

Crude odds ratios with accompanying 95% confidence intervals were calculated to measure the association between risk of BCC and SCC and oral steroid use (Table 2). Stronger increases in risk of each skin cancer were found for steroid use to treat (supposedly) non-atopic conditions, compared to nonusers. Steroid use to possibly treat atopic conditions was not found to be associated with either type of cancer. These findings suggest that the effects of atopic conditions may confound the association between glucocorticoids and skin cancer risk. The analysis is limited in that the odds ratios have not been adjusted for other confounding factors, although the adjusted odds ratios in the

original analysis were very similar in magnitude to the unadjusted odds ratios. Another limitation involves the fact that four cases (two BCC, two SCC) that received steroid treatment for conditions in more than one category were not identified as such in the original table, and so could not be adjusted for in this analysis. However, other analyses involving different assumptions about the possible joint conditions suggested that the findings would not be greatly influenced by this problem. Both of these issues could be addressed by the authors through reanalysis of the original study data. It would also be interesting to know whether a similar reanalysis of inhaled steroid use resulted in comparable findings.

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## Reply: Glucocorticoid use and skin cancers

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Sir,

We appreciate Dr Purdue's interest in our report on use of glucocorticoids and skin cancers. As suggested in his letter, we reclassified indication for steroid use into two categories: (1) atopic conditions (i.e. 'respiratory conditions and asthma' and 'allergies') and (2) non-atopic conditions (i.e. 'musculoskeletal and connective tissue disease', 'neoplasm', 'gastrointestinal disease', and 'other condition') (Table 1). In the reanalysis of the data, we noted an error in Table 1 of the original report. There were only two controls that used glucocorticoids for allergies (the seven controls in the original report included users of inhaled steroids). The correct numbers appear in Table 1 below and are restricted to oral users. The odds ratios associated with oral glucocorticoid use, stratified by Dr Purdue's classification, are shown in Tables 2 and 3. The results for 'any use' differ very slightly from the original report because we removed individuals with more than one indication or with missing data on the indication for use for this reanalysis.

**Table 1** Oral glucocorticoid use according to indication among skin cancer cases and controls

Steroid use <sup>a</sup>	Indication	Controls N (%)	BCC N (%)	SCC N (%)
No		491 (95.0)	534 (93.0)	245 (91.1)
Yes	Any use <sup>b</sup>	26 (5.0)	40 (7.0)	24 (8.9)
	Treat possible atopic conditions <sup>c</sup>	11 (2.1)	12 (2.1)	9 (3.4)
	Treat possible non-atopic conditions <sup>d</sup>	15 (2.9)	28 (4.9)	15 (5.6)

BCC = basal cell carcinoma; SCC = squamous cell carcinoma. <sup>a</sup>Use of oral glucocorticoid use for 1 month or longer. <sup>b</sup>Excludes three individuals with more than one indication (two BCC, one SCC) and two individuals with missing data on indication for use (one BCC, one SCC). <sup>c</sup>Includes 'respiratory conditions and asthma' and 'allergies'. <sup>d</sup>Includes 'musculoskeletal and connective tissue disease', 'neoplasm', 'gastrointestinal disease', 'other condition'.

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The data for basal cell carcinomas (BCC) provide some support for his hypothesis, that is, the association may be limited to non-atopic conditions (Table 2). However, lack of precision in our risk estimates prevents us from drawing any firm conclusions. In our original report, the association was stronger for squamous cell carcinomas (SCC), and for this cell type, the risk associated with oral glucocorticoid use does not differ much by type of condition (Table 3). Unfortunately, we were unable to perform the recommended analysis of inhaled steroid use since the indications for use almost exclusively fell into the atopic category (Table 4). The potential effect of immune response and immunosuppression on the incidence of skin cancer is of considerable interest to us. We hope that further studies will address commonly used immune-modulating drugs along with atopic conditions, and that this, in turn, will shed light on this pathway to human malignancies.

**Table 2** Association between oral glucocorticoid use and BCC, with further analysis by indication

Steroid use <sup>a</sup>	Indication	BCC	BCC
		Crude OR (95% CI)	Age, sex adjusted OR (95% CI)
No		1.00 (reference)	1.00 (reference)
Yes	Any use <sup>b</sup>	1.45 (0.87, 2.41)	1.43 (0.86, 2.38)
	Treat possible atopic conditions <sup>c</sup>	1.00 (0.44, 2.29)	0.97 (0.42, 2.23)
	Treat possible non-atopic conditions <sup>d</sup>	1.72 (0.91, 3.25)	1.70 (0.90, 3.24)

BCC = basal cell carcinoma; OR = odds ratio; CI = confidence interval. <sup>a</sup>Use of oral glucocorticoid use for 1 month or longer. <sup>b</sup>Excludes two cases with more than one indication and one case with missing data on indication for use. <sup>c</sup>Includes 'respiratory conditions and asthma' and 'allergies'. <sup>d</sup>Includes 'musculoskeletal and connective tissue disease', 'neoplasm', 'gastrointestinal disease', 'other condition'.

**Table 3** Association between oral glucocorticoid use and SCC, with further analysis by indication

Steroid use <sup>a</sup>	Indication	SCC	SCC	SCC
		Crude OR (95% CI)	Age, sex adjusted OR (95% CI)	Age, sex, skin type <sup>b</sup> adjusted OR (95% CI)
No		—	—	—
Yes	Any use <sup>c</sup>	1.93 (1.09, 3.41)	1.98 (1.10, 3.57)	2.21 (1.21, 4.04)
	Treat possible atopic conditions <sup>d</sup>	1.64 (0.67, 4.01)	1.68 (0.67, 4.19)	1.75 (0.68, 4.46)
	Treat possible non-atopic conditions <sup>e</sup>	2.00 (0.96, 4.17)	2.10 (0.99, 4.47)	2.49 (1.16, 5.36)

SCC = squamous cell carcinoma; OR = odds ratio; CI = confidence interval. <sup>a</sup>Use of oral glucocorticoid use for 1 month or longer. <sup>b</sup>Skin reaction to sun exposure. <sup>c</sup>Excludes one case with more than one indication and one case with missing data on indication for use. <sup>d</sup>Includes 'respiratory conditions and asthma' and 'allergies'. <sup>e</sup>Includes 'musculoskeletal and connective tissue disease', 'neoplasm', 'gastrointestinal disease', 'other condition'.

**Table 4** Indication for glucocorticoid use among those who use inhaled steroids

Indication for steroid use	Inhaled only	Inhaled+oral <sup>a</sup>
Respiratory conditions and asthma	29	10
Allergy	7	1
Musculoskeletal and connective tissue disease	1	0
Gastrointestinal disease	0	1
Other condition	3	2

<sup>a</sup>Three people have more than one reason for steroid use.