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Comments on: 'Four-year data from use of the nut and soya testing protocol before treatment with isotretinoin and alitretinoin': reply from authors

doi: 10.1111/ced.14517

We read with interest and accept some of the points made by McCarthy *et al.*¹ and Ostlere and Bansal² on our paper regarding drug challenge and skin prick testing with isotretinoin. In response to this, we are now referring selected patients with severe acne and suspected soya and nut allergy to our drug allergy service for drug challenges and/or skin prick testing with isotretinoin and its capsule. Our reported protocol^{3,4} is a means of mitigating and categorizing risk for our patients, and we are pleased that it is generating debate that may potentially inform practice. Without clear prospective evidence in larger patient numbers to the contrary, we propose that it may still be risky to recommend isotretinoin when allergy tests are positive to specific soya and nut proteins.

Regardless of the low theoretical risks, how many patients (and their parents) would be prepared to take an initial drug challenge of 1–2 h in duration,^{2,5} and then take a prolonged treatment course of 4–6 months with a named ingredient to which they are potentially allergic, albeit at low risk levels?

The Summary of Product Characteristics (SPC) for isotretinoin 10 and 20 mg soft capsules clearly states that this drug is contraindicated in patients who are allergic to peanuts or soya. Roche, the original isotretinoin licence holder, confirmed to us in writing (Roche, personal communication) in October 2020 that prescribing isotretinoin in this context is 100% off-licence, thus it then becomes the full responsibility of the clinician if there are any future reactions. This is also in line with European Medicines Agency (EMA) guidelines.⁶

The latest data in October 2020 from Roche states that its isotretinoin capsule formulated to contain 20 mg isotretinoin also contains 215.8 mg refined soya oil, 15.4 mg hydrogenated soya oil and 61.4 mg partially hydrogenated soya oil (total 292.6 mg soya bean oil).⁷ Hence, the average dosages of 40–60 mg of isotretinoin will contain

double or triple the listed soya oil content per day. The total soya oil content will vary with different manufacturers. The soya oils in the capsules are not tested for residual protein content (Roche, personal communication).

Hence, this risk may not be appropriate to completely ignore (as was suggested¹ for the throat swelling in our index patient in the original 2016 paper, who did proceed to have further symptoms on rechallenge with isotretinoin). Unfortunately, we could not retrieve any further information or do further testing on this index patient as they have been lost to follow-up. In a recent literature search we could find no evidence documenting other patients who reacted to the capsule of these tablets rather than the active ingredient or other excipients.

We agree that further study is needed to clarify the full clinical significance of soya and nut allergy in relation to tolerance of these drugs, but would emphasize that our protocol has been useful for risk stratification in our patient cohort. Further such study should provide more detailed information for our patients to choose their preferred treatment options, balancing risk and benefits.

We agree that relying on anecdotal reports of safety with drug challenges in small numbers of patients may not be the best evidence to determine future clinical practice. Further prospective studies are needed, and drug challenge testing and potential skin prick testing of selected patients with isotretinoin and its constituents is the next step if no alternative treatments are suitable. As with other contraindications for isotretinoin (and other similar drugs), treatment options will need to be considered with shared decision-making with the patients and their guardians.

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Linked articles: McCarthy S *et al.* *Clin Exp Dermatol* 2020; **45**: 1071; Ostlere L, Bansal A. *Clin Exp Dermatol* 2020; **45**: 1070.

Conflict of interest: the authors declare that they have no conflicts of interest.

Accepted for publication 19 November 2020

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Adherence to treatment with prescribed topical corticosteroid therapy and potential barriers to adherence among women with vulvar lichen sclerosis: a prospective cross-sectional study

doi: 10.1111/ced.14527

Lichen sclerosis (LS) is a chronic inflammatory dermatosis that predominantly affects the anogenital region. Potential complications of vulvar LS include scarring, loss of vulvar architecture and development of vulvar squamous cell carcinoma (SCC). It has been suggested that individualized treatment regimens with long-term topical corticosteroid (TCS) may modify the course of disease in

LS and reduce the risk of complications such as SCC.¹ Guidelines for the management of LS now advocate consideration of an individualized treatment regimen of long-term TCS to maintain disease control.²

TCS have been a mainstay in the treatment of inflammatory skin conditions for decades, and there is ample evidence to support their long-term efficacy and safety. Despite this, several studies have demonstrated suboptimal compliance with prescribed TCS therapy among patients with dermatological conditions.³ There are limited data available in the literature on compliance with prescribed TCS among patients with LS. The aims of this prospective study were to measure adherence to prescribed TCS among women with vulvar LS, to identify possible reasons for nonadherence and, to explore advice being received by patients from pharmacists and general practitioners (GPs) about TCS use.

The Clinical Research Ethics Committee (Cork, Ireland) approved the study. Female patients aged ≥ 18 years with a diagnosis of LS attending the vulvar dermatology clinic in our centre were invited to participate by completing anonymous questionnaires, which included patient demographics, Morisky Medication Adherence Scale (MMAS)-4 modified for LS, reasons for nonadherence to TCS use, and frequency of messages received from pharmacists and GPs regarding TCS-related risks and benefits.

Of 101 patients who were invited to participate in the study, 76 completed the questionnaire. Mean age was 57.4 years (median 59, range 25–82 years). All patients were prescribed TCS at least once weekly. Using the validated MMAS-4, 22.4% of participants ($n = 17$) were classified as high adherers, 51.3% ($n = 39$) medium and 26.3% ($n = 20$) low. The most frequently reported reasons for missing treatment applications included

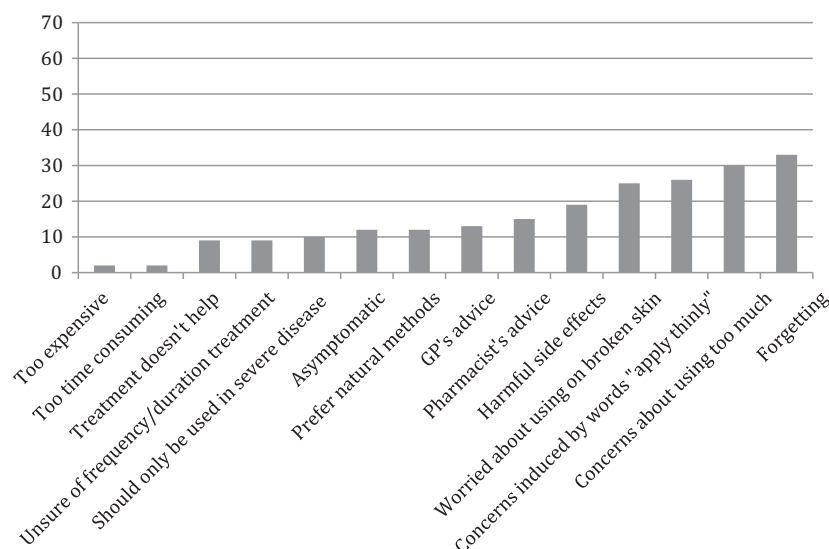


Figure 1 Reported reasons for nonadherence to treatment with topical corticosteroid as prescribed.