The prevalence of hidradenitis suppurativa outside the hospital setting: the impact of the undiagnosed

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Patients with hidradenitis suppurativa (HS) experience a significant delay from disease onset to diagnosis, estimated globally at 7·2 years.[1] This is related to multiple factors including under-recognition by doctors, embarrassment and stigma associated with the disease, and socioeconomic barriers.[1–3] Global prevalence estimates vary widely, from as low as 0·1% up to 4% in one European study.[4–6] This wide-ranging prevalence estimate is likely to be due to the different methodologies employed in studies, including the use of population and healthcare databases and both validated and nonvalidated screening questionnaires with and without clinical diagnostic confirmation. The use of healthcare insurance databases probably underestimates the prevalence due to socioeconomic healthcare barriers and diagnostic delay affecting patients with HS, while nonvalidated screening questionnaires without clinical confirmation may overestimate the prevalence.

In this issue of the *BJD*, Prens *et al.* report the largest study thus far utilizing validated HS screening questions, in the prospective Lifelines Cohort Study in the Northern Netherlands.[7] They received 58 198 out of a possible 135 950 responses. Patients in the study were asked if they had been diagnosed with HS. Those respondents who answered no were asked to complete two validated screening questions with a high sensitivity and specificity. Clinical photographs of HS lesions and the three Hurley stages were provided as a diagnostic aid for respondents.

Overall, 448 respondents reported a previous diagnosis of HS and 708 respondents answered positively to the two screening questions (1156 total prevalent cases of HS). The overall prevalence was thus 2·1%. Only 49 participants were receiving treatment for their HS (4·2%), with 30 of those receiving treatment under the care of a dermatologist. If the authors had utilized the data on medically diagnosed HS alone to estimate prevalence it would be much lower at 0·8%, highlighting the gap in prevalence, which may be related to the lengthy diagnostic delay.

Comorbidity analysis in this large cohort confirmed the association of HS with significant comorbidities including obesity, type 2 diabetes, chronic obstructive pulmonary disease, depression and Crohn disease. There were several newly identified comorbidities including fibromyalgia, irritable bowel syndrome, chronic fatigue syndrome and migraine.

A previous systematic review and network meta-regression analysis identified an overall prevalence of 0·4% in studies from Europe, the USA and Australia.[4] This identified the disparity between clinical samples in healthcare settings, with a pooled prevalence of 1·7%, and population-based studies including the use of healthcare databases and screening questionnaires, which had a much lower pooled prevalence of 0·3%. Prens *et al.* demonstrate this in a large population-based study, with a gap in prevalence rates between patients at inclusion in the cohort study (0·8%) and patients in the final analysis (2·1%). The strengths of this study are in the use of validated screening questions and the large sample size representative of an entire population and not just patients within a hospital setting. The prevalence rate of 2·1% seen in this study is likely to be most representative of the actual prevalence of HS, and once again highlights the diagnostic delay and the need for increased awareness of HS among physicians and patients.

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Niamh Kearney [1,2] and Brian Kirby [1,2,3]

[1]*Department of Dermatology, St Vincent's University Hospital, Dublin, Ireland;* [2]*School of Medicine, University College Dublin, Dublin, Ireland and* [3]*Charles Institute of Dermatology, University College Dublin, Dublin, Ireland*
Email: nkearne@tcd.ie

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References

1 Saunte DM, Boer J, Stratigos A *et al.* Diagnostic delay in hidradenitis suppurativa is a global problem. *Br J Dermatol* 2015; **173**:1546–9.
2 Howells L, Lancaster N, McPhee M *et al.* Thematic synthesis of the experiences of people with hidradenitis suppurativa: a systematic review. *Br J Dermatol* 2021; **185**:921–34.
3 Rick JW, Thompson AM, Fernandez JM *et al.* Misdiagnoses and barriers to care in hidradenitis suppurativa: a patient survey. *Australas J Dermatol* 2021; **62**:e592–4.
4 Jfri A, Nassim D, O'Brien E *et al.* Prevalence of hidradenitis suppurativa: a systematic review and meta-regression analysis. *JAMA Dermatol* 2021; **157**:924–31.
5 Jemec GB, Heidenheim M & Nielsen NH. [Prevalence of hidradenitis suppurativa in Denmark]. Ugeskr Laeger 1998; 160:847–9 (in Danish).

6 Ingram JR, Collins H, Atkinson MD, Brooks CJ. The prevalence of hidradenitis suppurativa is shown by the Secure Anonymised Information Linkage (SAIL) Databank to be one per cent of the population of Wales. *Br J Dermatol* 2020; **183**:950–2.
7 Prens LM, Bouwman K, Troelstra LD *et al.* New insights in hidradenitis suppurativa from a population-based Dutch cohort: prevalence, smoking behaviour, socioeconomic status and comorbidities. *Br J Dermatol* 2022; **186**:814–22.

Polygenic risk scores for melanoma: a stepwise process towards clinical implementation

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Early detection of melanoma or, even better, preventing melanoma by educating and stimulating sun-protective behaviour, are still essential steps to reducing its global burden. However, evidence is insufficient to demonstrate the benefit of population-based screening by total body skin examination.[1] Potentially, focusing the screening on high-risk individuals may be cost effective. Clinical implementation of polygenic risk scores (PRSs) is increasingly mentioned to facilitate this identification of high-risk individuals (i.e. genetic risk stratification).

Although nowadays multiple PRSs for melanoma exist, external validation of the predictive performance of a PRS in an independent population is often absent. However, reproducibility is mentioned as an important issue in last year's published PRS Reporting Standards (PRS-RS).[2] Therefore, the paper by Steinberg *et al.*,[3] in this issue, is an important study that evaluates three melanoma PRSs in addition to basic clinical characteristics derived from meta-analysis in two independent large cohorts.

The predictive performance of a model can be tested by the discriminant accuracy or area under the receiver operating characteristic curve (AUCROC). This determines if people who get a melanoma have a higher risk prediction than those who do not. Steinberg *et al.* showed that in both the UK Biobank (UKB) and Melbourne Collaborative Cohort Study (MCCS) discriminant ability increased from 0·03 to 0·10 by adding a PRS to age and sex, i.e. an integrated risk model.[3] However, the overall AUCROC was still moderate at 0·69, suggesting that for population-based screening, the tested integrated risk models are not useful. The inclusion of single-nucleotide polymorphisms beyond those that meet stringent genome-wide association study significance levels or adding traditional melanoma risk factors may be considered to boost future predictive performance.

Most PRS studies present relative risks of melanoma. However, the authors of this study calculated the PRS-based sex- and age-specific 10-year absolute risk of melanoma. Absolute risk scores provide more interpretable results and can even motivate behavioural changes. Using these absolute risk scores, the authors were also able to test the model's calibration, which compares the agreement between the expected and observed number of melanoma cases. Overall, they found that the model underpredicted incidence of melanoma, that is, fewer melanomas, compared with expected incidence. This would lead to falsely excluding high-risk patients. By adding the PRS to the risk model, estimations were closer to the observed number of cases in the UKB, but not in the MCCS sample. Different local healthcare systems and risk exposures per population are important reasons for misleading model outcomes.[4] These findings emphasize the need to calibrate model performance in different settings.

In this study, Steinberg *et al.* show that implementation of PRSs in practice is still a considerable challenge, but they point us in the right direction.

Marlies Wakkee

Department of Dermatology, Erasmus MC Cancer Institute, University Medical Center Rotterdam, Dr Molewaterplein 40, 3015 GD, PO Box 2040, Rotterdam, 3000 CA, the Netherlands
Email: m.wakkee@erasmusmc.nl

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References

1 US Preventive Services Task Force: Bibbins-Domingo K, Grossman DC, Curry SJ *et al.* Screening for skin cancer: US Preventive Services Task Force recommendation statement. *JAMA* 2016; **316**:429–35.
2 Wand H, Lambert SA, Tamburro C *et al.* Improving reporting standards for polygenic scores in risk prediction studies. *Nature* 2021; **591**:211–19.
3 Steinberg J, Iles MM, Lee JY *et al.* Independent evaluation of melanoma polygenic risk scores in UK and Australian prospective cohorts. *Br J Dermatol* 2022; **186**:823–34.
4 Van Calster B, McLernon DJ, van Smeden M *et al.* Calibration: the Achilles heel of predictive analytics. *BMC Med* 2019; **17**:230.

Janus kinase inhibitors for hidradenitis suppurativa: expanding the therapeutic toolbox

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In this issue of the BJD, Alavi *et al.* report two multicentre phase II trials designed to evaluate the safety and tolerability of the Janus kinase (JAK)1 inhibitor INCB054707 in patients with moderate-to-severe hidradenitis suppurativa (HS).[1] Treatment of patients with HS can be challenging, with variable and unpredictable responses to available treatments and no single