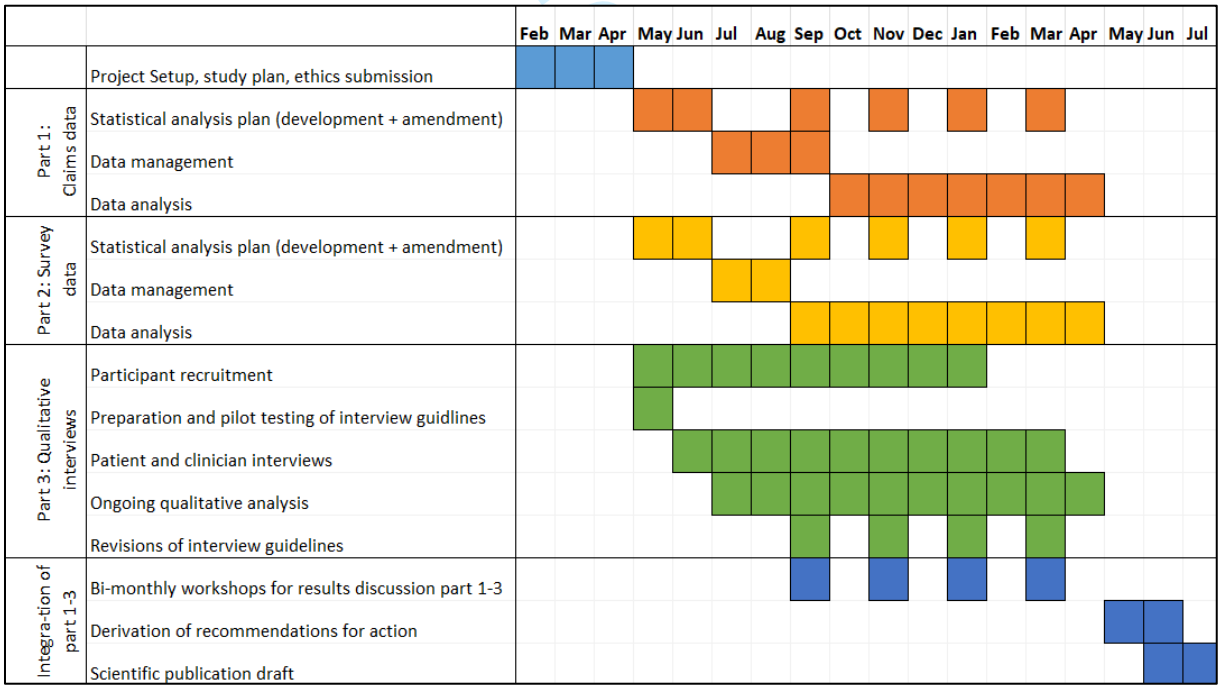
6.8 Dissemination of project outcomes

Study findings will be published in peer-reviewed dermatological journals and shall be submitted to national and international conferences including the congress of the European Academy of Dermatology and Venereology (EADV), the congress of the DDG (German Dermatological Society), the German convention ‘Dermatologie KOMPAKT & PRAXISNAH’, and the German ‘DERM’ conference.

The evidence-based recommendations derived from our study findings will be directed to the German decision bodies including federal ministries of health and social affairs, the Federal Joint Committee, and the payers. The target audience of dermatologists can be reached via the journal 'The Hautarzt', which has high coverage among dermatologists in Germany; results and recommendations will also be communicated to the state associations within the Professional Association of the German Dermatologists (BVDD), to all dermatologists in Germany, and to the regional AD networks. People with AD and/or AA can be reached via patient information events, patient journals, self-help groups, patient websites, and the IVDP's social media channels.

7 Timeline

The work packages are listed below separately for the overall study including the integration of the three study parts (blue), part 1 (claims data; orange), part 2 (survey data; yellow), and part 3 (qualitative study; green). The project will last 18 months in total. Scientific publications will be submitted afterwards; timing of abstract submission to scientific conferences will depend on the respective conference deadlines.



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UKE HAMBURG

Healthcare situation and disparities of patients with alopecia areata – A mixed methods analysis by *Toni Maria Janke, Beke Hester, Katharina Müller, Christine Blome, Theresa Klinger*

Supplement Tables S1 and S2: Relevant treatment and therapy (ATC and EBM) in claims data

Table S1: Relevant treatment of AA

Drug Group	Active ingredient	Anatomical Therapeutic Chemical [ATC] definition system	Ambulatory doctors fee schedule [EBM]
Topical treatments	Antibiotics	D06A	
	Antihistamines	D04AA	
	Crisaborole	D11AH06	
	Cromoglicic acid	D11AH03	
	Carbamide products	D02AE	
	Corticosteroids, dermatological preparations	D07	
	- Group I	D07AA	
	- Group II	D07AB	
	- Group III	D07AC	
	- Group IV	D07AD	
	- Corticosteroids, combinations with antiseptics	D07B	
	- Corticosteroids, combinations with antibiotics	D07C	
	- Corticosteroids, other combinations	D07X	
	Pimecrolimus	D11AH02	
	Psoralens	D05AD	
	Tacrolimus	D11AH01	
	Tars	D05AA	
Systemic biologics	Dupilumab	D11AH05	
Systemic non-biologics (conventional)	Methotrexate	L01BA01, L04AX03, M01CX01	
	Mycophenolic acid	L04AA06	
	Alitretinoin	D11AH04	
	syst. Antibiotics	J01	
	syst. Antihistamines	R06A	
	Azathioprine	L04AX01	
	Ciclosporin	L04AD01	
	Methoxsalen	D05BA02	
	Trioxysalen	D05BA01	

Drug Group	Active ingredient	Anatomical Therapeutic Chemical [ATC] definition system	Ambulatory doctors fee schedule [EBM]
Systemic GCS	Glucocorticosteroids - Betamethasone depot - Methylprednisolone depot - Prednisolone depot - Triamcinolone depot	H02AB H02AB51 H02AB54 H02AB56 H02AB58	
Ultraviolet light (UV) therapy	Selective phototherapy Supplement photochemotherapy, PUVA Balneophototherapy		30430 30431 10350

Table S2: Ambulatory doctors fee schedule [EBM] of outpatient psychotherapy

Ambulatory doctors fee schedule [EBM]	**Description**
22220	psychotherapeutic interview
23220	psychotherapeutic interview
35100	Differential diagnostic clarification of psychosomatic disease states
35110	Verbal intervention in psychosomatic disease states
35111	Exercise interventions, individual treatment
35112	Exercise interventions, group treatment
35113	Exercise interventions for children and adolescents, group treatment
35120	Hypnosis
35130	Determination of the obligation to pay benefits for the initiation of short-term therapy
35131	Determination of the obligation to pay benefits for the initiation / extension of long-term therapy
35140	Biographical anamnesis
35141	In-depth exploration
35142	Supplementary assessment of neurological and psychiatric findings
35150	Probationary session
35151	Psychotherapeutic consultation
35152	Acute psychotherapeutic treatment
35200	Depth psychology-based psychotherapy (short-term therapy, individual treatment)
35201	Depth psychology-based psychotherapy (long-term therapy, individual treatment)
35202	Depth psychology-based psychotherapy (short-term therapy, large group)
35203	Depth psychology-based psychotherapy (long-term therapy, large group)
35205	Depth psychology-based psychotherapy for children and adolescents (short-term therapy, small group)
35208	Depth psychology-based psychotherapy for children and adolescents (long-term therapy, small group)
35210	Analytical psychotherapy (individual treatment)
35211	Analytical psychotherapy (large group)
35212	Analytical psychotherapy for children and adolescents (small group)
35220	Behavioural therapy (short-term therapy, individual treatment)

Ambulatory doctors fee schedule [EBM]	**Description**
35221	Behavioural therapy (long-term therapy, individual treatment)
35222	Behavioural therapy (short-term therapy, small group)
35223	Behavioural therapy (long-term therapy, small group)
35224	Behavioural therapy (short-term therapy, large group)
35225	Behavioural therapy (long-term therapy, large group)
35251	Supplement I
35252	Supplement II
35253	Supplement III
35300	Test procedures, standardised
35301	Test procedures, psychometric
35302	procedures, projective
35401	Depth psychological psychotherapy (1, individual treatment)
35402	Depth psychological psychotherapy (2, individual treatment)
35405	Depth psychological psychotherapy (individual treatment)
35411	Analytical psychotherapy (1, individual treatment)
35412	Analytical psychotherapy (2, individual treatment)
35415	Analytical psychotherapy (individual treatment)
35421	Behavioural therapy (1, individual treatment)
35422	Behavioural therapy (2, individual treatment)
35425	Behavioural therapy (individual treatment)
35503	Depth psychological psychotherapy, 3 participants
35504	Depth psychological psychotherapy, 4 participants
35505	Depth psychological psychotherapy, 5 participants
35506	Depth psychological psychotherapy, 6 participants
35507	Depth psychological psychotherapy, 7 participants
35508	Depth psychological psychotherapy, 8 participants
35509	Depth psychological psychotherapy, 9 participants
35513	Depth psychological psychotherapy, 3 participants
35514	Depth psychological psychotherapy, 4 participants
35515	Depth psychological psychotherapy, 5 participants
35516	Depth psychological psychotherapy, 6 participants
35517	Depth psychological psychotherapy, 7 participants
35518	Depth psychological psychotherapy, 8 participants
35519	Depth psychological psychotherapy, 9 participants
35523	Analytical psychotherapy, 3 participants
35524	Analytical psychotherapy, 4 participants
35525	Analytical psychotherapy, 5 participants
35526	Analytical psychotherapy, 6 participants
35527	Analytical psychotherapy, 7 participants
35528	Analytical psychotherapy, 8 participants
35529	Analytical psychotherapy, 9 participants
35533	Analytical psychotherapy, 3 participants
35534	Analytical psychotherapy, 4 participants
35535	Analytical psychotherapy, 5 participants
35536	Analytical psychotherapy, 6 participants
35537	Analytical psychotherapy, 7 participants

Ambulatory doctors fee schedule [EBM]	**Description**
35538	Analytical psychotherapy, 8 participants
35539	Analytical psychotherapy, 9 participants
35543	Behavioural therapy, 3 participants
35544	Behavioural therapy, 4 participants
35545	Behavioural therapy, 5 participants
35546	Behavioural therapy, 6 participants
35547	Behavioural therapy, 7 participants
35548	Behavioural therapy, 8 participants
35549	Behavioural therapy, 9 participants
35553	Behaviour therapy, 3 participants
35554	Behavioural therapy, 4 participants
35555	Behaviour therapy, 5 participants
35556	Behavioural therapy, 6 participants
35557	Behavioural therapy, 7 participants
35558	Behavioural therapy, 8 participants
35559	Behavioural therapy, 9 participants
35571	Surcharge for individual therapy
35572	Surcharge for group therapy
35573	Surcharge for consultation/acute treatment
35600	Test procedures, standardised
35601	Test procedures, psychometric
35602	procedures, projective

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Supplement Table S3 and S4 Category systems of patients with alopecia areata and dermatologists

Table S3: Category system of patients with AA

1st	2nd	3rd	4th level of category system
Health care			
	Therapy Options		
		Local therapies	
			Cryotherapy
			Pulse therapy
			PRP
			DCP
			Further therapy options
			UV therapy
			Cortisone cream / topical cortisone
		Systemic therapies	
			Immunosuppressants
			Biologics
			Further therapy options
			Cortisone injection
			Cortisone tablet
		Other therapies	
			Participation in study
			Shampoo
			Wig and other assistive devices
			Lifestyle change
		Decision against therapy	
	Therapy-related behaviour and attitude		
		Medical consultation	
			With medical consultation
			Without medical consultation
		Costs and external conditions	
		Critical aspects of therapy	
			No long-term improvement
			Lack of continuity
			Scepticism towards potential side effects
			Lack of information by physician
			Lacking participation in therapy decisions
			Scepticism towards medication

		Few therapies offered
		Mode of administration
		Aversion to/caution with cortisone
		Exclusively symptomatic treatment
	Testing various therapies and products	
	Taking therapies according to need	
		Escalation steps
Medical providers		
	Dermatologists	
		Monitoring of disease/therapy progression
		Visits according to need
		Loyalty towards practice
		Cancer screening
		Consultation hour for hair loss
	General practitioner	
		Referral to specialist
		Examination at general practitioner
		No relevant provider
	Outpatient clinic	
	Other physicians	
		Rheumatologist
		Initial examination
	Psychological providers	
Non-medical provider		
	Alternative medical options	
		Use of alternative medical options
		No use of alternative medical options
	Pharmacy	
Aspects and criticism towards healthcare		
	Reasons for physician visits	
		Repeated prescription
		Blood tests
		Visibility of AA
		No provider visited
	Empathy of providers	
		Lack of empathy / not being taken seriously
		Empathy / being taken seriously
	Competencies of provider	
		Lack of competencies / expert knowledge
		Trust in competencies / expert knowledge
	Availability pf physicians	
		Problems finding good dermatologists
		Waiting time
	Change of physicians	
		Due to expertise

		Due to location
		Not changed despite dissatisfaction
	Side effects and contraindications	
	Patient education	
Life with AA		
	Familial case history	
	Misdiagnosis	
	Triggers	
	No obvious trigger	
	Physical changes	
	Seasonal influence	
	Infections	
	Stress	
	Co-morbidities	
	Information and exchange	
	Spontaneous remission	
	Symptoms	
	Handling of disease	
	Support by friends and family	
	Acceptance	
	Everyday life	
	Hope for spontaneous remission	
	Mental burden	
	Resignation/frustration	
	Visibility	
	Feeling uncomfortable	
	Research for causes	
	Repression	
	Desperation	

Table S4: Category system of dermatologists

1st	2nd	3rd	4th level of category system
Health care stations			
	Dermatologists		
	General practitioner		
	Outpatient clinic		
	Inpatient clinic visits		
	Psychological support		
	Alternative medical options		
	Pharmacy		
	No previous therapy		
	Information and exchange		
	Lifestyle change		
	Waiting time		
Treatment			
	Treatment options		
		Local therapies	
			Calcineurin inhibitors
			Cortisone intralesional
			Topical cortisone
			DCP therapy
			Local therapy - not specified
			PRP therapy
			UV therapy
			Further products
		Systemic therapies	
			Biologics
			Systemic cortisone
			ciclosporin
			JAK inhibitors
			Minoxidil
			MTX
		New therapies	
			Off-label therapies
			Study inclusion
		Wigs and other assistive devices	
		Issues regarding the therapy	
			Localisation of the disease
			Limited therapy options
			Non-response to therapies
			Reimbursement of therapies
			Reoccurrence after treatment end
	Monitor disease and treatment		
		Phasing out therapy	

1st	2nd	3rd	4th level of category system
		Observation of the course of disease	
		Disease duration as decision-making criterion	
		Laboratory examination and diagnostics	
		Assessment of scores	
		Tolerability of therapy and side effects	
	Spontaneous remission		
	Characteristics and life circumstances of patients		
	Patient involvement		
		Drug samples for patients	
		Building trust	
		Patient preferences	
		Adherence	
		Patient education	
	Re-presentation		
Reasons for visits at dermatologists			
	Disease symptoms		
	Fear and worry		
	Awareness for disease		
	Infections		
	Information about disease and its causes		
	New therapies and treatment options		
	Visibility		
	Stress		
	Desperate search and suffering		
	Wish for improvement		
	Time of disease progression		

UKE HAMBURG

IVDP Institut für Versorgungsforschung in der Dermatologie und bei Pflegeberufen

Healthcare situation and disparities of patients with alopecia areata – A mixed methods analysis by *Toni Maria Janke, Beke Hester, Katharina Müller, Christine Blome, Theresa Klinger*

Supplement 4: Recommendations for action developed in the expert panel

Background:

The AMEDA study (*Inequalities in access to medication for atopic dermatitis and alopecia areata in Germany: A mixed-methods study*) aimed to describe the care of adult patients with AD (AD) and alopecia areata (AA) in Germany. In particular, treatment pathways of patients and inequalities in care should be described.

An expert meeting was held on 01.06.2023 to present the results. The aim of the meeting was to **develop recommendations for action to reduce inequalities in the care of patients with AD and AA**.

Participants of the Expert Meeting:

- Patient representatives (Karin Mecklenburg from the German Neurodermatitis Association and Eva Lück-Beumler from Alopecia Areata Deutschland e.V.)
- Dermatologists (Prof. Dr. med. Matthias Augustin and Prof. Dr. med. Sabine Steinke)
- UKE scientists (PD Dr. Christine Blome, Dr. Kristina Hagenström, Beke Hester, Katharina Müller)

In the following, the results regarding AA will be presented.

Summary of the recommendations for action:

Alopecia Areata:

- Evidence of poorer care for patients with statutory health insurance → Reconsider the classification of AA as a lifestyle disease in order to provide access to adequate care for patients with statutory health insurance

- Evidence of regional differences in the quality of care → Development of an information platform to inform dermatologists about current scientific results and to strengthen the empowerment of patients

Alopecia Areata

Evidence of poorer care for patients with statutory health insurance

1. Background: In a decision of 18.10.2018, the G-BA restricted the treatment of alopecia areata (AA) as follows: "*There is no question that the treatment of alopecia areata in the various degrees of severity is a medical treatment and represents a burden for those affected, nevertheless the criteria leading to the classification as so-called lifestyle medicinal products are fulfilled*."[1]. The classification of AA to the area of lifestyle diseases excludes the reimbursement of costs for medicinal products for the treatment of AA by statutory health insurances.
2. Quantitative data: The analyses of the SHI routine data showed that 150 thousand people in Germany are treated for AA every year. Almost 35% suffer from a moderate to severe form of AA. The medication care of these insured persons in 2020 showed that the majority is treated with topical steroids or systemic non-biological drugs. JAK inhibitors can only be represented to a limited extent with SHI routine data, as these have only been approved for severe AA since 2022. The initial care of SHI-insured persons with an incidental AA diagnosis is primarily provided by with dermatologists. Subsequently, the majority of insured persons switch to a general practitioner.
3. Qualitative data: The analysis of the qualitative data indicates that due to this allocation, statutory patients are less well cared for, as the costs for high-priced therapies such as JAK inhibitors are not covered: "*In the case of alopecia areata, when we talk about therapy options, especially in the area of JAK inhibitors. Reimbursement of the costs of JAK inhibitors for the diagnosis of alopecia areata is very, very difficult. This is more likely*

[1] https://www.g-ba.de/downloads/40-268-5354/2018-10-18_AM-RL-II-Ergaenzung-Aktualisierung_TrG.pdf

to be the case with private patients. Then you have a better chance. It's certainly always an individual decision by the health insurance company." (dermatologist, code D08)

Recommendation for action: In order to ensure that patients with statutory health insurance receive the same level of care as those with private health insurance, the guidelines on access to medication need to be revised. In order to provide all patients with access to adequate care, **we recommend that** the **G-BA** recognises AA as an autoimmune disease instead of classifying it as a lifestyle disease. In doing so, we join a petition that is already being considered by the German Bundestag[2] .

Evidence of regional differences in the quality of care

1. Background: Data on AA show that patients have differences in care depending on where they live. This is shown, for example, by the fact that access to dermatologists is more difficult in rural areas due to longer waiting times and sometimes long travel times.
2. Quantitative data: The drug supply showed some regional differences on the basis of the SHI routine data. Significantly more insured persons in urban areas consulted a specialist compared to insured persons in rural areas.
3. Qualitative data: The qualitative interviews also revealed that it is difficult for patients to find dermatologists who have sufficient expertise and information about AA. "*I think very few GPs or dermatologists know that. And you have to be really lucky to find a doctor who is currently interested in it and/ is really actively involved in the science nowadays, or at least passively reads along. And that depends on the doctor. You have to be lucky, my time was too valuable, where I actually read: wait and see and then it will fit*" (patient with AA, code AA03). The interviews with dermatologists confirm this: "I think the *more severe the alopecia is, the fewer medical colleagues you will find who are willing to treat the alopecia. (…) I think the willingness to deal with such a disease, to even say: Okay' I'll see if I can help the patient somehow. As I said, that is the individual*

[2] https://epetitionen.bundestag.de/content/petitionen/_2023/_03/_27/Petition_148387.html (as at: 07.06.23)

attitude of the doctor. And, as I said, that is often not so great, unfortunate"y." (dermatologist, code D07)

Recommendation for action: The data show that dermatologists need more information on the disease in order to provide adequate care. We therefore recommend that the **G-BA** and **IQWiG** develop an information platform on AA that presents current scientific results. Such a platform is not only helpful for dermatologists, but also for patients. The empowerment of patients is also crucial: well-informed patients can demand more co-determination in the choice of therapy and thus also improve care.

Other important findings on AA from the Expert panel were:

- The stigmatisation of the disease is very stressful for patients; making AA more widely known will create more understanding and reduce stigma.
- Patients have expressed the wish that dermatologists and general practitioners first exclude other diseases by testing the blood values when making a diagnosis. In addition, patients would like specialists to point out other possible treatment options, such as nutritional counselling to reduce nutrient/vitamin deficiencies.
- Self-help and exchange among AA patients play a major role. Interdisciplinary meetings between patients and doctors should be promoted more strongly.

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Identifying barriers and disparities in the healthcare of patient with alopecia areata – A mixed-methods analysis using claims data and qualitative interview data

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Identifying barriers and disparities in the healthcare of patient with alopecia areata – A mixed-methods analysis using claims data and qualitative interview data

Running head: Healthcare situation and disparities of patients with alopecia areata

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Abstract

Objectives

Alopecia areata (AA) is a chronic immune-related disease with non-scarring hair loss. Treatment may reduce disease activity but cannot cure. Even though AA can be very burdensome to patients, the German social act has categorized AA as a "lifestyle disease" and treatment is not covered by statutory health insurances (SHI). We aimed to characterise the healthcare situation of patients with AA in Germany, including potential inequalities, and to derive recommendations for action.

Design

This mixed-method study combined (1) semi-structured qualitative interviews with patients and dermatologists, analysed through qualitative content analysis and (2) claims data analyses of a large nationwide German SHI from 2016 to 2020. Both types of data were collected and analysed in parallel to enable integrated analysis. Consecutively, an expert panel derived recommendations for action.

Setting

Interviews were conducted online or via telephone.

Participants

Patients were recruited conveniently via a dermatological outpatient clinic, patient organisations and social media. Dermatologists were recruited from a nationwide network and the dermatological societies.

Primary and secondary outcome measures

Exploration of healthcare situation of adult persons with AA in Germany, investigating potential barriers to adequate care and identifying potential inequalities of access to care.

Results

We interviewed 20 patients (average age 40.7 years; 75.0% female) and 14 dermatologists (age 48.4 years, 50.0% female). SHI data included 4,692 persons with AA in 2020 (prevalence 0.23%; mean age 55.8 years; 76.2% female). The lack of reimbursement was criticised by both patients and dermatologists. Though 57.5% of patients received at least one drug prescription, mostly topical therapies, access to approved systemic drugs was very low. Drugs were prescribed mostly by general practitioners (41.1%) and dermatologists (32.8%). Some patients were sceptical regarding side effects of treatment and criticised exclusively symptomatic treatment. Patients reported an urge for information and exchange with others as well as

different ways of handling their disease, such as acceptance, and frustration or desperation. Patients living in urban areas received topical therapies more often than patients in rural areas. Furthermore, women were more likely to receive treatment than men. Recommendations for action include reimbursement of AA medication and developing a platform providing information on AA to physicians and patients.

Conclusions

Disease burden and frustration of patients with AA is high, mostly caused by limited treatment options and lack of reimbursement, limiting access to approved drugs such as JAK inhibitors. Through the mixed-method-design, we were able to combine patient experiences and quantitative data reflecting the reality of healthcare in Germany.

Strengths and Limitations of this study

- In the interviews, only German-speaking patients could participate and due to the nature of qualitative data, no quantitative assumptions can be made.
- Claims data analyses cover only services that are reimbursed by the statutory health insurance and data might be over- or underestimated due to insufficient or inadequate differential diagnoses, misclassifications, or coding behaviour of the practitioner.
- The major strength of this study is the mixed-methods design, in which the different methods compensated for their limitations.
- The mixed-methods approach allowed to generate and investigate additional research questions and enabled a comprehensive interpretation of the results.

Funding statement

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Competing interests

TMJ, BH, KM, TK and KH have no conflict of interest.

CB has received speaker honoraria and/or research grants from Amgen/Celgene, AstraZeneca, Bauerfeind, Deutsche Gesellschaft für ME/CFS, Hartmann, Lilly, Mapi Group, medi, Pfizer, Sanofi, UCB, and Urgo.

BS has received honoraria and consulting fees for lectures, scientific presentations, medical advisory and / or received grants and / or participated in clinical trials including the following companies: Abbvie, Almirall Hermal, Amgen, Bayer, Beiersdorf, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Eli Lilly, Galderma, GSK, Incyte, Janssen-Cilag, LEO Pharma, Medac, Novartis, Pierre Fabre, Pfizer, Sanofi Aventis, and UCB.

MA has served as a consultant, lecturer, researcher, and/or has received research grants from companies manufacturing drugs for alopecia areata, including AbbVie, Eli Lilly, Incyte and Pfizer.

Introduction

Alopecia areata (AA) is an inflammatory, immune-mediated disease leading to non-scarring hair loss. It is associated with other chronic inflammatory skin and autoimmune diseases.[1,2] Furthermore, AA can be triggered by numerous factors.[2] In patients with milder forms, around two thirds experience spontaneous remission.[1] However, an increased risk of recurrences remains. AA is characterised by a mostly high psychosocial burden. Since mostly visible body areas are affected, most patients experience or perceive stigmatisation, interpersonal strain and increased levels of psychosocial stress.[3,4]

Disease-halting drugs used for AA traditionally include topical glucocorticosteroids (TGCs) and calcineurin inhibitors (TCI), systemic glucocorticosteroids (SGCs) and immunosuppressants such as methotrexate and Janus kinase inhibitors (JAKi). With the JAKi baricitinib (since 2022) and ritlecitinib (since 2023) the first systemic drugs have been approved in Europe. Psychosocial support is indicated in many patients.[5,6] The first German therapy guideline for AA is expected to be available in 2026.[7]

The prevalence of AA is about 1.6% worldwide [8] and 0.2% in Germany.[9] Few studies have been conducted on the care of AA patients. The statutory health insurance (SHI) data from the USA show that 44.2% of patients remained untreated after diagnosis[10]and that the male gender predicted fewer medical visits.[11] In the UK, access to care was influenced by gender, socioeconomic status, ethnicity, and urban residence.[12] Patients reported high out-of-pocket costs.[13]

In Germany, the German Social Act V includes a “lifestyle paragraph” excluding drugs from reimbursement by the SHI when they serve for improving hair growth. From the perspective of the Federal Joint Committee regulating details of healthcare in the SHI system, this applies to all forms of hair loss, including AA;[14] resulting, drugs for AA are generally not covered by the SHI. Hence, approved and evidence-based therapies such as JAK inhibitors are rarely used in patients with SHI status (constituting 89% of the German population)[15] but in markedly more patients who have private health insurance.

Thus, quality of care for AA in Germany is suboptimal and there seems to be an unmet need for adequate and equal treatment in this burdensome disease. This study being part of the project "Inequalities in access to medication for atopic dermatitis (AD) and AA in Germany: A

mixed-methods study (AMEDA)" (Supplement 1) aimed to analyse the healthcare situation of adult persons with AA in Germany by a) investigating potential barriers to adequate care and b) identifying potential inequalities of access to care. Recommendations for action were to be derived from the results and addressed to the stakeholders in the German health system.

Design

The mixed-method study design combined qualitative interviews and claims data from a large nationwide German SHI.

Qualitative analyses

Online or telephone interviews were conducted between June 2022 and April 2023. We used a semi-structured, pilot-tested interview guideline (Supplement S2 and S3) based on the research questions and literature. If necessary, the guideline was adapted throughout the study to allow for integrating new aspects found in previous interviews and in the claims data analysis. The interviews were conducted by two female researcher associates (health scientists, M.Sc.; BH, TMJ) experienced in conducting qualitative interviews through their university education and previous qualitative studies. We took a neo-positivist philosophical position with a realist approach, meaning that we sought approaching objective reality.[16] Data collection and analysis were not theory-based.

Patients were recruited conveniently via a dermatological outpatient clinic, patient organisations and social media. Dermatologists were recruited from a nationwide network and the dermatological societies, representing >95% of professionally working German dermatologists. All participants gave written informed consent. Participants had the right to withdraw their consent at any time until pseudonymised data was anonymised. Only members of the study team had access to interview data and information on the participants. For patients, it was stated explicitly that a non-participation had no influence on their treatment. The interviewers had no personal, professional or therapeutic relation with the interviewees, except for one dermatologist working at the same institute. Interviews introduced themselves, their background and the aim of the study prior to the interview. Recruitment stopped as soon as further interviews added no additional content, meaning that thematic saturation was reached. For this, we documented which categories were newly developed per

interview. We defined thematic saturation to be reached once no new categories emerged on the two highest levels of the category system.

All interviews were audiorecorded and transcribed verbatim, in the process of which the interviews were pseudonymised. Data were analysed with MAXQDA v. 24 (VERBI GmbH, Berlin, Berlin, Germany) using qualitative content analysis according to Kuckartz[17]: Two researchers (BH, TMJ) formulated research questions and derived main categories from these. Afterwards, both researchers familiarised with the interview transcripts and case summaries and categorised the first transcript jointly. Based on this, they revised the main categories. One researcher categorised three subsequent transcripts and the categorisation was checked by the other. In the further categorisation, additional (levels of) subcategories were developed, if necessary. The category system was frequently discussed by the study team (BH, CB, TMJ).

Claims data analyses

The analysis was based on an anonymised 40% sample (N=2,513,860; 58.0% women, average age 55.1 years in 2020) of all persons (aged at least 18 years) who were insured for at least one day with the DAK-Gesundheit (DAK-G) between 01/01/2016 and 31/12/2020. Based on the guidelines and recommendations for ensuring good secondary data (GPS) and good epidemiological practice (GEP), these data from the SHI system do not require an ethical vote or the consent of the insured persons.[18,19] This is because these data sets are based on existing data originally collected for other purposes. In addition, the data are anonymized, which prevents the identification of individuals and thus minimises the associated risks. The use of the project's data base is well protected by legal and institutional regulations, such as the GPS and the GEP. These regulations ensure ethical and responsible use of the data.

Prevalent insured persons were considered to have AA (ICD-10 GM L63) if they had at least one confirmed outpatient or inpatient main or secondary diagnosis. Incident cases had to have a three-year diagnosis-free period in 2020.[9]

The utilisation of outpatient care for prevalent AA was determined based on all physician contacts.[20] AA-related drug prescriptions (coded by the Anatomical Therapeutic Chemical [ATC] definition system) and defined daily doses (DDD) or treatments (ambulatory doctors fee schedule [EBM]) were only recorded if an AA (Supplement S4, Table S1) diagnosis was made in the same quarter.

In the sensitivity test, systemic antibiotics and their proportion of prescriptions in the total population were analysed to determine the population effect. The treatment history of AA patients was followed over four quarters using drug prescriptions. The proportion of outpatient psychotherapy (at least one prescription; Supplement S4, Table S2) was compared between prevalent AA patients and other skin diseases (ICD-10 'L' diagnosis excluding L63). Hospitalisation rates for full and partial inpatient stays with a principal diagnosis of AA were also recorded.

The administrative estimates of period prevalence and incidence (annual) were expressed as percentages with 95% confidence intervals (CI) and were standardised according to the German federal statistics institute DESTATIS as of 31 December for the observation year. Descriptive statistics and multivariate analysis methods were used according to the data level of variables. For comparative analyses, the data were adjusted for age, sex, and federal state using 1:3 nearest neighbour propensity score matching (PSM). Logistic regression was utilised to compute propensity scores (PS). Relative risks (RR) and 95% CI were calculated to assess differences between the comparison cohorts. The analyses were performed with SAS Version 9.4 German (SAS Institute, Cary, North Carolina, USA).

Mixed-methods approach

Both types of data were collected and analysed in parallel to enable integrated analysis: The study team met on a monthly basis to discuss interim results of all parts of the study. Hence, patterns found in one study part were presented and possibilities discussed to investigate from this originating hypotheses in the other study part. As an example, we detected a high use of antibiotics in the claims data analysis. Accordingly, we asked dermatologists in interviews if they prescribe antibiotics for patients with AA and, if so, in which cases and we probed this topic in interviews with patients.

The data were synthesised into an overall conclusion and from this, recommendations for action were derived.

Development of recommendations for action

Based on the results of all study parts, an expert meeting was held with two dermatologists, two patient representatives and four scientists (researchers responsible for analyses of

qualitative and claims data). Within the meeting, recommendations for action to reduce inequalities in the care of patients with AA were developed.

Patient and Public Involvement

In the expert panel, members of a patient organisation participated to discuss results and develop recommendations. At the end of the project, all participants received a lay summary of the results.

Results

Sample description and baseline characteristics

In the qualitative interviews (Table 1), 20 patients and 14 dermatologists participated (duration 20–85 minutes).

>>Insert Table 1<<

For each patient and dermatologist, distinct category systems were established through qualitative content analysis. The category system was considered final, when the last two participant interviews and the three last dermatologist interviews had revealed no new categories on the two highest levels of the category system. Main categories in patient data were “healthcare” and “life with AA”. Main categories derived from dermatologist interview were: “healthcare stations”, “treatment” and “reasons for visits at dermatologist”. For the full category system see Supplement S5, Tables S3 and S4.

According to claims data, the standardised prevalence of AA in 2020 was 0.23% (N=4,692; mean age 55.8 years (standard deviation 19.0, median 57); 76.2% female) and incidence was 0.09% (N=1,565; 2019), corresponding to about 150,000 prevalent and 53,000 incident persons across Germany. The prevalence and incidence increased with age.

Treatments for AA

Following the claims data, 57.5% of the persons with AA received at least one drug prescription in 2020. Topical and systemic non-biological drugs were prescribed to 36.8% and 35.1%, respectively; among the topical drugs, 95.3% were TGCs (mostly class III and IV) and

11.1% received SGCs (Table 2). Less than 0.02% (n=9) used JAK inhibitors, namely tofacitinib and baricitinib (each 0.06%), ruxolitinib (0.04%) and upadacitinib (0.02%). Ultraviolet light (UV) therapy received 0.53% of the insured persons with AA in 2020 (0.78% in 2016) with selective phototherapy being the most common form of treatment. With 32.0% of insurees with AA receiving psychotherapeutic treatment, they were 19% (RR 1.19, CI 1.13-1.25) more likely to receive psychotherapy than persons with another skin disease (according to PSM).

>>Insert Table 2<<

The total prescription volume decreased continuously. The number of DDD dispensed fell from around 288,398 in 2016 to 233,264 in 2020. Only systemic biologics (i.e., Dupilumab) showed a slight increase from 1,206 DDDs in 2018 to 2,580 DDDs in 2020 (Figure 1).

>>Insert Figure 1<<

41.1% of the AA-related drugs were prescribed by general practitioners (GPs), 32.8% by dermatologists and 4.2% by internists. GPs prescribed antibiotics (65.6%), TGCs class I (63.4%), systemic antihistamines (53.4%), azathioprine (66.7%) and SGCs (50.4%) more often than dermatologists (Figure 2). Dermatologists prescribed the majority of biologics (i.e., Dupilumab; 75.0%). A total of 27.3% of insured persons with AA received a systemic antibiotic, compared to 21.7% of the general population (all insured persons without AA).

>>Insert Figure 2<<

In the qualitative data, patients reported the use of different **therapeutic options** including ***local***, ***systemic***, and ***further therapies*** or products. Some patients ***decided against therapy*** (Table 3, Q1.1), mostly due to experienced lack of improvement. Some reported the therapy was too time-consuming or was not likely to be successful (Q1.2). Female patients also reported ending treatment due to pregnancy.

Patients who received ***topical therapies*** reported different therapeutic success: in some patients, hair started growing again, while others did not see improvement.

Many reported wearing headgear (Q1.3), having permanent make-up, or using specific shampoos. Furthermore, patients reported lifestyle changes to improve hair growth.

For ***systemic therapies***, patients reported the use of immunosuppressants (Q1.4), oral or intralesional systemic corticosteroids, and (in few patients) JAKis and biologics through participation in a clinical study or as an off-label therapy. The patient with JAKi reported improvement of symptoms.

Most patients reported ***having tested various therapies and products***, including prescribed therapies and over-the-counter products or home remedies. They also mentioned ***critical aspects regarding therapy***: most patients were frustrated because of few therapeutic options. When receiving treatment, many felt lacking shared decision-making (Q1.5). Many reported scepticism towards medication and side effects. This scepticism includes a general scepticism not only against conventional medicine but also towards JAKi. Some patients criticised the exclusively symptomatic treatment and that no long-term improvement was achieved. Some wanted their practitioner to provide more information about the disease and therapy options (Q1.6). The most discussed aspects regarding therapy options were ***costs and external conditions***. Patients reported major differences in cost reimbursement between different SHIs and criticised that their insurance did not pay for the necessary equipment (e.g., wigs).

The dermatologists reported that they usually start treatment with ***local therapies***, mostly TGCs. Most dermatologists also mentioned therapies with diphenylcyclopropenone or platelet-rich plasma as treatment options; however, only few reported using these in practice. Also, both therapies could only be offered as privately paid treatments. Other local therapies were TCI and UV therapy.

Dermatologists also reported offering ***new therapies*** to patients, namely JAKi or immunomodulating therapies as off-label therapies. Study inclusion was reported as another possibility to offer persons with AA access to modern treatments (Q1.7). Regarding ***systemic therapies***, SGCs were described as a short-term, acute treatment. Dermatologists described JAKi as a very effective treatment (Q1.8), but as only a theoretical therapeutic option in Germany. As a treatment to "*simply stop this acute phase of the disease*" (dermatologist, male, 60–69 years), immunosuppressants such as cyclosporine and methotrexate, as well as minoxidil, were reported. Finally, dermatologists described that patients were often content

with using ***wigs and other supportive devices*** (Q1.9), and some patients did not require or want any additional treatment.

Dermatologists also reported ***issues regarding the therapy***, notably the overall limited therapy options, especially for those working in office-based practice. The second major aspect was the lack of reimbursement by the health insurances (Q1.10). Further issues were recurrence after treatment end (Q1.11) and non-respondence to therapies.

Almost all dermatologists reported **spontaneous remission** in many patients with mild AA. They encouraged these patients to wait and document the symptoms (Q1.12).

An important aspect of AA treatment was **patient involvement**, which could be achieved through ***patient education*** (Q1.13) or by considering ***patient preferences***. Dermatologists reported overall high levels of ***adherence*** (Q1.14).

>>Insert Table 3<<

Life with AA

Patients reported their **symptoms** describing different severity of hair loss ranging from few bald spots to total hair loss; most had severe AA including some with a long disease history. Few patients had experienced a **spontaneous remission**. Some reported **co-morbidities**, including allergies, bronchial asthma, and other autoimmune diseases, or a **family history of AA**.

Few patients reported ***no obvious trigger***; most patients assumed their AA to be triggered by different factors such as ***stress***, for example through work (Table 4, Q2.1), private life or relationships. Few patients had experienced their first symptoms after an ***infection***. Several female patients reported changes in their symptoms (both increased and reduced) in relation to ***physical or hormonal changes*** such as pregnancy, miscarriage, or breast feeding. Some patients experienced a ***seasonal influence*** on symptoms (Q2.2). Of these, all but one reported hair growth in spring/summer and hair loss in autumn/winter.

Information and exchange with other patients were very important for the participants, making use of social media, patient support groups or other ways of connecting with other patients. Some reported searching for new research results online. Few patients said they did not want or need exchange with other patients.

Patients have found different ways of **handling their disease**. Some patients reported having ***accepted the disease*** (Q2.3, Q2.4). Others talked about the ***mental burden***, ranging from "*of course, mentally you're not doing so great*" (female patient) to severe depression and suicidal thoughts. The ***visibility*** of the disease was a severe burden for many patients. They described ***resignation/frustration***, ***feeling uncomfortable*** and ***desperate***, or ***repressing*** thoughts about their AA.

Some patients described wanting to *understand the causes* of their disease and how to influence its progression (Q2.5); some ***hoped for a spontaneous remission***.

>>Insert Table 4<<

Patient pathways

In the qualitative interviews, for the initial examination of the AA, generally including blood tests, some patients visited a dermatologist while others first saw a GP. After this, the GP mostly was no longer a relevant provider for AA treatment. Visits at the dermatologist mostly happened as needed (Table 4, Q3.1), while some patients saw their dermatologist regularly for the monitoring of the disease/therapy progression. Some patients visited specific dermatologic consultations for hair loss. Pharmacies were only used by patients to pick up prescribed therapies (Q3.2). Most patients had made use of alternative options, including visits to homoeopaths or acupuncture therapy. Most of these patients reported no improvement in their symptoms and some mentioned the high costs of alternative providers; however, some appreciated that "*you are perceived quite differently. Of course, they have a completely different time register for you.*" (female patient). Some patients attained psychological care, mostly looking for help in handling their disease (Q3.3) but also hoping to reduce stress and improve the symptoms.

Most patients criticised a lack of empathy or felt like they were not taken seriously by the physician (Q3.4). However, some reported being taken seriously and appreciating the dermatologists' empathy and honesty (Q3.5). Some patients experienced a lack of competencies or expert knowledge (Q3.6) and therefore saw multiple different dermatologists. Patients mostly reported long waiting times until their appointment and difficulties finding good physicians.

Dermatologists reported that patients usually first visit GPs or dermatologists. GPs would usually do routine blood tests to exclude other diagnoses and then refer the patient to dermatologists. Patients with a long or complicated disease history are often referred to university clinics or specialised outpatient clinics (Q3.7). Inpatient clinic visits were reported to play a minor role. Furthermore, dermatologists reported that some patients used over-the-counter products from the pharmacy, for example shampoos against hair loss. Few mentioned suggesting the option of psychological support to patients.

Alternative medical options were mentioned by some dermatologists but reported that patients with AA generally make less use of these compared to other patient groups. Dermatologists also reported that information and exchange with other patients was important for many patients.

In 2019, 53.3% of the 1,565 patients with AA initially received prescriptions for AA. In the first quarter, 70.5% were treated by dermatologists and 31.5% by GPs, with 47.7% receiving prescriptions, falling to 39.6% in the third quarter. In the fourth quarter, the proportion of patients treated by GPs rose to 53.5%, while the proportion treated by dermatologists fell to 27.0% (Figure 3).

>>Insert Figure 3<<

The proportion of persons with AA having received systemic non-biologic drugs increased by age (Table 5). The user rate of topical treatment was significantly higher in women (26.2%; p<0.001) and those from urban areas (26.5%; p 0.002). Dermatologists prescribed topical and biological drugs more frequently (63.7%; 75.0%; each p<0.001), whereas GPs prescribed systemic non-biologics, especially GCs more frequently (60.3%; 48.1%; p<0.001).

>>Insert Table 5<<

Recommendations for action

In the expert meeting, recommendations for action to reduce barriers of access and/or inequalities in the healthcare of patients with AA were developed. The English translation on

the recommendations for action can be found in Supplement S6. In the following, a summary is provided.

1. Evidence of poorer healthcare for patients with SHI

   To ensure that patients with SHI receive the same level of care as those with private health insurance, we recommend that the German legislation body (Bundestag) recognises AA as relevant autoimmune disease instead of classifying it as a lifestyle disease.

2. Evidence of regional differences in the quality of care

   The data show that dermatologists need more information on AA to provide adequate care. We recommend the development of a platform on AA that presents data on current scientific results; this platform could also be helpful for patients and might empower them by being well-informed about their disease.

Discussion

This mixed-method study analysed the healthcare situation of adult persons with AA in Germany and investigated potential inequality, in particular regarding medication; from the study results, recommendations for action were derived.

Both the SHI data and the qualitative data reveal a large gap of healthcare for persons with AA in Germany. Concordantly they show that there is much less use of advanced therapies for AA as recommended. Baricitinib and ritlecitinib show efficacy in treatment[1] but have only been approved in 2022 and 2023 and, hence, after the time period represented by the claims data analysed for this study. At this time, these and other JAKis might have been only prescribed as off-label treatment. Our qualitative results confirm that prescribing advanced therapies still remains challenging due to the lack of reimbursement through the SHIs, which originates from the exclusion of drug treatments for AA by the Germans Social Act, which is based on a false interpretation of the terms alopecia (hair loss) and “drugs improving hair growth” by the legislators. The intention was to exclude reimbursement of treatments for simple hair loss as caused by androgenetic alopecia, a common and harmless disease. The legal process by the German parliament failed to consider that alopecia areata is a distinct severe immune disease with a different pathogenesis, disease course, phenotype and disease

burden. Being associated with a multitude of other immune-mediated diseases and autoimmune conditions, it needs stringent diagnostics and consequent treatment. The exclusion of such treatments thus violates the imperative of the German Social Act to provide support for persons with severe health conditions. Another reason for low prescribing rates might be the discussion about long-term safety of these new drugs. JAKis approved in the years before baricitinib received black box warning[21] and Alert warning[22] ("Rote Hand Brief"; BfARM Germany) which derived from data for the pan-JAKi tofacitinib in high treatment doses for patients with rheumatoid arthritis or colitis. These analyses were used for generalised warnings about increased risk of blood clots, serious heart-related events or cancer for several JAKis,[23] although their mode of action and targeted enzymes are different, e.g. baricitinib selectively and reversibly binds to JAK1 and JAK2, whereas its effect on JAK3 or TYK2 is low.[24,25] This will be under investigation and closer look for all further safety analyses, but created an alerted atmosphere for prescribers.

While expensive innovative drugs are not reimbursed, health insurances tend to pay for cheaper, often topical treatments. As in other dermatological diseases,[26] lower potency TGCs were mostly prescribed by GPs and higher potency TGCs by dermatologists. Additionally, in persons with AA, GPs might be hesitant to prescribe higher dosed medication due to limited research and experiences. While in the interviews GPs were often mentioned as first contact person but considered as not relevant in the treatment process, claims data showed that the number of patients contacting GPs increased over time. Throughout the observation period following the initial AA diagnosis, there was a notable decline in the prescription volume, from 48% in the first quarter to 40% in the third quarter. The results are in accordance with the findings from the US, which indicated that 44% of individuals with AA were not prescribed treatment in the year following diagnosis.[10] This corresponds to reports about resignation and ending treatment in case of lacking improvement. The participants emphasised their frustration with the lack of treatment options and sometimes inadequate knowledge by their healthcare provider. This may result from AA being a predominantly visual diagnosis. While patients expect to undergo more detailed examinations in the hope of finding triggers, once diagnosis has been confirmed, the patient is often left with regular monitoring, which might cause frustration.

Similar to previous findings,[27,28] patients reported high mental burden. A study on younger adolescents identified feeling isolated and being self-conscious as psychological strain for patients. AA was regarded as more than just hair loss and unpredictability whether hair would grow bas was seen as difficult experience.[29]Also, claims data show a higher probability to use psychotherapy compared to other skin diseases. Therefore, the mental health of people with AA should be considered and physicians should be made aware of this issue. Psychological interventions might not only help patients to cope with their disease but also improve AA through reduced stress levels of patients.[30]

Patients in the qualitative study part often reported lacking empathy and understanding by healthcare providers. This is in line with a previous study, which identified the need for more information and addressing the emotional impact in young patients (De Vere Hunt 2021).

We found higher prevalence and higher therapy prescription in women. A possible reason is that women might be more sensitive to hair loss than men due to cultural factors. Furthermore, treatment prescription grows with age. Patients in urban areas receive more topical medication. This might confirm considerations in the qualitative interviews that dermatologists in rural areas often lack knowledge about AA treatment or are worried about reimbursement. Additionally, long travel distances might reduce the acceptance of therapies requiring regular physician visits. Surprisingly, a marked proportion of patients received prescription drugs attributable to AA though they are legally excluded from reimbursement. Two reasons may contribute to this: Low-cost drugs may not be queried by the payers and thus are tolerated in spite of the ban. Second, further diagnoses may have been used to hide the use of drugs for an indication not covered by the SHI. For example, patients with comorbid rheumatism might receive JAKis more often as in these indications advanced therapies is more likely to be remunerated. This might also explain why JAKis were not prescribed by dermatologists in our claims data set.

As part of this study, recommendations for action to reduce health disparities were developed. Firstly, the expert panel recommended to recognise AA as an autoimmune disease instead of classifying it as a lifestyle disease. Through this recognition, all patients will be able to receive adequately reimbursed care. This would reduce the patient burden and improve

the healthcare situation significantly. Secondly, we the expert panel outlined the differences between urban and rural areas. Physicians should be better informed about AA, its treatment options and options for reimbursement and study inclusion; this should be done through an independent platform that informs about scientific results. The current development of treatment guidelines for AA will also help inform physicians better to enable providing adequate care for patients.

The major strength of our study is the mixed-methods design, which allowed us to generate additional research questions. Furthermore, the combination of the different results enabled a more comprehensive interpretation. Due to the nature of qualitative data, no quantitative assumptions can be made and results are not generalizable to the wider public. In the interviews, only German-speaking participants could participate, which excludes the experience of non-German speaking patients in the German healthcare system. Additionally, even though we recruited in different setting (dermatology clinics, patient organisation, social media) patients with higher severity, better online access and more engaged patients are most likely to participate, whereas patients with only light symptoms are likely to be underrepresented in the qualitative data. Claims data cover all patients who have received healthcare covered by the respective SHI, and they allow for an objective quantification of the healthcare received. Even if claims from private insurance are not included, the SHI covers about 90% of the population in Germany and thus provides an extremely robust and representative data base.[31] Its breadth and depth allow reliable statements to be made about the realities of health care in Germany, even though privately insured persons are not included. For example, there are differences between the groups of people insured by the various health insurance funds.[32] To minimise these differences, the prevalence rates have been adjusted for age and sex. However, only services that are reimbursed by the SHIs are recorded. Therefore, data on privately paid services are not collected. In addition, the proportion of patients with AA could be over- or underestimated, for example, due to insufficient or inadequate differential diagnoses, misclassifications, or coding behaviour of the practitioner. To account for this, we used validity criteria such as confirmed outpatient diagnoses.

Overall, this study provides important new data on the healthcare of persons with AA. By including interviews with patients and dermatologists and linking these with quantitative data, we draw a wide picture on the current healthcare of patients with AA. We were also able to show that the treatment conditions need to be improved through the health insurance to provide adequate care to all patients. Lastly, the recommendations for action that we developed based on our study results aim to reduce disparities in healthcare.

Author's contribution

All authors had substantial contributions to the analysis or interpretation of data for this paper, revised it critically for important intellectual content, approved it finally and agreed to be accountable for this work in ensuring its integrity of interpretation of data.

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Data availability statement: The datasets generated for the claims data cohort are not available, as the use of claims data is restricted to authorized researchers. The data underlying the qualitative analyses will be shared on reasonable request to the corresponding author.

Ethics statement: The study has been approved by the Local Ethics Committee at the University Medical Center Hamburg-Eppendorf (LPEK-0427). Participants of the interview study received information on the ethics and data protection and provided written informed consent.

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Tables

Table 1: Characteristics of patients and dermatologists participating in the interviews

	Mean (range) / n (%)	
	Patients (n=20)	**Dermatologists** (n=14)
Age (years)	40.7 (25–61)	48.4 (31–69)
Gender		
Female	15 (75.0)	7 (50.0)
Male	5 (25.0)	7 (50.0)
Education		
(Vocational) A-levels [12–13 years of education]	15 (75.0)	n.a.
10 years of education	3 (15.0)	n.a.
9 years of education	2 (10.0)	n.a.
Living/Practicing*		
Baden-Wuerttemberg	3 (15.0)	1 (7.1)
Bavaria	4 (20.0)	1 (7.1)
Berlin	1 (5.0)	0 (0)
Hamburg	1 (5.0)	1 (7.1)
Lower-Saxony	4 (20.0)	2 (14.3)
North Rhine-Westphalia	3 (15.0)	4 (28.6)
Rhineland-Palatine	1 (5.0)	4 (28.6)
Saxony	1 (5.0)	0 (0)
Saxony-Anhalt	0 (0.0)	1 (7.1)
Schleswig-Holstein	2 (10.)	1 (7.1)
Insurance		
Statutory	19 (95.0)	n.a.
Private	1 (5.0)	n.a.
Duration of AA symptoms (years)	16.3 (0.25–51)	n.a.
Missing hair		
Scalp	54% (0.0–100%)	n.a.
Face/body	62% (0.0–100%)	n.a.
Employment situation*		
Practice	n.a.	10 (71.4)
Clinic	n.a.	5 (35.7)
Experience as dermatologist (years)	n.a.	19.7 (7–37)

*multiple answers possible

Table 2: Alopecia areata (AA) related prescriptions in prevalent insured persons with AA and at least one drug prescription in 2020

Drug group	Drug therapy	Patients with AA-diagnosis (N)	≥1 Rx (n)	≥1 Rx (%)	Total DDD	Mean Rx per patient	Mean DDD per patient
Total	**Any therapy**	**4,692**	**2,701**	**57.57**	**233,305.49**	**2.67**	**86.38**
Topicals	**Total**	**4,692**	**1,726**	**36.79**	**121,928.74**	**1.85**	**70.64**
	Antibiotics	1,726	124	7.18	1,117.01	1.18	9.01
	Antihistamines	1,726	2	0.12	30.00	1.00	15.00
	Corticosteroids, dermatological preparations	1,726	1,644	95.25	117,745.80	1.78	71.62
	- Group I	1,726	41	2.38	1,589.17	1.20	38.76
	- Group II	1,726	153	8.86	6,312.73	1.35	41.26
	- Group III	1,726	1,064	61.65	75,501.70	1.57	70.96
	- Group IV	1,726	454	26.30	26,499.54	1.50	58.37
	Corticosteroids, combinations with antiseptics	1,726	28	1.62	592.00	1.18	21.14
	Corticosteroids, combinations with antibiotics	1,726	117	6.78	1,947.33	1.28	16.64
	Corticosteroids, other combinations	1,726	97	5.62	5,303.32	1.40	54.67
	Pimecrolimus	1,726	51	2.95	1,602.50	1.39	31.42
	Tacrolimus	1,726	42	2.43	860.00	1.31	20.48
	Tars	1,726	4	0.23	573.44	1.00	143.36
Systemics	**Total**	**4,692**	**1,649**	**35.14**	**111,376.749**	**2.44**	**67.54**
Biologics	Total - Dupilumab	**4,692**	**8**	**0.17**	**2,579.56**	**4.50**	**322.45**
Non-biologics	Total	**4,692**	**1,644**	**35.04**	**108,797.189**	**2.42**	**66.18**
	Methotrexate	1,640	41	2.49	8,829.95	3.41	215.36
	Mycophenolic acid	1,640	7	0.43	1,437.50	3.43	205.36
	Alitretinoin	1,640	2	0.12	465.00	4.50	232.50
	syst. Antibiotics	1,640	1,283	78.04	21,484.73	1.74	16.75
	syst. Antihistamines	1,640	142	8.64	15,380.99	1.89	108.32
	Azathioprine	1,640	18	1.09	3,249.99	4.83	180.55
	Cyclosporine	1,640	4	0.24	530.00	8.50	132.50
JAKi	Janus kinase inhibitors*	**4,692**	**9**	**0.19**	**42.00**	**4.67**	**4.67**
	Tofacitinib	9	3	33.33	1,163.40	6.67	387.80
	Upadacitinib	9	1	11.11	120.00	2.00	120.00
	Baricitinib	9	3	33.33	735.00	3.00	245.00
	Ruxolitinib	9	2	22.22	317.34	5.50	158.67
GCS	Glucocorticosteroids*	**4,692**	**520**	**11.08**	**57,377.03**	**2.21**	**110.34**
	- Prednisolone depot	520	6	1.15	92.50	1.17	15.42
	- Triamcinolone depot	520	52	10.00	3,705.96	1.13	71.27

Multiple counting was possible; *Sub-type of non-biological treatment

Note: Rx=prescription; DDD=defined daily dose

Table 3: Quotes by patients and dermatologists referring to therapy options

Quote Number	Quote	Participant
Q1.1	"*No, except for taking zinc supplements, I don't do anything anymore. I let it [the hair] come and go.*"	Patient, female, 30–39 years
Q1.2	"*I would have had to go to [city 8] I think, every week or so [...] and that, um, I would not have managed in terms of time, to be honest. I then also heard, as soon as the treatment is finished, the hair will fall out again.*"	Patient, female, 50–59 years
Q1.3	"*The wig I got quite early, without the wig I would feel very stigmatized, because I have neither the strength nor the self-confidence to walk around without hair on my head.*"	Patient, female, 30–39 years
Q1.4	"*That worked well. I was symptom-free for a relatively long time. My hair stopped falling out. […] Then it abruptly stopped working*"	Patient, female, 20–29 years
Q1.5	"*So it was always said [by the dermatologist]: change of medication. Let's look for something new. I didn't have much say in the matter.*"	Patient, female, 20–29 years
Q1.6	"*I would have liked to have the possibilities, treatment options in more detail, in an overview, […] but instead we get something different [different information] from every dermatologist*"	Patient, male, 40–49 years
Q1.7	"*If the patient has a high level of suffering, I would send him to the university hospital, with the idea of getting into a study, because there is currently a lot happening. In our practice, we don't do too much, I have to say*"	Dermatologist, female, 30–39 years
Q1.8	"*And with baricitinib, regarding the experience so far, you really have a great therapy option, but with the restriction that it is not reimbursed*"	Dermatologist, male, 50–59 years
Q1.9	"*Sometimes the wig is so well made that you don't even see it. [...] And they [the patients] are really happy. With the wig, you have to say, a new phase begins for them*"	Dermatologist, female, 40–49 years
Q1.10	"*But these are patients who have been to other places [physicians] and who are simply hoping that you will prescribe them a systemic therapy that you may not be able to get from other doctors. […] I used to put a lot of work into asking the health insurance companies to cover it. […] The answer is always: Yes, you can prescribe it, but it is a lifestyle medication*"	Dermatologist, female, 40–49 years
Q1.11	"*But for the patient, I think it's an agony. It [the DCP therapy] is very tedious and almost always leads to a relapse when they stop taking it*"	Dermatologist, male, 60–69 years
Q1.12	"*Of course, we have a number of patients where there is a spontaneous remission, who do not come back into the practice*"	Dermatologist, female, 30–39 years
Q1.13	"*What is important, patients must be educated well that this disease runs in relapses. This means that once we have brought on a 'cure', we cannot guarantee that a relapse will not occur at some point [...]*"	Dermatologist, male, 40–49 years

Q1.14	*"But they are actually/ do what we recommend. [...] I always explain to them that theoretically you can also just wait. [...] But they are very willing to undergo therapy"*	Dermatologist, female, 40–49 years

1

Table 4: Quotes by patients referring to life with Alopecia areata (Q2) and Quotes by patients and dermatologists referring to patient pathways and health care disparities (Q3)

Quote number	Quote	Participant
Q2.1	"*It started in 2015, a circular spot at the back of the head [...], I wanted to quit my job at the time and was afraid to tell my boss and I think that was the stress.*"	Patient, female, 30–39 years
Q2.2	"*With approaching winter [...] I already notice that the head hair is also thinner and not as good. [...] And in summer it grows again*."	Patient, female, 40–49 years
Q2.3	"*I'm feeling fine with it so far, in the sense that I have accepted it.*"	Patient, male, 40–49 years
Q2.4	"*For me in my everyday life this disease plays no role in this sense, [...] I am fine.*"	Patient, female, 20–29 years
Q2.5	"*What interests me now is whether I can influence it [...] by my actions, by my way of life, because although I have accepted it [...], I would like to understand it.*"	Patient, male, 40–49 years
Q3.1	"*I would say if I didn't need the prescription [for the wig], I wouldn't go there at all.*"	Patient, female, 50–59 years
Q3.2	"*I would say that pharmacists are not really educated about AA. I don't think they would suggest anything to you on their own.*"	Patient, female, 20–29 years
Q3.3	"*I started the therapy and that simply helps to focus on this stress management and partly also these fears that go along with it, to learn strategies.*"	Patient, female, 30–39 years
Q3.4	"*[…] to see the psychosocial side of this disease, that is not just your hair falling out, but what it does to the people and that would, I would just wish that [...] that is also addressed and is also dealt with sensitively with those affected, that they feel taken seriously.*"	Patient, female, 20–29 years
Q3.5	"*He was very empathetic. He explained well that you really can't do much.*"	Patient, female, 20–29 years
Q3.6	"*The dermatologists were very overwhelmed here in the area.*"	Patient, female, 20–29 years
Q3.7	"*If this attempt has brought no success over weeks, months, then the dermatologist in private practice usually stops the treatment. [...] And that is actually when the normal topical steroid has failed, that the patient is then referred to us [a university hospital].*"	Dermatologist, male, 40–49 years

Table 5: Subgroup analyses of prescribed treatment groups (bold printed figure display significant differences) in prevalent adult persons with Alopecia Areata in 2020 (N=4,692)

Treatment	Topicals	Sys. Biologics	Sys. non-biologics	Sys. GCS*
Age, p-value	**<0.001**	0.158	**<0.001**	**<0.001**
Up to 30, n(%)	**393 (7.9)**	2 (0.0)	**250 (5.0)**	**44 (0.9)**
> 30–45, n(%)	**377 (7.6)**	1 (0.0)	**285 (5.7)**	**64 (1.3)**
> 45–65, n(%)	**590 (11.9)**	5 (0.1)	**576 (11.6)**	**207 (4.2)**
> 65, n(%)	**499 (10.0)**	0 (0.0)	**611 (12.3)**	**215 (4.3)**
Gender, p-value	**<0.001**	0.471	**<0.001**	**<0.001**
Male, n(%)	**559 (11.2)**	4 (0.1)	**370 (7.4)**	**82 (1.6)**
Female , n(%)	**1,300 (26.2)**	4 (0.1)	**1,352 (27.2)**	**448 (9.0)**
Insurance district types, p-value	**0.002**	0.272	0.723	0.588
Urban, n(%)	**1,315 (26.5)**	4 (0.1)	1,176 (23.7)	365 (7.3)
Rural, n(%)	**543 (10.9)**	4 (0.1)	543 (10.9)	163 (3.3)
Specialist, p-value	**<0.001**	**<0.001**	**<0.001**	**<0.001**
None of both, n(%)	**131 (7.0)**	**2 (25.0)**	**523 (30.4)**	**187 (35.3)**
General practitioner, n(%)	**367 (19.7)**	**0 (0.0)**	**1,038 (60.3)**	**255 (48.1)**
Dermatologist, n(%)	**1,184 (63.7)**	**6 (75.0)**	**116 (6.7)**	**80 (15.1)**
Both n(%)	**177 (9.5)**	**0 (0.0)**	**45 (2.6)**	**8 (1.5)**

* Sub-type of non-biological

Figure legends

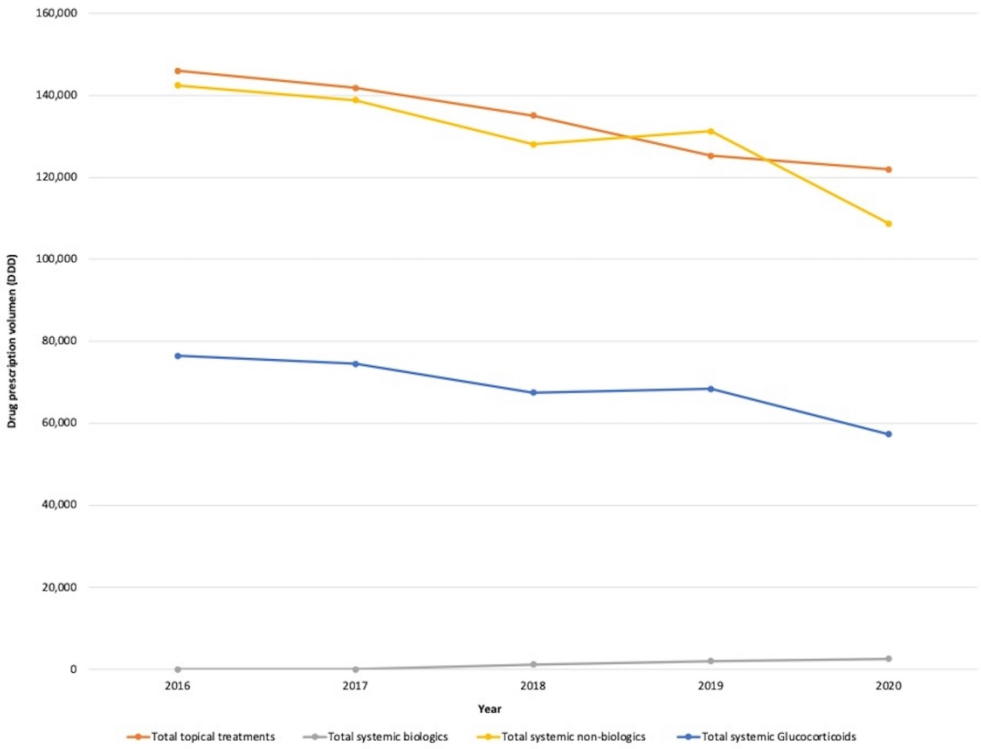
Figure 1: AA related drug prescription volume (defined daily doses [DDD]) in prevalent adult persons with AA and at least one prescription from 2016 to 2020 by drug group (2016 N= 3,337; 2017= 3,294; 2018 N= 3,321; 2019 N= 3,045; 2020 N= 2,699)

Figure 2: AA related topical prescriptions in prevalent adult persons with AA with at least one drug prescription by prescriber in 2020 (N= 1,726); Rx=prescription, multiple counting possible

Multiple counting; *Sub-type of non-biological drugs

Figure 3: Distribution of specialties treating incident adult persons with AA in 2019; person with at least one AA-related drug prescription were included (Quarter 1 N=803; Quarter 2 N=383; Quarter 3 N=342; Quarter 4 N=318), washout for incidence assessment 3 years

Note: The first observation quarter corresponded to the quarter in which the medication was prescribed



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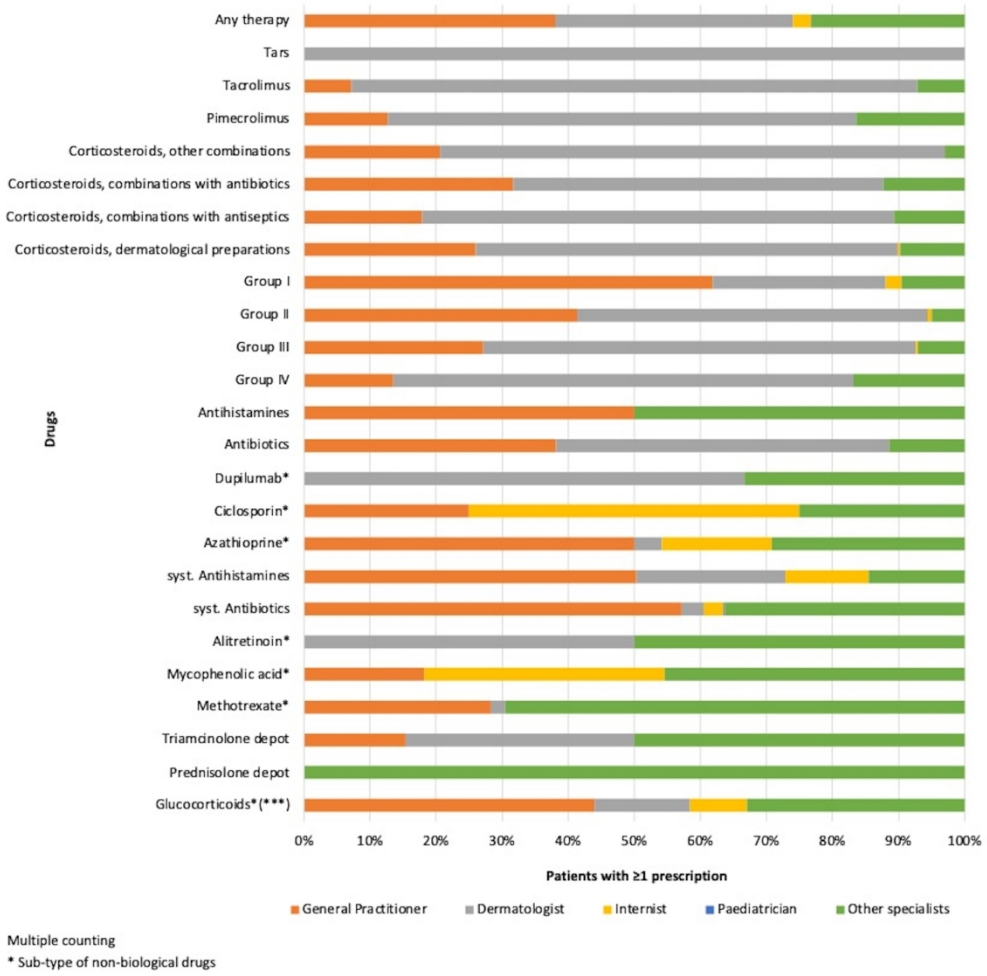

Multiple counting

* Sub-type of non-biological drugs

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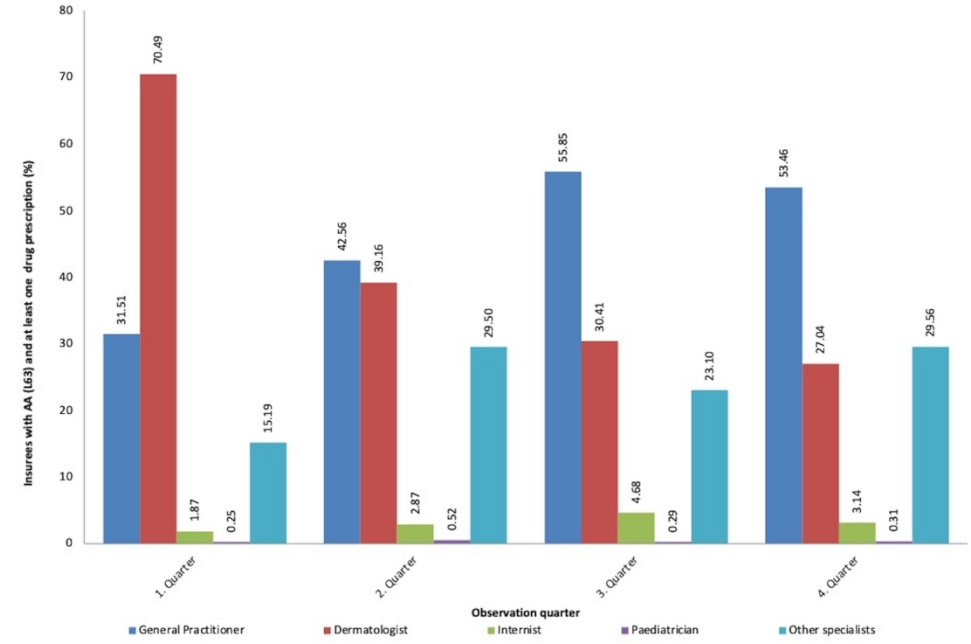

Note: The first observation quarter corresponded to the quarter in which the medication was prescribed

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Study plan

Inequalities in access to medication for atopic dermatitis and alopecia areata in Germany: A mixed-methods study (AMEDA)

Version: v1

Date: 17 February 2022

Principal investigator:

PD Dr. Christine Blome

Research Group Leader Patient-Reported Outcomes

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1 Synopsis

Study title	Inequalities in access to medication for atopic dermatitis and alopecia areata in Germany: A mixed-methods study
Financial support	Pfizer Inc. (Quality Improvement Grant RFP: Understanding healthcare disparities in Atopic Dermatitis and Alopecia Areata patients)
Objective	To describe and explain healthcare disparities in adult patients with atopic dermatitis (AD) and/or alopecia areata (AA) in Germany with a special focus on medication, and to deduce recommendations for action.
Target population	Adult patients diagnosed with AD or alopecia areata AA; dermatologists treating adult patients with AD or AA (in part 3)
Design	Mixed-methods study
Data basis	Part 1: claims data: nationwide data-on-file from the statutory health insurance DAK-G including 2.2 million insured people in 2016-2019; billing-relevant information from outpatient and inpatient care Part 2: survey data: nationwide data-on-file from the AtopicHealth study conducted in 2017-2019; patient- and clinician-reported data, such as patient characteristics, information on health care; patient-reported outcomes Part 3: qualitative study: in-depth interviews with patients with AD, patients with AA, and dermatologists using pilot-tested, semi-structured interview guidelines
Estimated number of participants	Part 1: claims data including approx. n=72,820 patient with AD and n=9,900 patients with AA Part 2: survey including n=1,291 patients with AD Part 3: qualitative sample including approx. n=25 patients with AD, n=25 patients with AA, n=20 dermatologists
Data analysis	Part 1: Prescription prevalence and health care utilization will be analyzed by medication, region and patient characteristics including co-morbidities, age, and gender; trends over time will be analyzed Part 2: Analysis of health care disparities by patient subgroups using appropriate descriptive and inferential statistical methods

	Part 3: Transcripts of interviews will be analyzed using qualitative content analysis Integration of study parts: The three study parts will be conducted in parallel. Interim findings and newly developed hypothesis from each study will be exchanged and discussed in the project team on a regular basis in order to determine which of these can also be investigated with the respective other data sources.
Study duration	February 2022 – July 2024
Quality assurance	The study will be conducted following the criteria for Good Scientific Practice by the German Research Foundation (Deutsche Forschungsgemeinschaft, DFG) as well as the Bylaws for Safeguarding Good Scientific Practice and Avoiding Scientific Misconduct at University Hamburg; claims data analysis will follow the Good Practice of Secondary Analysis. CVderm has been certified in accordance with DIN ISO 9001:2015 in the scope of the certification of the University Medical Center Hamburg-Eppendorf. In addition, CVderm follows its own standard operating procedures.
Ethics	The conduction of the study follows the legal requirements for data protection. The study has been approved by the Local Psychological Ethics Committee at the University Medical Center Hamburg-Eppendorf (LPEK-0427, 12 January 2022)

		03 May 2022
Principal investigator	PD Dr. Christine Blome University Medical Center Hamburg-Eppendorf IVDP Martinistr. 52 (CPW 3) D-20246 Hamburg	date
		03 May 2022
Sub-principal investigator	Kristina Hagenström, PhD University Medical Center Hamburg-Eppendorf IVDP Martinistr. 52 (Building 342) D-20246 Hamburg	date

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2 Abbreviations

AA	Alopecia areata
AD	Atopic dermatitis
CVderm	German Center for Health Services Research in Dermatology
IVDP	Institute for Health Services Research in Dermatology and Nursing
UKE	University Medical Center Hamburg-Eppendorf

3 Responsibilities and addresses

3.1 Coordinating center and investigators

German Center for Health Services Research in Dermatology (CVderm)

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PD Dr. Christine Blome; Principal investigator

Kristina Hagenström, PhD; Sub-principal investigator

Toni Maria Klein, M. Sc.; Study coordinator, survey analysis and qualitative study

Claudia Garbe, M. Sc.; Claims data analysis

3.2 Name and address of financially supporting company

Pfizer Inc., a Delaware corporation

235 East 42nd Street

New York, NY10017

USA

4 Introduction

The need for improved health care for AD in Germany and the corresponding research gaps can be derived from a large body of previous research from our group, including the AtopicHealth study series (Langenbruch et al. 2014; Langenbruch et al. 2021). In summary, there is evidence of considerable patient burden and unmet patient needs (Augustin et al. 2020; Beikert et al. 2014; Steinke et al. 2014), high economic burden (Mohr et al. 2021), and significant comorbidity (Radtke et al. 2017; Zander et al. 2020). Quality of care often does not comply with guidelines (Werfel et al. 2016; Werfel et al. 2021; Hagenström et al. 2021; Steinke et al. 2018; Langenbruch et al. 2014) including insufficient access to prevention and education (Zyriax et al. 2021).

To ensure that this project does not duplicate existing work, we conducted a PubMed/Medline literature search in September 2021 using the following search term:

(Atopic dermatitis[TiAb] OR neuroderm*[TiAb] OR eczema[TiAb] OR alopecia areata[TiAb]) AND (healthcare[TiAb] OR (health AND care[TiAb]) OR medication[TiAb] OR prescription[TiAb])

There are limited studies addressing health disparities among patients with AD (Davis et al. 2021). For the US, it was found that resource utilization differed by age (Alexander et al. 2018; Singh & Silverberg 2019), AD severity (Drucker et al. 2018), and region (Wu et al. 2021). Two studies conducted in the UK and Denmark identified age, gender, ethnicity, socio-economic status, disease severity, co-morbidity with allergic rhinitis or asthma, smoking history, and urban setting as predictors of health care access (de Lusignan et al. 2020; Thyssen et al. 2020).

For Germany, we described the overall health care situation of patients with AD using 2019 claims data (Hagenström 2021). We found that only one-third of patients are treated by a specialist; that there is significant underuse especially of innovative drugs; and that women receive prescription drugs more often. Further studies described the situation of the overall AD population in Germany without differentiating by patient characteristics (Heratizadeh et al. 2020; Zietze et al. 2021) or are outdated (Schmitt et al. 2009 using data from 2003-2004).

Thus, there is a lack of knowledge on whether health care disparities found internationally also apply to German AD patients. Furthermore, both internationally and in Germany, reasons for disparities are not well understood.

For AA, literature on the health care situation is scarce, and we found none from Germany. A recent US claims data analysis showed that 44% of patients were not prescribed treatment in the year following AA diagnosis, but no analysis by patient subgroup was reported (Senna et al. 2021). An earlier US study showed male gender to be predictive of fewer physician visits (Farhangian et al. 2015); the

same was found for primary care visits in the UK (Harries et al. 2021). The latter study further identified gender, socio-economic status, ethnicity, and living in urban or deprived areas as predictors of health care access.

Not least given upcoming targeted treatments for both AD and AA, and the fact that quality of care is still suboptimal in Germany, it is crucial to understand health care disparities in these patients in order to enable improvement measures. This study will therefore build upon the methodology used successfully in our previous study on AD (Hagenström et al. 2021), extended by a detailed analysis of subgroups with inadequate access to high quality health care, and widening the analysis to a 4-year data set. The same analysis will be performed for patients with AA, which to our knowledge will be the first systematic analysis of the health care situation of this patient group in Germany. Claims data analysis will be integrated with survey (AD) and qualitative (AA and AD) data, enabling a broader perspective that also uncovers potential explanations of health care disparities.

5 Goals and objectives

This project aims to describe and explain healthcare disparities in adult patients with AD and/or AA in Germany with a special emphasis on medication, and to deduce recommendations for action.

Disparities associated with the following patient characteristics will be considered: age; gender; socio-economic status, including education and working situation; family situation; region of residence; disease severity and co-morbidities (insofar as associations with health care are not clinically substantiated, e.g., more potent medication for more severely affected patients).

Aspects of health care to be evaluated include: prescribed medication (type of medication; prescription frequency); treatment by dermatologists vs. other physicians with other specialties; number of physician consultations.

As found for other dermatological indications in Germany, as well as for AD and AA internationally, we hypothesize that access to health care and quality of care will be disparate, depending on several of the characteristics described above and/or interactions between these characteristics.

In using an innovative mixed-methods approach that combines large quantitative data bases with qualitative in-depth interviews, the study aims to both describe and explain group differences in health care and is thereby closely aligned with the RFP focus on understanding healthcare disparities. This understanding is fundamental for deriving suitable recommendations for action, which will be done as the last step of the project based on the integrated analysis of our data.

6 Study design

The study will use a mixed-methods design combining

- claims data (part 1)
- survey data on health care in AD (part 2)
- qualitative patient and physician interviews (part 3).

While part 1 and 2 focus on identifying healthcare disparities in AD and AA, part 3 aims to derive possible explanations.

The three study parts will be conducted in parallel to enable integrated analysis, with the different methodological approaches supplementing and enriching each other. Quantitative findings shall be addressed in the qualitative interviews in order to derive explanations, and analysis of the qualitative data will generate additional hypotheses to be tested with the quantitative data.

The three study parts are described in more detail in the following subheadings.

6.1 Part 1: Claims data

6.1.1 Objectives

To describe the care paths of adults with AD or AA, including prescription prevalence and health care utilization

6.1.2 Patients and data

Nationwide data-on-file from the statutory health insurance DAK-G including 2.2 million insured people in 2016-2019. Based on AD prevalence of 3.31% and AA prevalence of 0.58%, a sample of 72,820 patients with AD and 9,900 patients with AA can be assumed. The data set covers all billing-relevant information from outpatient and inpatient care, including all drugs prescribed for outpatients. Master data of the insured persons contain age and gender, district municipality code as well as start and end of the insured period (incl. reason for leaving).

6.1.3 Data management and statistical analysis

The data set contains de-identified health-insurance data. A linkage number allows to combine data from all service areas to analyse care paths of patients, mostly based on day-specific coding of medical services. Prescription prevalence and health care utilization will be analyzed by medication, federal state level and patient characteristics including co-morbidities, age, and gender. Trends over time will

be analyzed. More detailed information on data management and statistical analyses can be drawn from the statistical analysis plan for part 1.

6.2 Part 2: Survey data

6.2.1 Objectives

To describe the health care situation of adults with AD, including the analysis of health care disparities between patient subgroups.

6.2.2 Patients and data

Nationwide data-on-file from the AtopicHealth study conducted in 2017-2019 including 1,291 adult patients with AD and their treating physicians from 111 dermatological practices and ambulant clinics. Data includes patient characteristics (such as age, gender, family situation, working situation, school and professional education, region, disease severity (SCORAD), and comorbidities), information on health care (AD treatment, physician/clinic visits), and patient-reported outcome measurements (such as Dermatology Quality Life Index, and Patient Benefit Index).

6.2.3 Data management and statistical analysis

The data set of the AtopicHealth study is already available at the IVDP. Data will be prepared as needed (including calculation of scores, if not yet available, and grouping of variables). Analysis of healthcare disparities will be investigated through analysis by patient subgroup using the appropriate descriptive and inferential statistical method. More detailed information on data management and statistical analyses can be drawn from the statistical analysis plan for part 2.

6.3 Part 3: Qualitative Interview

6.3.1 Objectives

To explore patient journeys of adults with AD or AA and to explain healthcare disparities.

6.3.2 Participants and data

Patients will be recruited from the dermatological ambulant clinic at the UKE, from outpatient dermatologists, via patient organizations, and via social media. Dermatologists will be recruited from the broad networks of dermatologists available at the IVDP, including outpatient dermatologists and ambulant clinics, as well as dermatological associations. The final sample size cannot be determined beforehand due to the character of qualitative studies. Recruitment of patients will stop when interviews reveal no decisive added value and result in no further additional content. Based on

previous experiences, it is estimated that this will be reached after interviewing 50 participants (n=25 with AD, n=25 with AA) and 20 dermatologists.

In-depth interviews will be conducted using pilot-tested, semi-structured interview guidelines. The interview guideline will be based on the research question and existing literature. Throughout study conduct, the interview guideline will be adapted to allow for in-depth exploration of the findings from the quantitative study parts and for additional topics that may result from the respective previous interviews. The study team regularly reviews the current interviewing procedure, gives each other feedback on their interview guidance, and discusses preliminary findings.

6.3.3 Data management and qualitative analysis

All interviews will be audio-recorded and transcribed verbatim while clearing identifiers (e.g., names or places). Transcripts of the interviews will be analyzed using qualitative content analysis according to Kuckartz (2018) with regard to the research question.

Categorization will be conducted using the NVivo software.

6.4 Integration of study parts 1 to 3

All study parts will be conducted in parallel in a *convergent design*. Throughout the study conduct interim results of all study part will be discussed in the project team in a regular workshop, taking place bi-monthly after onset of the data analysis phase. This will allow for patterns and associations found in one study part to be explored also in the other study parts, if applicable. Thereby, quantitative results can be addressed and explored in the qualitative study part and qualitative findings can lead to additional quantitative analyses. Additionally, quantitative study parts can enrich each other as claims data analyses might evoke questions regarding additional clinician- and patient-reported outcomes, not captured in billing data, while analysis of AtopicHealth data may provoke longitudinal research questions. Accordingly, exchange between the study parts can lead to additional research questions, that might evoke amendments in the statistical analysis plans (quantitative parts) and changes in interview guidelines and sampling strategy (qualitative part). Qualitative and quantitative findings will be compared in terms of where they converge, diverge, or complement each other (Curry & Nunez-Smith, 2014, pp.229-258); if they diverge, it will be discussed whether this points at bias in one of the study parts or whether the findings can be reconciliated (i.e. plausible interpretations are sought).

6.5 Derivation of recommendations for action

The results of all study parts will be considered for derivation of recommendations for action. Results will be presented and discussed in an interdisciplinary expert group, including psychologists, health

scientists, statisticians, and physicians. Within this group, results will be analyzed with regard to political decisions and resource allocation as well as everyday clinical practice. From this, recommendations for action will be deduced.

6.6 Quality assurance

The study will be conducted following the criteria for Good Scientific Practice by the German Research Foundation (Deutsche Forschungsgemeinschaft, DFG) as well as the Bylaws for Safeguarding Good Scientific Practice and Avoiding Scientific Misconduct at University Hamburg; claims data analysis will follow the Good Practice of Secondary Analysis (Swart et al. 2015). The CVderm has been certified in accordance with DIN ISO 9001:2015 in the scope of the certification of the University Medical Center Hamburg-Eppendorf. In addition, the CVderm follows its own standard operating procedures.

6.7 Data protection and ethics

The conduction of the study follows the legal requirements for data protection.

Claims data will be processed only in a de-identified manner so that data cannot be linked to individuals. A linkage number allows to combine data from different service areas while keeping data de-identified.

Atopic Health data has been pseudonymized with the study team not being able to so link that data to the respective persons.

Qualitative data will be pseudonymized, that is, encrypted with a numerical code (only the qualitative study team is able to allocate personal data), and will only be analyzed in this pseudonymized way. Audio records will be transcribed without names, addresses or other information that allow identification of the participant. Personal data of the participant will be destroyed three years after data collection at the latest, and hence, data will be anonymized.

The study has been approved by the Local Ethics Committee at the University Medical Center Hamburg-Eppendorf (LPEK-0427, 12 January 2022).

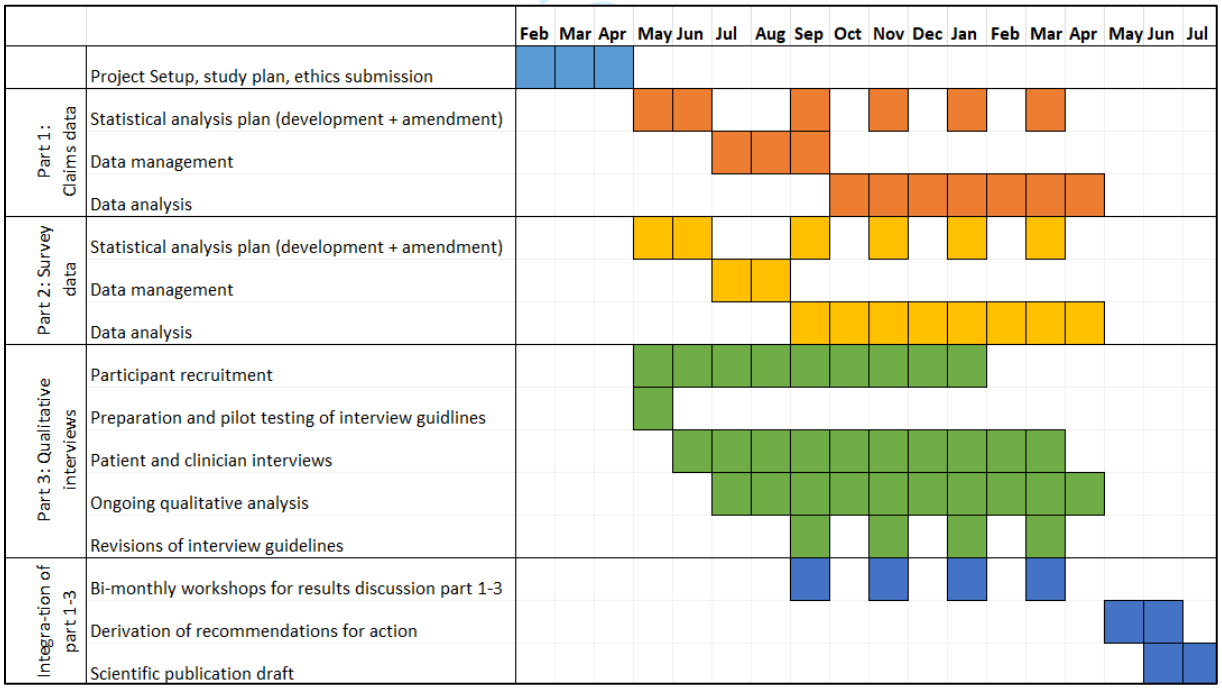
6.8 Dissemination of project outcomes

Study findings will be published in peer-reviewed dermatological journals and shall be submitted to national and international conferences including the congress of the European Academy of Dermatology and Venereology (EADV), the congress of the DDG (German Dermatological Society), the German convention ‘Dermatologie KOMPAKT & PRAXISNAH’, and the German ‘DERM’ conference.

The evidence-based recommendations derived from our study findings will be directed to the German decision bodies including federal ministries of health and social affairs, the Federal Joint Committee, and the payers. The target audience of dermatologists can be reached via the journal 'The Hautarzt', which has high coverage among dermatologists in Germany; results and recommendations will also be communicated to the state associations within the Professional Association of the German Dermatologists (BVDD), to all dermatologists in Germany, and to the regional AD networks. People with AD and/or AA can be reached via patient information events, patient journals, self-help groups, patient websites, and the IVDP's social media channels.

7 Timeline

The work packages are listed below separately for the overall study including the integration of the three study parts (blue), part 1 (claims data; orange), part 2 (survey data; yellow), and part 3 (qualitative study; green). The project will last 18 months in total. Scientific publications will be submitted afterwards; timing of abstract submission to scientific conferences will depend on the respective conference deadlines.



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AMEDA Interview Guide

Patients with alopecia areata

Thank you for agreeing to take part in the study.

The aim of this study is to investigate the treatment pathways of adult patients with alopecia areata. In doing so, we would like to learn about different stages in the treatment pathway and, in particular, find out more about access to medication for these conditions. We also want to uncover inequalities so that we can address and minimize them later.

In order to gain a comprehensive insight, today we would like to look at your entire history with alopecia areata - what you have experienced (and also taken) so far. We don't just want to look at certain stages, but focus in particular on how decisions and paths were taken.

While you are telling me your story, I will take a few notes on a PowerPoint slide to make it easier to follow the process and illustrate your journey. So please don't be surprised if I don't look at the camera in the meantime - I'll continue to listen to you but will make notes on the second screen. During the conversation, I will share my screen from time to time so that we can take a look together. This illustration does not have to be worked out down to the last detail, but should rather serve as an aid and orientation.

We look forward to learning more about your personal treatment path and getting to know your views. There is no right or wrong. Tell us openly what you would like to tell us about the topic.

I will keep asking questions and drawing our attention to certain aspects - although I will try to keep my own speaking time to a minimum so that we can learn more about you and from you.

We will record our conversation and then write it down verbatim. However, this will be pseudonymized, i.e. all names, places and the like will be omitted so that no conclusions can be drawn to your person. Everything you say remains confidential. Apart from the pseudonymized data (e.g. verbatim quotes to substantiate a statement), none of the information provided here will be shared with anyone outside the study team.

If we bring up anything you don't want to talk about, please let us know.

The interview will last a maximum of 90 minutes - if we are finished earlier, this is not a problem and is at least as informative for us as a longer appointment. The duration always depends very much on the individual treatment history. In any case, the interview will not take longer than 90 minutes. However, you can stop at any time or take a break.

Do you have any questions? Then I would start the recording now.

Introductory questions
To start with, I would like you to tell me briefly how you are currently feeling with your alopecia areata.
I would like to learn more about your personal patient history - from the first symptoms to the present day. If you were to divide this time into stages or phases, what would they be? Please tell me about the phases you have gone through since the beginning of your illness.
Details of patient history
Explore individual phases further • What did you experience during this time with regard to the treatment of AA? • What steps have you taken? / What stages were there within this phase?
Focus on: subjective feelings, personal experiences, reasons: • What prompted you to ...? • How did it come about that you ... visited / ... took / ...? • Please tell me how you to this decision. • How did it come about that you decided for/against the [doctor's visit/medication/other help/...]? have decided? • What was important to you when you made your decision? • *Downstream: How did you feel about [symptoms/stress/visits to the doctor/medications/side effects/...]?*
Request specific area/settings
Further inquiries about specific areas/settings, whether they played a role/what role they played: • To what extent did XX play a role in your patient history? • What experiences have you had at/with XX? • Feel free to tell me more about your journey to XX. • Please tell me more about your experience at XX. • Why have you no experience with XX? *Areas/Settings:* - *General practitioners* - *Dermatologists* - *Medication* - *Other products (including basic care)* - *Pharmacy* - *Self-help groups* - *Internet* - *Alternative practitioner:in and other alternative medicine* - *Other*
Overall view
When you look back on your previous patient history, would you have liked something to have gone differently? (happened earlier / happened later / left something out / missed something / ...)

Differences in care
Towards the end, I would like to take a broader view. As I mentioned earlier, we would like to find out what differences there might be in care. I would therefore now like to look at specific aspects that may have affected your situation with alopecia areata. In the following, I will mention some personal or disease-related characteristics and would like to know from you how these affect how you feel about your alopecia areata, whether you go to the doctor and how you are treated. Of course, you can talk about your own experience and history, but perhaps you have already noticed some of these aspects or you can imagine situations in which they might come into play. *Follow-up: To what extent could you imagine that these characteristics could have an impact on the care situation of patients* • Severity of alopecia areata • Comorbidities • Health insurance • Place of residence / region • Age • Family situation (partnership, children) and living situation (with family, living alone) • Professional background and educational qualifications • Gender Are there any other personal or disease-related characteristics that you feel have an impact on the care of your alopecia areata? *Or are there other characteristics that you can imagine having an impact on the patient's care situation?*
Conclusion
Is there anything else that you consider important that has not yet been discussed? (with regard to your own patient history *or the care of patients with alopecia areata as a whole*),

Query of socio-demographic data for our sample description:

- Estimation of the participant's hair loss (in %)
- Estimation of the participant's:in by proportion of total hair missing (in %)
- Age
- Gender
- Highest school-leaving qualification
- Place of residence
- Duration of the disease
- Type of insurance (private/statutory)

Clarify at the end:

- Account details for expense allowance
- Note that payment of the expense allowance can take up to 8 weeks
- Open questions
- Information that participants will receive a brief summary of the study results at the end of the study

I would like to thank you very much for taking the time to conduct this interview with me and for your openness during our conversation. These are very important insights for us.

AMEDA Interview Guide

Dermatologists

Thank you for agreeing to take part in the study.

The aim of this study is to investigate the treatment pathways of adult patients with alopecia areata. In doing so, we would like to get to know different phases in the treatment pathway and, in particular, learn more about access to medication for these conditions. We also want to uncover inequalities in the treatment of different patient groups so that we can address and minimize them later.

We are interviewing both patients with these two conditions and dermatologists in order to gain a comprehensive insight into the treatment paths and options for patients with alopecia areata. We would therefore like to hear about your personal experiences in treating these patients and what you consider to be important or special.

I would like to learn as much as possible about your experiences from everyday practice.

I will record our conversation and then transcribe it verbatim. However, the transcript of our conversation will be pseudonymized so that no conclusions can be drawn to your person. Everything you say will remain confidential. Apart from the pseudonymized data (e.g. verbatim quotes to substantiate a statement), none of the information given here will be shared with anyone outside the study team.

The interview will last about an hour.

Do you have any further questions? Then I would start the recording now.

Notes for interviewers

- Questions are aimed at the care provided by the doctor being interviewed.
- Focus: what the doctor sees and experiences him/herself
- If the doctor answers on a "meta-level", ask specifically:
  - What is it like for you personally?
  - Can you give me an example of this from your everyday practice?
  - How was it with your last patient?

Patient history
Alopecia areata
First of all, I would like to look at the patient stories of patients with alopecia areata that you see in your daily practice:
What are the triggers or reasons why patients with alopecia areata come to your practice? • What specific triggers are named by the patients? In your opinion, which reasons are of particular importance? • At what point in the illness does this happen and what concerns do patients come with? • From what you learn from patients: what paths have they already taken before they come to your practice? • What else do patients do on the side? Which providers/service providers do they visit; what do they try out?

Medication	
Alopecia areata	
Now I would like to look at the treatment options, especially drug therapies, for patients with alopecia areata?	
What treatment options do you consider for patients with alopecia areata? How do you come to a decision for individual patients? • Please tell me about the decision-making process for or against certain drugs and treatment options? • How does the decision-making process work together with the patient? • What factors play an important role for you in the process? • What do you look out for in the course of therapy?	*Reminder for interviewers:in:* • *Standard therapy (no guideline available)* • *System therapy* • *Spontaneous healing* • *Cortisone*
After the patients have been with you: • How does the patient's journey continue once they have been to your practice?	

Differences in the supply situation
Atopic dermatitis & alopecia areata
I would now like to take another look at the overall care situation for adults with alopecia areata. I am interested in specific aspects that could influence the care of patients. I'm going to go through a list of characteristics one after the other and would ask you to tell me everything you can think of about how these aspects could affect care.
To what extent do you feel that the following characteristics of patients or the disease itself have an influence on whether patients come to you for care and how they are cared for • Severity of the *(Question: How exactly does this affect you? How does this influence your treatment approach?)* • Existing concomitant diseases • Place of residence / region • Health insurance • Age • Family situation (partnership, children) and living situation (with family, living alone) • Professional background and educational qualifications • Gender Are there any other characteristics that come to mind that have or could have an impact on the care situation of patients with atopic dermatitis?
The care situation can be improved through different approaches. Such approaches are often first tried out in regional pilot projects before they can find their way into standard care. Since we are recruiting throughout Germany, we are interested in whether there are already approaches somewhere that improve the care situation of patients with alopecia areata. Do you know of any pilot projects in Germany that aim to improve the care of patients with alopecia areata? Or do you know of pilot projects from other areas that you think would be well suited to patients with alopecia areata?
Conclusion
Is there anything else that you consider important (with regard to your everyday practice with patients alopecia areata or to the care of these patients as a whole) that has not yet been discussed?

I would like to thank you very much for taking the time to conduct this interview with me and for your openness during our conversation. These are very important insights for us.

Query of socio-demographic data for our sample description:

- Age
- Gender
- Location
- Practice or clinic
- Duration active as dermatologist

Clarify at the end:

- Account details for expense allowance
- Note that payment of the expense allowance can take up to 8 weeks
- Open questions

UKE HAMBURG

Healthcare situation and disparities of patients with alopecia areata – A mixed methods analysis by *Toni Maria Janke, Beke Hester, Katharina Müller, Christine Blome, Theresa Klinger*

Supplement Tables S1 and S2: Relevant treatment and therapy (ATC and EBM) in claims data

Table S1: Relevant treatment of AA

Drug Group	Active ingredient	Anatomical Therapeutic Chemical [ATC] definition system	Ambulatory doctors fee schedule [EBM]
Topical treatments	Antibiotics	D06A	
	Antihistamines	D04AA	
	Crisaborole	D11AH06	
	Cromoglicic acid	D11AH03	
	Carbamide products	D02AE	
	Corticosteroids, dermatological preparations	D07	
	- Group I	D07AA	
	- Group II	D07AB	
	- Group III	D07AC	
	- Group IV	D07AD	
	- Corticosteroids, combinations with antiseptics	D07B	
	- Corticosteroids, combinations with antibiotics	D07C	
	- Corticosteroids, other combinations	D07X	
	Pimecrolimus	D11AH02	
	Psoralens	D05AD	
	Tacrolimus	D11AH01	
	Tars	D05AA	
Systemic biologics	Dupilumab	D11AH05	
Systemic non-biologics (conventional)	Methotrexate	L01BA01, L04AX03, M01CX01	
	Mycophenolic acid	L04AA06	
	Alitretinoin	D11AH04	
	syst. Antibiotics	J01	
	syst. Antihistamines	R06A	
	Azathioprine	L04AX01	
	Ciclosporin	L04AD01	
	Methoxsalen	D05BA02	
	Trioxysalen	D05BA01	
Systemic GCS	Glucocorticosteroids	H02AB	
	- Betamethasone depot	H02AB51	
	- Methylprednisolone depot	H02AB54	
	- Prednisolone depot	H02AB56	

Drug Group	Active ingredient	Anatomical Therapeutic Chemical [ATC] definition system	Ambulatory doctors fee schedule [EBM]
	- Triamcinolone depot	H02AB58	
Ultraviolet light (UV) therapy	Selective phototherapy Supplement photochemotherapy, PUVA Balneophototherapy		30430 30431 10350

Table S2: Ambulatory doctors fee schedule [EBM] of outpatient psychotherapy

Ambulatory doctors fee schedule [EBM]	**Description**
22220	psychotherapeutic interview
23220	psychotherapeutic interview
35100	Differential diagnostic clarification of psychosomatic disease states
35110	Verbal intervention in psychosomatic disease states
35111	Exercise interventions, individual treatment
35112	Exercise interventions, group treatment
35113	Exercise interventions for children and adolescents, group treatment
35120	Hypnosis
35130	Determination of the obligation to pay benefits for the initiation of short-term therapy
35131	Determination of the obligation to pay benefits for the initiation / extension of long-term therapy
35140	Biographical anamnesis
35141	In-depth exploration
35142	Supplementary assessment of neurological and psychiatric findings
35150	Probationary session
35151	Psychotherapeutic consultation
35152	Acute psychotherapeutic treatment
35200	Depth psychology-based psychotherapy (short-term therapy, individual treatment)
35201	Depth psychology-based psychotherapy (long-term therapy, individual treatment)
35202	Depth psychology-based psychotherapy (short-term therapy, large group)
35203	Depth psychology-based psychotherapy (long-term therapy, large group)
35205	Depth psychology-based psychotherapy for children and adolescents (short-term therapy, small group)
35208	Depth psychology-based psychotherapy for children and adolescents (long-term therapy, small group)
35210	Analytical psychotherapy (individual treatment)
35211	Analytical psychotherapy (large group)
35212	Analytical psychotherapy for children and adolescents (small group)
35220	Behavioural therapy (short-term therapy, individual treatment)
35221	Behavioural therapy (long-term therapy, individual treatment)
35222	Behavioural therapy (short-term therapy, small group)
35223	Behavioural therapy (long-term therapy, small group)
35224	Behavioural therapy (short-term therapy, large group)
35225	Behavioural therapy (long-term therapy, large group)

Ambulatory doctors fee schedule [EBM]	**Description**
35251	Supplement I
35252	Supplement II
35253	Supplement III
35300	Test procedures, standardised
35301	Test procedures, psychometric
35302	procedures, projective
35401	Depth psychological psychotherapy (1, individual treatment)
35402	Depth psychological psychotherapy (2, individual treatment)
35405	Depth psychological psychotherapy (individual treatment)
35411	Analytical psychotherapy (1, individual treatment)
35412	Analytical psychotherapy (2, individual treatment)
35415	Analytical psychotherapy (individual treatment)
35421	Behavioural therapy (1, individual treatment)
35422	Behavioural therapy (2, individual treatment)
35425	Behavioural therapy (individual treatment)
35503	Depth psychological psychotherapy, 3 participants
35504	Depth psychological psychotherapy, 4 participants
35505	Depth psychological psychotherapy, 5 participants
35506	Depth psychological psychotherapy, 6 participants
35507	Depth psychological psychotherapy, 7 participants
35508	Depth psychological psychotherapy, 8 participants
35509	Depth psychological psychotherapy, 9 participants
35513	Depth psychological psychotherapy, 3 participants
35514	Depth psychological psychotherapy, 4 participants
35515	Depth psychological psychotherapy, 5 participants
35516	Depth psychological psychotherapy, 6 participants
35517	Depth psychological psychotherapy, 7 participants
35518	Depth psychological psychotherapy, 8 participants
35519	Depth psychological psychotherapy, 9 participants
35523	Analytical psychotherapy, 3 participants
35524	Analytical psychotherapy, 4 participants
35525	Analytical psychotherapy, 5 participants
35526	Analytical psychotherapy, 6 participants
35527	Analytical psychotherapy, 7 participants
35528	Analytical psychotherapy, 8 participants
35529	Analytical psychotherapy, 9 participants
35533	Analytical psychotherapy, 3 participants
35534	Analytical psychotherapy, 4 participants
35535	Analytical psychotherapy, 5 participants
35536	Analytical psychotherapy, 6 participants
35537	Analytical psychotherapy, 7 participants
35538	Analytical psychotherapy, 8 participants
35539	Analytical psychotherapy, 9 participants
35543	Behavioural therapy, 3 participants
35544	Behavioural therapy, 4 participants
35545	Behavioural therapy, 5 participants

Ambulatory doctors fee schedule [EBM]	**Description**
35546	Behavioural therapy, 6 participants
35547	Behavioural therapy, 7 participants
35548	Behavioural therapy, 8 participants
35549	Behavioural therapy, 9 participants
35553	Behaviour therapy, 3 participants
35554	Behavioural therapy, 4 participants
35555	Behaviour therapy, 5 participants
35556	Behavioural therapy, 6 participants
35557	Behavioural therapy, 7 participants
35558	Behavioural therapy, 8 participants
35559	Behavioural therapy, 9 participants
35571	Surcharge for individual therapy
35572	Surcharge for group therapy
35573	Surcharge for consultation/acute treatment
35600	Test procedures, standardised
35601	Test procedures, psychometric
35602	procedures, projective

Healthcare situation and disparities of patients with alopecia areata – A mixed methods analysis by
Toni Maria Janke, Beke Hester, Katharina Müller, Christine Blome, Theresa Klinger

Supplement Table S3 and S4 Category systems of patients with alopecia areata and dermatologists

Table S3: Category system of patients with AA

1st	2nd	3rd	4th level of category system
Health care			
	Therapy Options		
		Local therapies	
			Cryotherapy
			Pulse therapy
			PRP
			DCP
			Further therapy options
			UV therapy
			Cortisone cream / topical cortisone
		Systemic therapies	
			Immunosuppressants
			Biologics
			Further therapy options
			Cortisone injection
			Cortisone tablet
		Other therapies	
			Participation in study
			Shampoo
			Wig and other assistive devices
			Lifestyle change
		Decision against therapy	
	Therapy-related behaviour and attitude		
		Medical consultation	
			With medical consultation
			Without medical consultation
		Costs and external conditions	
		Critical aspects of therapy	
			No long-term improvement
			Lack of continuity
			Scepticism towards potential side effects
			Lack of information by physician
			Lacking participation in therapy decisions
			Scepticism towards medication

		Few therapies offered
		Mode of administration
		Aversion to/caution with cortisone
		Exclusively symptomatic treatment
	Testing various therapies and products	
	Taking therapies according to need	
		Escalation steps
Medical providers		
	Dermatologists	
		Monitoring of disease/therapy progression
		Visits according to need
		Loyalty towards practice
		Cancer screening
		Consultation hour for hair loss
	General practitioner	
		Referral to specialist
		Examination at general practitioner
		No relevant provider
	Outpatient clinic	
	Other physicians	
		Rheumatologist
		Initial examination
	Psychological providers	
Non-medical provider		
	Alternative medical options	
		Use of alternative medical options
		No use of alternative medical options
	Pharmacy	
Aspects and criticism towards healthcare		
	Reasons for physician visits	
		Repeated prescription
		Blood tests
		Visibility of AA
		No provider visited
	Empathy of providers	
		Lack of empathy / not being taken seriously
		Empathy / being taken seriously
	Competencies of provider	
		Lack of competencies / expert knowledge
		Trust in competencies / expert knowledge
	Availability pf physicians	
		Problems finding good dermatologists
		Waiting time
	Change of physicians	
		Due to expertise

		Due to location
		Not changed despite dissatisfaction
	Side effects and contraindications	
	Patient education	
Life with AA		
	Familial case history	
	Misdiagnosis	
	Triggers	
	No obvious trigger	
	Physical changes	
	Seasonal influence	
	Infections	
	Stress	
	Co-morbidities	
	Information and exchange	
	Spontaneous remission	
	Symptoms	
	Handling of disease	
	Support by friends and family	
	Acceptance	
	Everyday life	
	Hope for spontaneous remission	
	Mental burden	
	Resignation/frustration	
	Visibility	
	Feeling uncomfortable	
	Research for causes	
	Repression	
	Desperation	

Table S4: Category system of dermatologists

1st	2nd	3rd	4th level of category system
Health care stations			
	Dermatologists		
	General practitioner		
	Outpatient clinic		
	Inpatient clinic visits		
	Psychological support		
	Alternative medical options		
	Pharmacy		
	No previous therapy		
	Information and exchange		
	Lifestyle change		
	Waiting time		
Treatment			
	Treatment options		
		Local therapies	
			Calcineurin inhibitors
			Cortisone intralesional
			Topical cortisone
			DCP therapy
			Local therapy - not specified
			PRP therapy
			UV therapy
			Further products
		Systemic therapies	
			Biologics
			Systemic cortisone
			ciclosporin
			JAK inhibitors
			Minoxidil
			MTX
		New therapies	
			Off-label therapies
			Study inclusion
		Wigs and other assistive devices	
		Issues regarding the therapy	
			Localisation of the disease
			Limited therapy options
			Non-response to therapies
			Reimbursement of therapies
			Reoccurrence after treatment end
	Monitor disease and treatment		
		Phasing out therapy	

1st	2nd	3rd	4th level of category system
		Observation of the course of disease	
		Disease duration as decision-making criterion	
		Laboratory examination and diagnostics	
		Assessment of scores	
		Tolerability of therapy and side effects	
	Spontaneous remission		
	Characteristics and life circumstances of patients		
	Patient involvement		
		Drug samples for patients	
		Building trust	
		Patient preferences	
		Adherence	
		Patient education	
	Re-presentation		
Reasons for visits at dermatologists			
	Disease symptoms		
	Fear and worry		
	Awareness for disease		
	Infections		
	Information about disease and its causes		
	New therapies and treatment options		
	Visibility		
	Stress		
	Desperate search and suffering		
	Wish for improvement		
	Time of disease progression		

UKE HAMBURG

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Healthcare situation and disparities of patients with alopecia areata – A mixed methods analysis by *Toni Maria Janke, Beke Hester, Katharina Müller, Christine Blome, Theresa Klinger*

Supplement 4: Recommendations for action developed in the expert panel

Background:

The AMEDA study (*Inequalities in access to medication for atopic dermatitis and alopecia areata in Germany: A mixed-methods study*) aimed to describe the care of adult patients with AD (AD) and alopecia areata (AA) in Germany. In particular, treatment pathways of patients and inequalities in care should be described.

An expert meeting was held on 01.06.2023 to present the results. The aim of the meeting was to **develop recommendations for action to reduce inequalities in the care of patients with AD and AA**.

Participants of the Expert Meeting:

- Patient representatives (Karin Mecklenburg from the German Neurodermatitis Association and Eva Lück-Beumler from Alopecia Areata Deutschland e.V.)
- Dermatologists (Prof. Dr. med. Matthias Augustin and Prof. Dr. med. Sabine Steinke)
- UKE scientists (PD Dr. Christine Blome, Dr. Kristina Hagenström, Beke Hester, Katharina Müller)

In the following, the results regarding AA will be presented.

Summary of the recommendations for action:

Alopecia Areata:

- Evidence of poorer care for patients with statutory health insurance → Reconsider the classification of AA as a lifestyle disease in order to provide access to adequate care for patients with statutory health insurance

- Evidence of regional differences in the quality of care → Development of an information platform to inform dermatologists about current scientific results and to strengthen the empowerment of patients

Alopecia Areata

Evidence of poorer care for patients with statutory health insurance

1. Background: In a decision of 18.10.2018, the G-BA restricted the treatment of alopecia areata (AA) as follows: "*There is no question that the treatment of alopecia areata in the various degrees of severity is a medical treatment and represents a burden for those affected, nevertheless the criteria leading to the classification as so-called lifestyle medicinal products are fulfilled.*"[1]. The classification of AA to the area of lifestyle diseases excludes the reimbursement of costs for medicinal products for the treatment of AA by statutory health insurances.
2. Quantitative data: The analyses of the SHI routine data showed that 150 thousand people in Germany are treated for AA every year. Almost 35% suffer from a moderate to severe form of AA. The medication care of these insured persons in 2020 showed that the majority is treated with topical steroids or systemic non-biological drugs. JAK inhibitors can only be represented to a limited extent with SHI routine data, as these have only been approved for severe AA since 2022. The initial care of SHI-insured persons with an incidental AA diagnosis is primarily provided by with dermatologists. Subsequently, the majority of insured persons switch to a general practitioner.
3. Qualitative data: The analysis of the qualitative data indicates that due to this allocation, statutory patients are less well cared for, as the costs for high-priced therapies such as JAK inhibitors are not covered: "*In the case of alopecia areata, when we talk about therapy options, especially in the area of JAK inhibitors. Reimbursement of the costs of JAK inhibitors for the diagnosis of alopecia areata is very, very difficult. This is more likely to be the case with private patients. Then you have a better chance. It's certainly always an individual decision by the health insurance company.*" (dermatologist, code D08)

[1] https://www.g-ba.de/downloads/40-268-5354/2018-10-18_AM-RL-II-Ergaenzung-Aktualisierung_TrG.pdf

Recommendation for action: In order to ensure that patients with statutory health insurance receive the same level of care as those with private health insurance, the guidelines on access to medication need to be revised. In order to provide all patients with access to adequate care, **we recommend that** the **G-BA** recognises AA as an autoimmune disease instead of classifying it as a lifestyle disease. In doing so, we join a petition that is already being considered by the German Bundestag[2] .

Evidence of regional differences in the quality of care

1. Background: Data on AA show that patients have differences in care depending on where they live. This is shown, for example, by the fact that access to dermatologists is more difficult in rural areas due to longer waiting times and sometimes long travel times.
2. Quantitative data: The drug supply showed some regional differences on the basis of the SHI routine data. Significantly more insured persons in urban areas consulted a specialist compared to insured persons in rural areas.
3. Qualitative data: The qualitative interviews also revealed that it is difficult for patients to find dermatologists who have sufficient expertise and information about AA. "*I think very few GPs or dermatologists know that. And you have to be really lucky to find a doctor who is currently interested in it and/ is really actively involved in the science nowadays, or at least passively reads along. And that depends on the doctor. You have to be lucky, my time was too valuable, where I actually read: wait and see and then it will fit*" (patient with AA, code AA03). The interviews with dermatologists confirm this: "I think the *more severe the alopecia is, the fewer medical colleagues you will find who are willing to treat the alopecia. (…) I think the willingness to deal with such a disease, to even say: Okay' I'll see if I can help the patient somehow. As I said, that is the individual attitude of the doctor. And, as I said, that is often not so great, unfortunate"y.*" (dermatologist, code D07)

Recommendation for action: The data show that dermatologists need more information on the disease in order to provide adequate care. We therefore recommend that the **G-BA** and

[2] https://epetitionen.bundestag.de/content/petitionen/_2023/_03/_27/Petition_148387.html (as at: 07.06.23)

IQWiG develop an information platform on AA that presents current scientific results. Such a platform is not only helpful for dermatologists, but also for patients. The empowerment of patients is also crucial: well-informed patients can demand more co-determination in the choice of therapy and thus also improve care.

Other important findings on AA from the Expert panel were:

- The stigmatisation of the disease is very stressful for patients; making AA more widely known will create more understanding and reduce stigma.
- Patients have expressed the wish that dermatologists and general practitioners first exclude other diseases by testing the blood values when making a diagnosis. In addition, patients would like specialists to point out other possible treatment options, such as nutritional counselling to reduce nutrient/vitamin deficiencies.
- Self-help and exchange among AA patients play a major role. Interdisciplinary meetings between patients and doctors should be promoted more strongly.