Reviewer's report

Title: Factors accounting for the association between anxiety and depression, and eczema: The Hordaland Health Study (HUSK)

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Reviewer: Parker Magin

Reviewer's report:

The manuscript contains some interesting findings but I have some concerns with the paper as presented, particularly the focus on IgE which distracts from the findings that are of genuine interest.

1) Major compulsory revision

The main problem is in the definition and measurement of eczema.

• As the authors point out, eczema (or dermatitis) includes not only atopic dermatitis but a whole range of other clinical entities that share common pathological features: seborrhoeic dermatitis, contact dermatitis, dishydrotic eczema etc

• Atopic eczema has been strongly associated with atopy/IgE but not other forms of eczema/dermatitis

• The question “Have you had eczema (red, itching, sensitive, or fissured skin) on any occasion during the last year?” will elicit a positive response from subjects with atopic eczema, but also from those with other forms of eczema/dermatitis and quite possibly from those with other inflammatory skin diseases (such as psoriasis, tinea, and a number of less common skin diseases) – especially if the skin condition has not yet been given a diagnosis by a health professional. The problem is in disease definition – other dermatoses besides eczema may have “red, itching, sensitive, or fissured skin”.

But, equally, not all inflammatory skin conditions will be elicited – the form of the question will tend to cause subjects whose skin condition (though red, itching, sensitive or fissured) has been given a “non-eczema” diagnosis to answer negatively.

Thus, findings from the analyses presented in the manuscript relate to a population with a much broader range of dermatoses than atopic eczema. Using such a population, inferences can’t be made concerning IgE and atopic eczema. I can’t see the data regarding IgE and atopy being of relevance to what I see as the bigger picture presented in the paper (that is, the association of skin disease with depression and anxiety).

Additionally, for this research question, the relevance of conducting a sub-study only in current and ex-hairdressers is problematic. The generalisability of results to the general population is limited.
Furthermore, the authors should be careful in extrapolating validity of self-reported symptoms/diagnoses from studies of hand eczema to other body sites as examined in this study. Hand dermatitis is a singular clinical entity.

Other points

• 2) Minor essential revision

The Participants and data collection should be made clearer.

It is not altogether apparent just what is the final response rate (once completion of the valid responses on the eczema and mental health variables is accounted for). It looks as though it may be approximately 44% for the main analyses, but can’t be calculated from the material provided. And it is certainly less than the figures of 57% / 70% / 73% / 81% that are cited for separate study populations at earlier stages. This has implications for the external validity of the study.

A flow chart of numbers of inclusions/exclusions at the steps prior to inclusion in the various analyses would help overcome this problem.

The final paragraph of The Participants and data collection needs is also unclear, even after reading the cited paper.

From the sentence structure, it appears that

The first, which was identical for all participants, included a self-administered questionnaire and a health examination with blood samples where the participants received a second form that was returned by prepaid mail.

all refers to the first stage of data collection. What was the second stage of data collection? What data was elicited at the examination and in the two questionnaires?

• 3) Discretionary revision

The authors are rightly careful to claim that there data demonstrates an association (and don’t claim to have provided evidence for causality), but more should be made in the discussion of the fact that this is a cross-sectional study and as such is unable to make inferences regarding causality. This of great importance in psychodermatology where stress and other psychological and psychiatric morbidity has been proposed to be causative of skin disease, as well as skin disease being proposed to be causative of anxiety, depression, stress and other psychological and psychiatric morbidity.

A major limitation of interpretation of results from the study is its cross-sectional nature and this should be made explicit.

In addition, in the wording in Page 4, paragraph 3:

The aim of the present study is therefore to examine the relevance of some proposed mechanisms

The use of the word “mechanisms” could be interpreted as implying evidence for causation. The wording could be reconsidered.
• 4) Discretionary revision
Page 4, 2nd paragraph
The sentence:
On the other hand, the advantage of clinical studies is the presumed good reliability of eczema, anxiety, and depression
I suspect this should read
is the presumed good reliability of diagnoses of eczema, anxiety, and depression

• 5) Discretionary revision
Page 9, paragraph 1
Using a simple list of questions derived from the somatisation diagnostic criteria doesn’t have the same validity as employing a validated instrument, and this should be made clear as a limitation of this aspect of the study.

• 6) The statistical aspects require more expert review than mine

Statistical analysis
I think expert statistical review may be of value.

Even as a non-statistician, I would have expected to have been provided with more information about the regression analyses – whether forward or backwards processes were used and criteria for inclusion and exclusion of independent variables in and from the models.

The rationale for using logistic regression in one set of analyses and linear regression in another when the dependent variable was HADS results in both circumstances needs to be stated.

Again as a non-statistician, I’m not sure why the successive iterations of regression modelling are presented (Table 5) rather than the final models which I would have thought would convey more useful information.

Conclusion
My overall assessment is that the question of IgE/atopy and it’s relation to depression and anxiety in atopic eczema is not able to be answered with the data presented here.

The paper does present data from a wider study of the association of anxiety and depression with skin disease. It also examines the role of somatisation and health anxiety in this association. This is of interest.

Thus the study adds some further insight to the existing cross-sectional literature on depression and anxiety in eczematous skin diseases. I think the paper would be best reframed as such, with its main limitation being the diagnostic validity of the self-diagnosis of eczema – this will result in a heterogeneous patient population of atopic and non-atopic eczema/dermatitis diagnoses. It is also likely that some measurement bias will be inherent in the survey question and some participants with non-eczematous inflammatory dermatoses will be included.
But, as the authors rightly state, a trade-off of diagnostic sensitivity/specificity versus power and generalisability is inherent in the psychodermatological findings of all previously-reported large population-based studies – studies which, so far at least, do not include clinical skin examinations.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests