Author’s response to reviews

Title: Cost And Effectiveness Of Prescribing Emollient Therapy For Atopic Eczema In UK Primary Care in Children and Adults: A Large Retrospective Analysis Of The Clinical Practice Research Datalink

Authors:

George Moncrieff (melissa.mandell@envisionpharmagroup.com;georgemoncrieff@hotmail.com)

Annie Lied-Lied (ALIEDLIE@ITS.JNJ.com)

Gill Nelson (gnelson1@ITS.JNJ.com)

Chantal Holy (CHoly1@its.jnj.com)

Rachel Weinstein (RWeinst1@its.jnj.com)

David Wei (dwei8@ITS.JNJ.com)

Simon Rowe (simon.m.rowe@gmail.com)

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Note: The below is also attached as Word document for easier reading.

Dear Editors:

Re: Reviewers comments to our article entitled: “Cost and effectiveness of prescribing emollient therapy for atopic eczema in UK primary care in children and adults: a large retrospective analysis of the Clinical Practice Research Datalink”.

We would like to thank you and the reviewers for a thorough review of our work. We believe the thoughtful comments from the reviewers will help make our work more accessible to readers. Please find below our comments and corrections for all comments raised by reviewers. Our comments are in bold letters.

Sincerely,

The Authors.
From: Emiliano Antiga (Reviewer 1): The paper entitled "Cost and effectiveness of prescribing emollient therapy for atopic eczema in UK primary care in children and adults: a large retrospective analysis of the Clinical Practice Research Datalink" is an interesting investigation about the role of the use of emollients in patients with the diagnosis of dry skin and atopic eczema. The paper is well written and the results are interesting.

The main concern is about the diagnosis of "dry skin and atopic eczema", that is quite generic and it includes (as reported in table 1) several entities that are very different from atopic dermatitis, including itch, pruritus, seborrhoeic dermatitis that account for about 25% of the non-emollient group and only of about 5-6% of emollient group. Although it is clearly difficult in this type of retrospective research to have homogeneous groups with clear-cut diagnoses, this may lead to a bias that should be clearly reported within the limitations of the study.

For all analyses, cohorts were matched using direct matching methodology. One of the variables that was used for matching was index diagnosis – that fact was important to make sure that patients treated with emollient were indeed compared to patients not treated with emollients but identified with similar index diagnoses.

This fact was further highlighted in the Methods section (former lines 166-167).

We have added the following sentence in the first paragraph of the section “Limitations” (line 360, p16):

“Disease types included for initial cohort identification were broad (Table 1); however, the analysis was based on groups matched exactly for index diagnosis.”

Please check the use of the acronyms. For example, in the introduction, the term "atopic dermatitis" is reported even after the use of its acronym AD.

Thank you, we have checked our use of abbreviations and corrected three lapses into full-term use.

We also added five abbreviations to the list of abbreviations (line 402, p19).

Robert T. Brodell (Reviewer 2): I enjoyed reading the article, "Cost and effectiveness of prescribing emollient therapy for atopic eczema in UK primary care in children and adults: a large retrospective analysis of the Clinical Practice Research Datalink." On the surface the article validates my clinical experience ....the use of emollients early and often in children with atopic dermatitis is an effective and cost-saving approach. However, I would like the limitation section (lines 385-392) to more strongly state a major limitation of this study. It was not possible to determine that the severity of disease in the groups who obtained Aveeno and those that did not.

We had previously raised the issue of severity of disease not being available in the CPRD (former line 385, p17) and “we tried to minimise the effect of a severity bias by matching for age and type of disease”; however, we appreciate the limitation does warrant greater clarity to the reader. We
have added text as suggested: (line 366, p16) “More severe patients prescribed a TCS may not receive a prescription for an emollient that visit because the prescriber is focussed on using the TCS.” (line 368, p16) “…should cases in the Emollient groups (including Aveeno groups) have been less severe…in a group expected to have fewer visits and lower costs.”

It is equally plausible that busy primary care physicians may have used emollients more commonly in patients with mild disease. Perhaps in some of the visits with milder disease, emollients were all they needed. More severe patients prescribed a topical steroid may not have received an emollient that visit as the prescriber focused on using the topical steroid. Thus, the findings of lower cost and fewer visits might be expected in the emollient group who had overall less severe disease. One approach to this conundrum would be to go back and assess the strength of topical steroid used in these groups. If more patients treated with mild steroid (hydrocortisone cream) were present in the emollient group and stronger topical steroids were used in the steroid-only group, there would be an indication supporting the possibility that the two groups were not equally severe.

Although an excellent suggestion (for which we thank the reviewer), re-analysis of the database would take considerable time without guarantee of a definitive answer in what remains a hypothesis-generating analysis. After consideration, our preference is to more clearly highlight the limitation regarding disease severity. To the conclusion we have added (line 392, p17) “though disease severity is an unknown and potential confounder in this analysis.”

Ultimately, a large, prospective study is required to settle this point. It would be difficult to blind this study since patients and physician will know if they received an emollient in addition to a topical steroid or non-steroid topical. There could be two treatment groups, one with Aveeno-Oatmeal and a second with a ceramide component.

Because of this deficiency, I would tone down the conclusions (lines 432-441). I agree that this study "demonstrated" fewer visits, fewer other prescriptions and reduced cost in the emollient group. This could be related to improvement in the skin barrier. BUT, lines 438-441 uses the verb "resulted in" suggesting it was causative. That is NOT clear.

Thank you for this observation. Our study, as with all retrospective analyses, cannot lead to causative conclusions and we agree with Dr Brodell that this needs to be rewritten. The statement was changed accordingly. Please see changes in lines 390-400, p18.

Similarly, in the abstract, lines 54-56…I agree "was associated with" is correct, but I would like to see some additional qualification here so that the reader who only skims the abstract is not left with the impression that a causative relationship has been proven. Perhaps the conclusion could say, "Recognizing limitations inherent in a study design where severity of disease could not be documented, prescription of emollients to treat DS&E was associated with…"

The abstract statement was changed accordingly and edits made earlier in the abstract to accommodate the additional words. Please see changes in lines 53-54, p3.
Editor Comments: I found your article entitled “Cost and effectiveness of prescribing emollient therapy for atopic eczema in UK primary care in children and adults: a large retrospective analysis of the Clinical Practice Research Datalink” interesting. In addition to the esteemed reviewers’ comment, I request you to shorten your article a bit.

We have removed circa 550 words from the body text, despite the additions requested below, by removing and summarizing some of the former detail from mainly the introduction and discussion (see tracked changes).

In addition, please admix the section “Implications” in “Discussion”.

This section is now addressed in paragraphs 1 and 2 of the discussion and the subtitle “Implications” has been deleted.