

cell carcinoma, and the two cancers had similar localizations, possibly an indication of common pathophysiological mechanisms.


Over the past decades, routinely collected data have been frequently used as data sources in dermatological research, and such data are often used to describe disease burden and generate hypotheses regarding mechanisms behind disease development.<sup>5,6</sup> The paper by De Giorgi *et al.* is an excellent example of how essential information can be extracted from large datasets and put into clinical context. In contrast to retrospective studies where recall bias and selection bias often are major issues, surveillance bias may be an important limitation in the present study, especially as CAC and squamous cell carcinoma both are cutaneous malignancies, and increased monitoring of patients following one skin cancer is common. However, overall these novel observations may help in the general understanding of CAC and sets a foundation for future research. The paper brings new attention to an understudied area in dermatology and warrants an international effort towards better treatment and management guidelines for these tumours.

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## Conflicts of interest

None to declare.

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## References

- 1 LeBoit PE, Burg G, Weedon D, Sarasain A. *World Health Organization Classification of Tumours. Pathology and Genetics of Skin Tumours*. Lyon: IARC Press, 2006.
- 2 Martinez SR, Barr KL, Canter RJ. Rare tumors through the looking glass. *Arch Dermatol* 2011; **147**:1058.
- 3 Avraham JB, Villines D, Maker VK *et al.* Survival after resection of cutaneous adnexal carcinomas with eccrine differentiation: risk factors and trends in outcomes. *J Surg Oncol* 2013; **108**:57–62.
- 4 De Giorgi V, Salvati L, Barchielli A *et al.* The burden of cutaneous adnexal carcinomas and the risk of associated squamous cell carcinoma: a population-based study. *Br J Dermatol* 2019; **180**:565–73.
- 5 Dizon MP, Yu AM, Singh RK *et al.* Systematic review of atopic dermatitis disease definition in studies using routinely collected health data. *Br J Dermatol* 2018; **178**:1280–7.
- 6 Lomas A, Leonardi-Bee J, Bath-Hextall F. A systematic review of worldwide incidence of nonmelanoma skin cancer. *Br J Dermatol* 2012; **166**:1069–80.

## The long road to valid outcomes in vitiligo

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There are only two mistakes one can make along the road to truth; not going all the way, and not starting.

– Buddha

A key element in evidence-based medicine is that the results of clinical trial outcomes are trustworthy. For ages clinicians had personal preferences about which outcomes should be measured to evaluate the effectiveness of a certain treatment. This has led to confusion, which frustrates the comparison of studies and leads to a waste of research efforts. Similar to atopic eczema, in vitiligo different outcomes are continuously being measured and a variety of outcome measurement instruments are used to measure similar outcomes. To illustrate, Eleftheriadou *et al.* reported that 48 different outcome measurement instruments have been used to measure repigmentation in 54 controlled trials.<sup>1</sup> This is an unwarranted situation and deserves attention.

Although Eleftheriadou *et al.* revealed the large number of outcomes used,<sup>1</sup> it was Vrijman *et al.* who revealed the lack of evidence on the measurement properties of the outcome measurement instruments used in patients with vitiligo.<sup>2</sup> Therefore, recent studies in vitiligo focused on ‘what’ to measure (i.e. the outcomes)<sup>3</sup> and ‘how’ to measure these outcomes (i.e. outcome measurement instruments)<sup>4</sup> aiming to come to a consensus, among a large group of international stakeholders (including patients and healthcare professionals), about which outcomes are considered most important and which instruments are most suitable to measure these.

A milestone in vitiligo outcome research was the e-Delphi consensus on the core outcome set for clinical trials in vitiligo.<sup>5</sup> This procedure involved all relevant stakeholders and identified a minimal set of core outcome domains to be included in all clinical trials in vitiligo: repigmentation, side-effects/harms and maintenance of gained repigmentation. Now that we know what to measure we need to find out how to measure the core outcome domains. New measurement instruments, such as the Vitiligo Extent Score have been developed and validated.<sup>6</sup>

In addition to reach a consensus on what and how to measure, a next step was to achieve consensus on the definition of successful repigmentation. In other words, when is the treatment effective in terms of repigmentation? In previous studies, the definitions of ‘successful repigmentation’ varied from ‘any repigmentation’ to 100% repigmentation. In the past, these definitions were typically defined by physicians, but it is obvious that patients should have the most important voice in this matter.

In this issue of the *BJD*, Eleftheriadou *et al.* present the results of a consensus study on the definition of 'successful repigmentation' from the patients' perspective.<sup>7</sup> In three different focus groups involving a total of 73 patients with vitiligo, consensus was reached that 80% repigmentation of a target lesion is regarded successful by patients. Moreover, patients considered the face, neck and hands to be the most important sites of their bodies in terms of achieving satisfactory results. Also, patients recommended an objective and a subjective scale to measure repigmentation. Remarkably, this consensus was unanimous with a 100% agreement.

Does that mean that treatments where we anticipate much less than 80% improvement should not be started at all? It is wise not to jump too quickly to conclusions; for individual patients, substantially lower repigmentation rates may be acceptable or even successful. Other patients may just want to stop the progression of their vitiligo instead of aiming for repigmentation.<sup>8</sup> In the age of 'shared decision making' we need to discuss expectations and anticipated outcomes with our patients and achieve the best possible management of their skin condition. Inevitably, this study raises new questions and now needs to be repeated in other settings and other populations. These results also clarify that our treatments are not nearly as effective as patients require today. Given the great impact vitiligo may have on patient's quality of life, we need to follow a course for more effective treatments but also for valid outcomes in vitiligo.

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## Conflicts of interest

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## References

- 1 Eleftheriadou V, Thomas KS, Whitton ME *et al.* Which outcomes should we measure in vitiligo? Results of a systematic review and a survey among patients and clinicians on outcomes in vitiligo trials. *Br J Dermatol* 2012; **167**:804–14.
- 2 Vrijman C, Linthorst Homan MW, Limpens J *et al.* Measurement properties of outcome measures for vitiligo. A systematic review. *Arch Dermatol* 2012; **148**:1302–9.
- 3 Williamson PR, Altman DG, Bagley H *et al.* The COMET Handbook: version 1.0. *Trials* 2017; **18**:280.
- 4 Prinsen CA, Vohra S, Rose MR *et al.* How to select outcome measurement instruments for outcomes included in a "Core Outcome Set" - a practical guideline. *Trials* 2016; **17**:449.
- 5 Eleftheriadou V, Thomas K, van Geel N, Hamzavi I *et al.* Developing core outcome set for vitiligo clinical trials: international e-Delphi consensus. *Pigment Cell Melanoma Res* 2015; **28**:363–9.
- 6 van Geel N, Lommerts J, Bekkenk M *et al.* Development and validation of the Vitiligo Extent Score (VES): an international collaborative initiative. *J Invest Dermatol* 2016; **136**:978–84.
- 7 Eleftheriadou V, Hamzavi I, Pandya AG *et al.* International Initiative for Outcomes (INFO) for vitiligo: workshops with patients with vitiligo on repigmentation. *Br J Dermatol* 2019; **180**:574–79.
- 8 van Geel N, Desmedt V, De Schepper S *et al.* Cessation of spread as a treatment objective in vitiligo: perception from the patients' point of view. *Br J Dermatol* 2016; **174**:922–4.

## 'En route' to precision medicine

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In this issue of the *BJD*, McAleer *et al.* present interesting and important research on biomarkers measured in stratum corneum and plasma of infants with atopic dermatitis (AD).<sup>1</sup> Although AD is much more common in childhood, most biomarker research until now has focused on the disease in adults. With many new drugs for children with AD in different stages of development this research is timely.

There are many different uses for biomarkers in AD,<sup>2</sup> among these are the objective determination of disease severity and the prediction of treatment response. Until now, disease severity in patients with AD is mostly determined by using clinician-rated severity scores [e.g. Six Area, Six Sign Atopic Dermatitis, the Eczema Area and Severity Index (EASI) and the Severity Scoring of Atopic Dermatitis index (SCORAD)], each of which has advantages and disadvantages. The search for better clinician-rated disease severity measures in AD has resulted in more than 20 different scores being used in clinical studies, which hampers study comparability. Although the EASI and SCORAD are now the preferred measures, they also both have the problem of high inter- and intraobserver variability.<sup>3</sup> An objective biomarker for disease severity determined in blood or skin could greatly improve the way we measure disease severity in AD.

A recent systematic review showed serum CCL17/TARC levels to be the best objective biomarker for disease severity in adults with AD.<sup>4</sup> Now McAleer *et al.* have confirmed that AD plasma CCL17/TARC levels also correlates to disease severity in children.<sup>1</sup> Their study comprised the investigation of a set of potential biomarkers in stratum corneum. The user-friendly