

warnings of possible risks of mood change and suicidality, and these issues are of concern to patients and families as they participate in decision making about taking the medication.



In this issue of the *BJD*, the paper by Paljarvi *et al.* adds to the literature assessing whether treatment of acne with isotretinoin contributes to additional risk of neuropsychiatric conditions.<sup>3</sup> Utilizing a large electronic database of more than 12 million patients aged 12–27 years, the authors used a rigorous approach to compare the 12-month incidences of mental health conditions (including mood disorders, sleep, psychosis, anxiety and non-fatal self-harm) in different patient groups. The authors confirmed that acne diagnosis was associated with increased psychiatric risk compared with a matched population without acne (odds ratio 1.46). Furthermore, patients prescribed treatment for acne with topicals or oral antibiotics had a greater risk than patients with acne given no treatment, suggesting that acne severity impacts risk. This overall excess risk in people with acne was just maintained in patients treated with isotretinoin (odds ratio 1.06) but, importantly, the risk in patients treated with isotretinoin was reduced compared with those treated with oral antibiotics (odds ratio 0.8). Isotretinoin treatment therefore seemingly reduces the higher psychiatric risks associated with treatment-resistant acne. Data for self-harm followed a similar pattern to overall psychiatric risk, but suicide data were not available in the study.

Other studies support the perspective that isotretinoin is not associated with higher rates of neuropsychiatric events at the population level. A very large US population study<sup>4</sup> and a recent meta-analysis of 31 studies<sup>5</sup> showed no evidence to support an association between isotretinoin and depression. Singer *et al.*<sup>6</sup> showed that rates of completed suicide were lower in patients taking isotretinoin than in the general US population, and similar findings were presented by Droitcourt *et al.*<sup>7</sup> in a large population study in France.

Despite this evidence, individual cases of clinically significant depression and other neuropsychiatric events in association with isotretinoin are persistent in the literature, and numerous cases have been reported to regulatory agencies around the world. Continuing rare reports of completed suicide during and after treatment and are extremely distressing. Isotretinoin crosses the blood–brain barrier, and neurobiologists have identified plausible mechanisms to account for brain effects, particularly in young people.<sup>8</sup> Physical side-effects from isotretinoin may contribute to low mood, and it is also possible there are higher rates of awareness of psychiatric adverse events in patients on isotretinoin (ascertainment bias) due to regulatory requirements such as the ‘I-Pledge’ programme in the USA, which mandates monthly physician visits, giving more frequent opportunity to record mental health issues.

Isotretinoin is an extremely effective drug for acne, and in our practice we see improved affect, energy and self-confidence in many patients after effective acne treatment. It is essential that patients are screened at baseline for psychiatric history, which may be associated with increased risk of low mood and suicide during isotretinoin treatment.<sup>7</sup> Ongoing risk management should be practised consistently and referral

pathways put in place to support patients with mood concerns. However, this large population study provides some further reassurances that oral isotretinoin does not increase overall risks of psychiatric problems.

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## Identity and psychological distress in alopecia areata

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**Linked Article:** Macbeth *et al.* *Br J Dermatol* 2022; **187**:73–81.

In this issue of the *BJD*, Macbeth and her seven coauthors provide a timely article regarding mental health conditions associated with alopecia areata (AA).<sup>1</sup> In the past, this area has been neglected by many dermatologists and others when

considering the treatment of AA, a problem we discussed nearly 20 years ago.<sup>2</sup> Focusing specifically on depression and anxiety, as these are probably the most likely mental health concomitants of AA, this large-scale study found that both conditions are more common among people diagnosed with AA than among controls.

This is not a surprising finding. Hair is of fundamental importance in projecting the self-image, and a dramatic change in appearance can profoundly affect the way people see themselves.<sup>3</sup> In this sense AA is similar to other forms of disfigurement. We have long acknowledged the importance of the psychosocial aspects of, for example, facial disfigurement, but hair has similarities because it can be just as important for self-esteem as any other part of appearance. Many women (in particular) see their hair as their 'crowning glory', so the loss of hair can be particularly distressful for women.<sup>4</sup> Macbeth *et al.* did not compare sex differences. It would have been helpful to see whether previous findings regarding sex differences are repeated, or whether cultural change has altered the pattern of psychosocial problems experienced by men and women.

One important finding from the study of Macbeth *et al.* is not just that people with AA were more likely to experience depression and anxiety, but that they were also more likely to be issued time off work certificates and be recorded as unemployed. We know that hair loss can affect whether people take part in social activities such as sport<sup>5</sup> or sexual activity,<sup>6</sup> so this adds to the evidence regarding the inability of many people with AA to take part in normal social activities, presumably directly because of their hair loss.

The authors do recognize some of the limitations of their study. In addition to this, one problem may be the focus on medications as the main indicators of depression and anxiety. While this provides a reasonable measure of the classification of depression and anxiety, it is not without its faults. Many people experiencing symptoms of depression and anxiety do not go to their doctor and obtain medication. On the other hand, some people may be prescribed medication without a full assessment of their mental health. These issues are not likely to change the overall picture that many people with AA experience psychosocial problems.

Perhaps the most important point made by Macbeth *et al.* is that people with AA who experience psychological distress should be provided with appropriate support, and that we need to develop and test appropriate psychological therapies for use with AA. Psychologists do have appropriate therapies available. We must recognize the need for these among people with AA.

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## Weighing in on weight-based secukinumab dosing for psoriasis

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**Linked Article:** Augustin *et al.* *Br J Dermatol* 2022; **186**:942–954.

Therapeutic monoclonal antibodies directed against specific proinflammatory cytokines – a class of targeted therapies known as the biologics – have transformed the management of psoriasis.<sup>1</sup> Compared with the classical oral treatments, the latest generation of interleukin (IL)-17- and IL-23-blocking biologics has a higher likelihood of inducing sustainable treatment responses with complete clearance.<sup>2</sup> However, not all patients with psoriasis respond equally favourably. Patients who are obese, in particular, achieve lower treatment responses to biologics,<sup>3,4</sup> which could have a pharmacokinetic basis. Heavier patients attain higher drug clearance and lower drug concentrations to monoclonal antibody treatment.<sup>5,6</sup> Therefore, adjusting the dose of biologics might be a rational approach in patients with excess body weight.

In this issue of the *BJD*, Augustin and colleagues report findings from a multicentre randomized controlled clinical trial that assessed the merits of intensive, above-label dosing of secukinumab, an approved biologic targeting IL-17A, in patients with psoriasis weighing  $\geq 90$  kg.<sup>7</sup> In this trial, 331 patients with mean bodyweight of 111 kg (SD 18) were randomized to receive secukinumab according to the approved dosing regimen – i.e. 300 mg once per 4 weeks (Q4W) – or secukinumab in an intensified dosing regimen of 300 mg once per 2 weeks (Q2W). At week 16, a statistically significant greater proportion of patients achieved the primary endpoint of Psoriasis Area and Severity