PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Cohort profile: Patient characteristics and disease burden of alopecia areata in the Danish Skin Cohort
AUTHORS	Andersen, Yuki M F; Nymand, Lea; DeLozier, Amy M.; Burge, Russel T.; Edson-Heredia, E.; Egeberg, A;

VERSION 1 – REVIEW

REVIEWER	Bosseila, Manal A. -W. Cairo Univ, Dermatology
REVIEW RETURNED	04-Jul-2021

GENERAL COMMENTS	1- The associated comorbidities of AA are a very important issue and are well known and were mentioned by the authors in the introduction part of the manuscript. However, patients were not asked about them in the questionnaire; and thus are not mentioned in the results of this study. This a major defect in a disease registry. 2- It would have been interesting and of higher value if the authors would have performed statistical tests of correlations after obtaining the results of the questionnaires. Such as between disease severity or disease activity/flare or disease duration and associated findings of AA such as nail affection, positivity of family history, impact on quality of life (DQoL). But they merely described the available patient's characteristics with no attempt to correlate between the recorded findings. Specific Comments: Section Title in the manuscript Page Line Number The quoted text from the manuscript The comment/suggested correction/the missing information/ Abstract 3 16 was established to provide data that can serve as a tool in future AA research. This purpose is very vague and unspecific. The objective/aim needs to be specific and measurable. Abstract 4 35 history of cigarette smoking was comparable with the general population and slightly lower than for patients with psoriasi Why cigarette smoking specifically? Why comparing this feature with psoriasis in particular?? Both diseases are not related, so why was this chosen and not any other disease? This was clearer in the result section, but in the abstract section it is out of context. Abstract 4 44 31.4% At beginning of sentence the numbers should be written in letters.

	Strengths & limitations 5 17 Cohort is comprises a very number adults with AA that were interviewed by trained professionals The sentence needs to be written correctly Introduction 6 30 the condition is understudied compared with some other inflammatory skin diseases This statement is wrong: AA is an autoimmune disease not an inflammatory disease. And AA is actually well studied, with a lot of data on it. At time of this review there are 4877 publications on Pub med about Alopecia Areata. Patient & Public involvement 7 46 Patients were note involved in the development of ….. Patients were not involved in the development of ….. Patient Interviews 8 13 Information on patient demographics …. Why commonly associated Comorbidities such as atopic dermatitis, thyroid disorders, vitiligo, or Down's syndrome were not asked for?? Patient Interviews 8 34 , eye irritation, … It would have been more suitable to ask for eye dryness. With AA the eyes may show dry eyes, not eye irritation which is rather a symptom of atopy. Patient demographics 9 15 Our observation may partially reflect a higher awareness of hair loss among women. This could not be an explanation. Males and females become very much aware of patchy hair loss as occurring in AA. Also males have commonly shorter hairs and would detect a bald patch on their scalp much easier.

REVIEWER	Wu, JJ Kaiser Permanente Medical Center, Department of Dermatology
REVIEW RETURNED	07-Nov-2021

GENERAL COMMENTS	This is an excellent study in the understudied population of alopecia areata. It reads well. I do not see any issues in the conduct of this study.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1, Comment 1:

The associated comorbidities of AA are a very important issue and are well known and were mentioned by the authors in the introduction part of the manuscript. However, patients were not asked about them in the questionnaire; and thus are not mentioned in the results of this study. This a major defect in a disease registry.

Our reply:

We thank the reviewer for this comment, and we agree that AA-related comorbidities are important to study. Indeed, patients were not interviewed about these, since information on comorbidities can be obtained on individual-level by linking patients questionnaire responses with our nationwide registries in Denmark (e.g. the National Patient Registry, which contains ICD-10 codes for relevant comorbidities in these patients). Since physician-verified longitudinal information on comorbidities are in fact available for this cohort by registry linkage, there was no need to also as patients about this. Since this was already mentioned in the "Strengths and limitations" section, we respectfully suggest not to add further information on this topic in the manuscript at this stage.

Reviewer 1, Comment 2:

It would have been interesting and of higher value if the authors would have performed statistical tests of correlations after obtaining the results of the questionnaires. Such as between disease severity or disease activity/flare or disease duration and associated findings of AA such as nail affection, positivity of family history, impact on quality of life (DQoL). But they merely described the available patient's characteristics with no attempt to correlate between the recorded findings.

Our reply:

Thank you for this comment. This manuscript was submitted in the BMJ Opens "Cohort profile" section. The Author Guidelines for BMJ Open states that:

The cohort profile is an article type set up in BMJ Open to fill the space between a study protocol and a results paper. Cohort profiles should describe the rationale for a cohort's creation, its methods, baseline data and its future plans.

Furthermore, the guidelines state that a Cohort Profile paper should "summarise rather than present results".

We therefore only present baseline summary data of the overall cohort in this paper. For such descriptive data, the STROBE guidelines state that:

“Inferential measures such as standard errors and confidence intervals should not be used to describe the variability of characteristics, and significance tests should be avoided in descriptive tables.”

We agree that statistical tests of potential differences between the groups would be interesting, and we are in fact planning to conduct such analyses, but these would be the topic of another paper, since these are out of score for a “Cohort Profile”.

Reference: Vandenbroucke JP et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. Int J Surg. 2014 Dec;12(12):1500-24

Reviewer 1, Comments from table:

The quoted text from the manuscript	The comment/suggested correction/the missing information/	Author response
was established to provide data that can serve as a tool in future AA research.	This purpose is very vague and unspecific. The objective/aim needs to be specific and measurable.	We have now rephrased this sentence. However, since this is an inception cohort, rather than an individual “one-time study”, there is by design not one single “outcome”, but rather, the aim is to collect a multitude of different information about these patients that can serve as a resource for a number of different studies in the future.
	history of cigarette smoking was comparable with the general population and slightly lower than for patients with psoriasi	We agree that this was clearer in the result section, but due to the limitations in word count in the abstract, this was more difficult to describe thoroughly here. We have therefore removed this from the abstract.
31.4%	At beginning of sentence the numbers should be written in letters.	This has been corrected.

Cohort is comprises a very number adults with AA that were interviewed by trained professionals	The sentence needs to be written correctly	This has been corrected.
the condition is understudied compared with some other inflammatory skin diseases	This statement is wrong: AA is an autoimmune disease not an inflammatory disease. And AA is actually well studied, with a lot of data on it. At time of this review there are 4877 publications on Pub med about Alopecia Areata.	We agree that AA is an autoimmune disease, and apologize if the word "other" could be confusing in this regards. This has been rephrased. However, we disagree with the reviewer regarding AA being understudied. While there are <5,000 Pubmed indexed publications when searching for "alopecia areata", there are more than 31,000 records for Atopic dermatitis, and more than 56,000 records for Psoriasis (a more than 11-fold difference!). Given the considerable knowledge gaps about AA that still exist, we therefore submit that we feel that the disease is still relatively understudied compered to other diseases within dermatology.
Patients were note involved in the development of …..	Patients were not involved in the development of …..	This has been corrected
Information on patient demographics ….	Why commonly associated Comorbidities such as atopic dermatitis, thyroid disorders, vitiligo, or Down's syndrome were not asked for??	Because such information is already available though our existing data sources and can be linked to this dataset on individual-level (see our response to Reviewer 1, comment 1).
eye irritation, …	It would have been more suitable to ask for eye dryness. With AA the eyes may show dry eyes, not eye irritation which is rather a symptom of atopy.	The questions we used regarding Eye Irritation were specifically developed and used in clinical trials of novel AA therapies (baricitinib). We therefore chose to use the exact same questions that were used in these trials, to ensure comparability between the study cohorts in the clinical trials and patients in the Danish Skin Cohort.
Our observation may partially reflect a higher awareness of hair loss among women.	This could not be an explanation. Males and females become very much aware of patchy hair loss as occurring in AA. Also males have commonly shorter hairs and	We agree that this may not explain the entire difference, which was why we included the word "partially", however, we do believe that it could explain at lease some of the difference. Having a completely shaved head is arguably much more frequent among men than women. If a man is already shaving his head on a regular basis (by choice), there is a chance that he would not notice an AA-bald spot since his head was already always shaved

	would detect a bald patch on their scalp much easier.	

VERSION 2 – REVIEW

REVIEWER	Bosseila, Manal A. -W. Cairo Univ, Dermatology
REVIEW RETURNED	09-Dec-2021

GENERAL COMMENTS	To Editors of the journal: The authors have addressed all spelling mistakes written in the previous review. However, as regards the points of defect, such as wrong statements, they were not addressed or even discussed why they do not agree on correcting those statements in a separate response to reviewers.

VERSION 2 – AUTHOR RESPONSE

Reviewer 1, Comment 1:

The authors have addressed all spelling mistakes written in the previous review.

However, as regards the points of defect, such as wrong statements, they were not addressed or even discussed why they do not agree on correcting those statements in a separate response to reviewers.

Our reply:

We apologize if the reviewer did not feel that we adequately addressed the incorrect statements in our previous revision. The sentence regarding “other inflammatory diseases” has now been corrected (page 3). The defects/limitation regarding the lack of questions about comorbidities has now been discussed in the limitations section (page 11).