prognostic factors. In practice, the predictors of biomarkers will need to be assessed alongside clinical phenotypic and demographic factors.1

Biomarkers can potentially help us with the prediction of the cause of a disease, its progression, regression, outcome, diagnosis and, in the case of the scoping review in this issue of the BJD,2 the results of treatment. However, the sheer volume of the biomarker literature is in stark contrast to the few biomarkers that have established utility in clinical practice,3 especially in inflammatory disease.

Protagonists of what is possible with the translation of this approach into clinical practice envisage being able to assess a patient alongside their molecular screen with biochemical and genetic predictors that will enable personalized medicine choices to be made for optimal response, most cost-effective treatment pathways and avoiding harms.4

In this issue of the BJD, Corbett et al.2 present a comprehensive scoping review of the biomarker literature aimed at improving outcomes by predicting the effectiveness and safety of treatments for psoriasis. It is broad, including 71 studies and covering 17 different treatments, mostly biological therapies.

A significant failure rate with a treatment modality should lend itself to the biomarker approach. While conventional treatments were included in the scope, the authors found most potential biomarkers predict the response to antitumour necrosis factor therapy, with one marker for response to ustekinumab. However, none were ready for clinical application without further validation. For those working in this field, this scoping review helps signpost the areas for further research.

A good biomarker should be easy to sample and quantify and cost-efficient to process. It should be directly involved in disease pathogenesis. The authors have mapped the biomarkers onto the known pathways of importance for psoriasis including antigen processing and presentation (HLA-C*06:02), T-helper 17 cell differentiation [interleukin (IL)1B] and immune response (IL12B), and regulation of nuclear factor-kB activity (CARD14, IL17RA).5

Their critical appraisal of these studies showed that much of the evidence base was of poor quality, with methodological and reporting limitations that excluded many studies. This has led to important recommendations for future research which in turn should ensure more effective biomarker research, going forward.

Those biomarkers to take forward are clearer from the ‘catalogue’ presented by Corbett et al.2 To be useful, they will need to demonstrate strong association with the desired outcome and specificity, applying similar predictive testing to those applied to diagnostic tests. The complexity of psoriasis pathogenesis, its multiple pathways and the treatment modalities involved ensure that this will require much more work. Perhaps a less directed hypothesis-free approach, a more recent development, holds promise and could lead to new mechanistic insights. There may also be scope for timely integration of biomarkers into drug development in this rapidly changing therapeutic area.

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Melanoma overdiagnosis: why it matters and what can be done about it

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Cancer screening aims to reduce morbidity and mortality through early detection of preclinical disease. These potential benefits must be weighed against potential harms from diagnostic procedures, induced anxiety, false-positive or false-negative results and the detection of ‘indolent’ cancers, otherwise known as overdiagnosis. The actual benefits and harms from melanoma screening remain contested in the absence of robust evidence from randomized clinical trials.

The analysis by Whiteman and colleagues of a large Australian prospective cohort study is a valuable addition to the evidence base. Using a propensity score-based analysis, they obtained results that may approximately mimic those from a trial of melanoma screening.6 Participants who had a prior clinical skin examination were 30% more likely have a new diagnosis of melanoma than controls. Those who had a skin biopsy in the first year of follow-up were 50% more likely. The difference in cumulative risk increased over time to a
0–5% absolute risk difference at 5 years (screened 1.94%, unscreened 1.45%). More than 60% of new diagnoses were in situ melanomas. Restricting the primary analysis to invasive melanomas, the difference between screened and unscreened largely disappeared (adjusted hazard ratio 1.05, 95% confidence interval 0.72–1.63). These data strongly suggest substantial melanoma overdiagnosis because of screening, particularly overdiagnosis of melanoma in situ.

Limitations of the study, noted by the authors, would tend to underestimate overdiagnosis. These include use of proxies for screening (prior self-reported skin examination and incident skin biopsy), high background rates of screening (73% of people had prior skin checks), and considerable crossover (23% of those screened ‘dropped out’ of and 33% of those unscreened ‘dropped in’ to screening). Longer follow-up will increase certainty on the extent of overdiagnosis, and may also yield insights into potential beneficial impacts from screening on decreasing advanced-stage melanoma and melanoma mortality.

Overdiagnosis occurs when a person is diagnosed with melanoma but would never have experienced symptoms or harm from that lesion had it been left undetected and untreated. It causes harm through the melanoma diagnosis itself, and by leading to unnecessary treatment, investigations and treatment may be intensified) from potentially indolent ones (where de-intensification may be possible). Until then, melanoma overdiagnosis is largely identifiable only at a population level, and requires population-level interventions for its prevention. Such efforts are urgently needed to minimize harms from early melanoma detection, and ensure the delivery of sustainable, high-value healthcare.

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