clinical and dermoscopic examination and 14 (82.4%) were misclassified by OCT.

With additional use of OCT, the PPV increased from 95.6% (without OCT) to 99.2% (109 of 110) with OCT. The decrease in the percentage of misclassifications was not significant, but a study with enough power to detect differences in this order of magnitude would require a much larger sample size.

In another prospective study, the PPV of an OCT diagnosis that was made with high confidence was only 80%, but the BCC prevalence in that study was also lower (58.2%) than in the present study (95.6%). The PPV depends on prevalence and becomes lower if prevalence decreases.6

The use of OCT in addition to clinical and dermoscopic examination may reduce the risk of misclassification of non-BCC lesions as BCC; however, this study also shows that in cases of high clinical and dermoscopic suspicion of BCC, this risk is already very low. The gain from additional use of OCT in patients with high clinical suspicion of BCC must be balanced against the financial investment required for the purchase of an OCT device and training of OCT users.

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The BIOMarkers in Atopic Dermatitis and Psoriasis (BIOMAP) glossary: developing a lingua franca to facilitate data harmonization and cross-cohort analyses

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Dear Editor, The BIOMarkers in Atopic dermatitis and Psoriasis (BIOMAP) is a large European consortium aiming to advance personalized medicine for atopic dermatitis and psoriasis by identifying biomarkers that predict therapeutic response and disease progression. BIOMAP brings together clinicians, researchers, patient organizations and pharmaceutical industry partners, and encompasses data from over 60 individual studies, including randomized clinical trials, population-based cohorts and deeply phenotyped disease registries. The curation and harmonization of data and biosamples from these established studies will facilitate cross-cohort clinical and molecular analyses, increasing the potential to identify small-effect estimates and to better stratify disease subtypes. This research letter serves to disseminate BIOMAP’s pathway to data harmonization and will inform future collaborative research endeavours.

Pooling data from diverse studies presents inherent challenges. Each study has different methodologies, research objectives and outcomes. Data harmonization improves the comparability of existing studies by converting similar variables to a common format and creating ‘harmonized datasets’, which can be used for cross-cohort analyses. Figure 1 outlines how BIOMAP follows existing data harmonization guidelines,1 ensuring that clinically appropriate and meaningful conclusions can be drawn.

BIOMAP’s objectives were outlined in the project proposal (step 0). During protocol development, a list of variables pertinent to BIOMAP’s key research questions was devised. These predefined ‘BIOMAP categories’ included clinical phenotypes, disease associations, environmental/lifestyle factors, treatments and outcome measures. Next, a detailed mapping exercise was performed to explore what data were available in a subset of the studies underpinning BIOMAP. This involved the custodians of individual study datasets assigning a BIOMAP category to each variable in their study’s data dictionary. Annotated data dictionaries were assimilated

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into a clinical ‘metadata catalogue’ indexed according to the BIO-
MAP categories, generating a high-level overview of the clinical
variables recorded in this sample of BIOMAP studies (step 1). The
metadata catalogue identified similarities and discrepancies between
studies, and formed the foundation of the BIOMAP glossary.

The BIOMAP glossary defines a list of core variables, using
harmonized terminology and data format (step 2), and will be
used to create harmonized datasets. The Glossary Development
Team comprised clinical, bioinformatics, biostatistics and labo-
ratory expertise, and discussed the potential contents of the
glossary (11 members, representing five BIOMAP organiza-
tions). Discussions were informed by the metadata catalogue,
literature reviews and existing harmonization initiatives,
including the TREatment of ATopic eczema (TREAT) Registry
Taskforce,2 Harmonising Outcome Measures for Eczema3 and
the International Psoriasis Council.4

A BIOMAP webinar introduced data harmonization to the
wider BIOMAP consortium, illustrating the fundamental role
the glossary would play in downstream BIOMAP analyses. Fol-
lowing the webinar, glossary stakeholders were identified
(n = 67, including work-package leaders, dataset custodians,
clinicians and analysts from 28 BIOMAP organizations).

A draft glossary was circulated to the glossary stakeholders
who refined and approved the finalized glossary through a ser-
ies of three interactive Zoom meetings. Following group discus-
sion, any amendments to the proposed glossary were approved
or rejected through anonymous polling, using in-built Zoom
functionality (30 polls). The outcome of voting was accepted

Figure 1 The pathway to data harmonization of BIOMarkers in Atopic dermatitis and Psoriasis (BIOMAP) studies. (Left) Proposed steps for
retrospective data harmonization (adapted from the Maelstrom guidelines).1 (Right) Implementation of these steps for data harmonization in
BIOMAP. Overlapping boxes represent steps running concurrently. Following finalization of the BIOMAP glossary (step 2), harmonization of
individual study datasets started in a pragmatic and prioritized manner, based on the availability of data and proposed cross-cohort analyses.
Quality assurance (step 4) is integrated with step 3 in our harmonization pipeline, expediting the availability of harmonized datasets for cross-
cohort analyses.
with a simple majority (median agreement 100%; range 57–100) and the BIOMAP glossary version 1.0 was finalized.

Primary datasets are being transformed to conform to the content and structure of the BIOMAP glossary, creating harmonized datasets (step 3). Iterative discussions between each dataset custodian and the harmonization bioinformaticians culminate with a dataset-specific mapping document specifying how individual variables will be transformed to the glossary-defined dataset, thus ensuring accurately harmonized data (step 4). Harmonized datasets are made available on a secure, centralised and access-controlled data platform (step 5). Harmonized clinical datasets complement a carefully curated bioresource of archived and newly obtained biospecimens, which will be used for multivariate profiling of skin and blood.

The structure of the BIOMAP glossary was inspired by the internationally recognized Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM). The OMOP CDM adopts existing vocabularies, such as SNOMED Clinical Terms, and was developed to implement standardized analytical approaches on large observational datasets. During glossary development, deviations from the OMOP CDM were made where existing variables were not represented in the OMOP-defined terminology or where dermatological research required additional granularity (e.g. detailed information regarding phototherapy). The OMOP CDM tabular structure was adjusted to match BIOMAP analysts’ requirements. Full compatibility with the OMOP CDM is a priority for further development of the glossary.

The publicly available BIOMAP glossary may benefit investigators beyond the BIOMAP consortium who could prospectively align future studies with the glossary’s clinical variables, thus facilitating comparative analyses. Published dermatological research using OMOP approaches is currently limited. Cooperation between BIOMAP and OMOP, leading to the incorporation of BIOMAP customizations into the OMOP CDM is an appealing prospect. Collaboration could further enhance the potential for dermatological research using large observational datasets.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher’s website:

Appendix S1. Acknowledgements.
Appendix S2. Full list of author affiliations.
Appendix S3. Author conflicts of interest.

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Conflicts of interest: Appendix S3 (see Supporting Information).

Histopathological differential diagnosis of frontal fibrosing alopecia and fibrosing alopecia in a pattern distribution

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DEAR EDITOR, Frontal fibrosing alopecia (FFA) and fibrosing alopecia in a pattern distribution (FAPD) are forms of primary cicatricial alopecia, classified as subtypes of lichen planopilaris.1,2 FAPD and FFA may present with clinical overlap and similar histopathological and dermoscopic features.1 Parietal scalp involvement with frontal hairline recession can obscure the clinical delineation between FAPD and FFA. The aim of this study was to establish whether FAPD can be differentiated from FFA by histopathological analysis.

We conducted a cross-sectional analysis of biopsies from 43 women, all with a previous classical diagnosis of FAPD or FFA.1–4 All samples had horizontal sections in haematoxylin and eosin stain. Anisotrichia (hair fibre diversity) was present only in patients with FAPD. Twenty-one histopathological markers were critically compared and contrasted. Analysis of nonparametrically distributed data was performed using the Mann–Whitney U-test, and Person’s χ²-test was used to measure association. The research complied with Good Clinical Practice guidelines and was approved by an institutional review board.

Twenty-six cases of FAPD and 17 of FFA were selected for the study. Nine of 21 (43%) parameters were statistically different between the groups. In FAPD we found an increased average quantity of vellus hair in each sample, increased terminal follicles in the catagen or telogen phase, and lower telogen-to-vellus (T:V) ratio. In FFA, there were lower follicular scar counts, more vacuolar degeneration of the follicle epithelium and higher presence of perifollicular clefs at the infundibulum and isthmus, as well as lower amounts of arrector pili muscles (Table 1).

In our study, FAPD showed a statistically higher percentage of vellus hairs and terminal follicles in the catagen or telogen phase, as well as lower T:V hair ratio. These features are all known to be present in androgenic alopecia (AGA) and were not found to be relevant in the analysed FFA specimens. The clinical presence of diffuse hair thinning and dermoscopic features of anisotrichia are the most distinguishing signs of FAPD. FAPD shares its clinical presentation and pattern loss with AGA, but also has many clinical, dermoscopic and histopathological findings that overlap with FFA.1,3 The first description of FAPD, by Zinkernagel and Trüeb, noted an increase in telogen count as observed in patients with AGA. Zinkernagel and Trüeb found hair follicle miniaturization in 10 of 14 FAPD scalp biopsies.4 In a study of patients with FAPD, Teixeira et al. demonstrated histopathological findings of AGA in 16 of 16 biopsies and inflammation of vellus hair follicles in 10 of 16 scalp samples.5 Starace et al.,6 Chiu and Lin,7 and Griggs et al.1 used the higher presence of vellus hairs in FAPD as a histological criterion to separate FAPD from differential diagnoses of FFA and other lichenoid alopecias.

Although neither the intensity nor the location of inflammatory infiltrate was significantly associated with either diagnosis, the analysis of the inflammatory infiltrate demonstrated that FFA did show a significantly greater presence of inflammatory infiltrate associated with vacuolar degeneration of the follicular epithelium (FFA 63% vs. FAPD 30%, P = 0.034). We observed a higher frequency of perifollicular clefs in FFA (FFA 63% vs. FAPD 26%, P = 0.018), a greater amount of follicular scars in FFA than in FAPD (mean score 9.37 vs. 4.77, P = 0.004) and a reduction in arrector pili muscles in FFA (FFA 63% vs. FAPD 26% FAPD, P = 0.018), demonstrating that FFA causes greater structural disruption than FAPD.8

In conclusion, follicle classification and counts are a relatively simple way to differentiate FAPD from FFA. FAPD presents with findings reminiscent of AGA at sites of disease activity, with an increase in the vellus follicle number, a reduction in the T:V ratio, and an increase in the terminal follicles that are in the catagen or telogen phases. FFA shows features of more structural disruption than FAPD. This observation is consistent with the fact that FFA rapidly progresses to a cicatricial condition while FAPD follows a more indolent evolution over a comparable duration.

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