

University of Groningen

How reliable are scoring systems for hidradenitis suppurativa?

Oosterhaven, J A F

Published in:
The British journal of dermatology

DOI:
[10.1111/bjd.18249](https://doi.org/10.1111/bjd.18249)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2019

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):
Oosterhaven, J. A. F. (2019). How reliable are scoring systems for hidradenitis suppurativa? *The British journal of dermatology*, 181(3), 438-439. <https://doi.org/10.1111/bjd.18249>

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Predicting treatment success with biologics in psoriasis

DOI: 10.1111/bjd.18251

Linked Article: Mourad *et al.* *Br J Dermatol* 2019; **181**:450–458.

Drug survival analyses are frequently used to evaluate the performance of drugs used in chronic conditions in real-world practice, such as biologics for psoriasis.¹ The hypothesis is that a long drug survival indicates that the drug performs well. It is assumed that, if there were problems such as ineffectiveness or side-effects, the drug would have been stopped earlier.² Ultimately, it would be valuable for physicians to know beforehand which patients are likely to have successful or unsuccessful drug survival, enhancing personalized medicine. Predictive factors that guide physicians in decision making are needed to fulfil this purpose.

In this issue of the *BJD*, Mourad *et al.* report a systematic review and meta-analysis regarding predictive factors for drug survival of biologics in psoriasis.³ An extensive search has been carried out leading to the inclusion of 16 cohort studies ($n = 32\,194$) for the review. Three predictive factors were further investigated in a meta-analysis: sex, obesity and a diagnosis of psoriatic arthritis. Female sex and obesity were associated with a higher chance of discontinuation on a subset of biologics, while having a diagnosis of psoriatic arthritis led to lower rates of discontinuation. In a stratified analysis, it was shown that female sex and obesity led to more discontinuations because of adverse events, and that obesity was also associated with more discontinuations as a result of ineffectiveness.

The study by Mourad *et al.* provides important insights into which factors may pose a risk for discontinuation of specific biologics. It could be relevant to choose a drug based on prognostic factors that are present in a specific patient. This may guide physicians already in choosing the right biologic for the individual patient. It should be noted that a direct causal relationship between these prognostic factors and drug survival cannot be estimated from such observational studies. This should be an important topic for future aetiological research. For example, to improve drug survival in women, who more often stop biologics as a result of safety issues, different questions should be answered first. Important questions would be: do women have more safety issues when taking biologics or do they only report more issues? Which safety issues are present? Are preventive measures regarding safety possible? With regards to obesity, other questions are relevant, such as, is weight loss really leading to better survival rates before or during treatment? Should we base our dosages more on weight?

Studies like the present article by Mourad *et al.* are important in an era where multiple treatment options are available, as is the case in psoriasis care today. With many ongoing drug

developments, also for other chronic skin diseases, a careful examination of predictive factors for treatment success will remain relevant.

Conflicts of interest

J.M.P.A.v.d.R. carries out clinical trials for AbbVie, Celgene and Janssen and has received speaking fees from AbbVie and Janssen and reimbursement for attending a symposium from Celgene and AbbVie. All funding is not personal but goes to the independent research fund of the Department of Dermatology of Radboud University Medical Centre Nijmegen, the Netherlands.

Department of Dermatology, J.M.P.A. van den REEK 
Radboudumc, Nijmegen, the Netherlands
E-mail: Juul.vandenReek@radboudumc.nl

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How reliable are scoring systems for hidradenitis suppurativa?

DOI: 10.1111/bjd.18249

Linked Article: Thorlacius *et al.* *Br J Dermatol* 2019; **181**:483–491.

In order to conduct meaningful clinical trials on interventions for disease, the use of proper measurement instruments is key. This is increasingly acknowledged and large initiatives are being founded to improve the field of measurement in medicine. One of these initiatives is called COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN),¹ which mainly aims to develop core outcome sets (COSs), containing an agreed minimum set of outcomes that should be measured and reported in all clinical trials of a specific disease.² Such COSs are composed of high-quality

instruments that have been studied for their measurement properties, such as validity, reliability and responsiveness.

The increased attention on this subject has resulted in studies such as the one by Thorlacius *et al.*, featured in this issue of the *BJD*.³ The authors conducted a thorough study on the reliability of nine instruments used in hidradenitis suppurativa (HS); they studied outcome measurement instruments as well as staging systems. Reliability is defined by COSMIN as ‘the degree to which the measurement is free from measurement error’, as illustrated by the agreement of scores in unchanged patients for repeated measurements.¹ Twelve raters from different countries, with a profound clinical experience in HS, were asked to rate 24 patients. Before rating, all tested instruments were discussed during an introductory session. However, this session did not include bedside teaching with live patients.

The study team found wide limits of agreement for the instruments that measure changes in health status. This was also apparent from the high values for the minimal detectable change, reflecting that true change can only be determined with substantial changes on the instruments. In most classification instruments only fair inter-rater reliability was found. Intrarater reliability was not assessed.

It is clear that the comparison of scores in the literature on HS, even if evaluated using the same measurement instrument, may have been subject to misinterpretation until now. However, before researchers decide that this study warrants the development of even more new measurement instruments for HS, the added value of standardized rater-training procedures on how to use the existing instruments should definitely be considered to increase reliability.⁴

Acknowledgments

The author would like to acknowledge Dr Marie-Louise Schuttelaar and Angelique Voorberg for their critical revision of this commentary.

Conflicts of interest

None to declare.

Department of Dermatology, University Medical Center Groningen, University of Groningen, the Netherlands
 J. A. F. OOSTERHAVEN 
 E-mail: j.a.f.oosterhaven@umcg.nl

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Supporting Information

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Serum biomarkers in extramammary Paget disease

DOI: 10.1111/bjd.18250

Linked Articles: Mijiddorj *et al.* *Br J Dermatol* 2019; **181**:505–511. Nakamura *et al.* *Br J Dermatol* 2019; **181**:535–543.

Extramammary Paget disease (EMPD) is a rare intraepithelial cancer that usually presents with an eczematous-like rash in the axilla or anogenital region. The main challenges with the condition are accurate diagnosis, identifying the presence of underlying malignancy (usually anorectal or bladder adenocarcinoma) as well as the evaluation of potential metastatic spread, limited by a lack of credible diagnostic, prognostic and predictive biomarkers.

In the current issue of the *BJD*, two studies highlight potential biomarkers for EMPD: levels of serum cell-free (cf)DNA¹ and a combination of serum cytokeratin 19 fragment 21-1 (CYFRA) and serum carcinoembryonic antigen (CEA).² cfDNA is currently being studied in a range of fields from prenatal diagnosis of trisomy disorders,³ to its role as a diagnostic, prognostic and predictive biomarker in a host of cancer settings^{4,5} and refers to all nonencapsulated DNA in the bloodstream. CYFRA on the other hand is a fragment of cytokeratin 19, which forms an integral part of the epithelial cytoskeleton, whereas CEA is a cell surface glycoprotein. CYFRA and CEA are both found to be elevated in the serum of patients with a range of solid organ malignancies.²

Mijiddorj *et al.* report cfDNA levels in 19 healthy controls, 15 patients with localized EMPD and seven patients with metastatic EMPD, in which they highlight a significant increase in cfDNA in patients with EMPD compared with healthy patients.¹ Further comparison of cfDNA levels to serum CYFRA levels, revealed no significant difference in CYFRA levels between localized EMPD and healthy patients, whereas cfDNA, however, was able to discriminate between these two populations, collectively suggesting cfDNA as a putative diagnostic biomarker.

Studies of CYFRA expression levels in EMPD by Nakamura *et al.* provide further diagnostic information reporting no elevation in serum CYFRA levels or CEA in patients with primary invasive EMPD, but a significant increase of both