References

1 Caimmi SM, Manca E, Caimmi D *et al.* NSAID hypersensitivity in twins. *Pediatr Allergy Immunol* 2014; **25**:828–9.

2 Jurado-Escobar R, Doña I, Perkins JR *et al.* Polymorphisms in eicosanoid-related biosynthesis enzymes associated with acute urticaria/angioedema induced by nonsteroidal anti-inflammatory drug hypersensitivity. *Br J Dermatol* 2021; **185**:815–24.

3 Trait and disease association results available for the *ALOX5* rs28395868 variant across FinnGen, UK Biobank, and GWAS Catalog resources. Available at: https://genetics.opentargets.org/variant/10_45443229_G_A

4 Chen Y, Shan Y, Guo Z *et al.*Genetic and pharmacologic targeting of Alox5 attenuates *JAK2V617F* induced PV in mice. *Blood*. 2013;**122**: 112.

5 Crouch DJM, Bodmer WF. Polygenic inheritance, GWAS, polygenic risk scores, and the search for functional variants. *Proc Natl Acad Sci USA* 2020; **117**:18924–33.

6 Adams DR, Eng CM. Next-generation sequencing to diagnose suspected genetic disorders. *N Engl J Med* 2018; **379**:1353–62.

7 Soyer O, Sahiner UM, Sekerel BE. Pro and contra: provocation tests in drug hypersensitivity. *Int J Mol Sci* 2017; **18**:1437.

Data-driven prediction of biologic treatment responses in psoriasis: steps towards precision medicine

DOI: 10.1111/bjd.20625

Linked Article: Geifman *et al.* Br J Dermatol 2021; **185**:825–835.

In this issue of the *BJD*, Geifman *et al.* defined subgroups or 'trajectories' of patients with psoriasis with similar patterns of disease severity (Psoriasis Area and Severity Index, PASI). The patients were studied over time using a data-driven latent class mixed-modelling approach.[1] This modelling approach can be used to divide a heterogeneous population into a few homogeneous groups or 'trajectories'. As such, patient characteristics in specific trajectories can be used to predict health outcomes such as treatment success.[2,3] With the increase in (expensive) treatment options for psoriasis, but still a substantial number of nonresponders per biologic, these analyses are very welcome. In this study, data of patients who were treated with various biologics were included. Four PASI trajectories were identified, with differences in clinical characteristics such as body mass index, baseline PASI, psoriasis subtype and the specific biologics.

In pharmacoepidemiological studies, outcomes, exposures and presence of patient characteristics are often included in analyses according to a binary approach (present vs. not present). However, this might not accurately reflect the real-world situation, where outcomes, exposures and characteristics such as comorbidities can vary over time. Alternative modelling methods, such as trajectory modelling techniques, are able to summarize complex individual-level medication-utilization trajectories or time-varying exposures. Such models result in several groups of patients within a given population who share similar patterns of characteristics over time.[3] Within the study of Geifman *et al.*, an unsupervised data-driven approach was used to identify subgroups of patients with similar patterns of PASI scores over time. A strength of this approach is the possibility of handling large datasets and to be able to separate them into groups without bias of pre-existing knowledge. A possible disadvantage is that such unsupervised methods are at risk of overextraction or identifying groups that are not 'true'. In addition, different methods for clustering groups might produce different subgroups.[4] Reassuringly, the authors conducted the analysis in two independent cohorts, which showed overall similarities.

In the study of Geifman *et al.*, different biologics were grouped due to data availability.[1] As such, the trajectories were not biologic specific. However, a sensitivity analysis on adalimumab alone suggested that the identified trajectories were generic instead of treatment specific. From a clinical perspective, it would be interesting in future studies to define biologic-specific trajectories, as different biologics might provide different treatment responses over time. In addition, Geifman *et al.* indicated that in future studies additional molecular and pharmacological data could add to definitions of subgroups and eventually lead to a more accurate prediction of treatment responses. Treatment-specific trajectories and inclusion of biomarkers in these models would lift precision medicine to a higher level.

In conclusion, the ambitious data-driven approach used in the study of Geifman *et al.* is a promising first step in the use and evaluation of big (observational) data for the prediction of psoriasis treatment responses and treatment optimization in the future. Back-translation and implementation of such results into clinical practice will be an important future challenge. The ongoing rise of big data brings multiple opportunities, which require us to embrace an intensive collaboration between data scientists and clinicians.

L. S. van der Schoot and J. M. P. A. van den Reek

Department of Dermatology, Radboud University Medical Center, Nijmegen, the Netherlands

Correspondence: Juul M.P.A. van den Reek.

Email: juul.vandenreek@radboudumc.nl

Conflicts of interest: L.S.vdS. carries out clinical trials for Janssen and Novartis. All funding is not personal but goes to the independent research fund of the Department of Dermatology of the Radboud University Medical Center Nijmegen, the Netherlands. J.M.P.A.vdR. carries out clinical trials for AbbVie, Celgene and Janssen; has received speaking fees from and/or attended advisory boards for AbbVie, BMS, Almirall and Janssen; and has received 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 Center Nijmegen, the Netherlands.

References

1 Geifman N, Azadbakht N, Zeng J *et al*. Defining trajectories of response in patients with psoriasis treated with biological therapies. *Br J Dermatol* 2021; **185**:825–35.

2 Lennon H, Kelly S, Sperrin M *et al*. Framework to construct and interpret latent class trajectory modelling. *BMJ Open* 2018; **8**:e020683.

3 Nguena Nguefack HL, Pagé MG, Katz J *et al*. Trajectory modelling techniques useful to epidemiological research: a comparative narrative review of approaches. *Clin Epidemiol* 2020; **12**:1205–22.

4 Bauer DJ, Curran PJ. Distributional assumptions of growth mixture models: implications for overextraction of latent trajectory classes. *Psychol Methods* 2003; **8**:338–63.