This is a promotional advertisement from LEO Pharma for UK healthcare professionals.

For the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy.[1]

Adtralza® ▼ (tralokinumab)

Not an actual patient. For illustrative purposes only. Individual results may vary.

The first licensed biologic that inhibits IL-13 alone,[1,2] a key driver of atopic dermatitis signs and symptoms.[3]

Adtralza® maintained disease control for adult patients with atopic dermatitis at 2 years of treatment in the ECZTEND study.[4*]
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Adtralza® was generally well tolerated in ECZTEND at 2 years (n=1,442).[5**] The most common adverse events were viral upper respiratory tract infections (20.5%), atopic dermatitis (17.8%), upper respiratory tract infections (7.0%), headache (5.5%) and conjunctivitis (5.3%).[5**]

IL, interleukin.
*Interim analysis from ongoing open label extension study (data cut off: April 30 2021).[4] The 2-year cohort subgroup (n=86) included patients previously treated with Adtralza® monotherapy for 52 weeks in ECZTRA 1 and 2, followed by a washout period >15 weeks from last treatment in parent trial, then assigned to 104 weeks' treatment in ECZTEND study.[4] Primary endpoint was number of adverse events from baseline to last treatment visit (up to Week 268).[4]
**Data from 2-year interim safety analysis of the ECZTEND study, which included patients from parent trials ECZTRA 1, 2, 3, 4, 5 and 7.[5]

Prescribing information for Adtralza®▼ (tralokinumab) 150 mg solution for injection in pre-filled syringe
Please refer to the full Summary of Product Characteristics (SmPC) (www.medicines.org.uk/emc) before prescribing.
▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. **Indications:** Treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy. **Active ingredients:** Each pre-filled syringe contains 150 mg of tralokinumab in 1 mL solution (150 mg/mL). **Dosage and administration:** *Posology:* The recommended dose of tralokinumab is an initial dose of 600 mg (four 150 mg injections) followed by 300 mg (two 150 mg injections) administered every other week as subcutaneous injection. Every fourth week dosing may be considered for patients who achieve clear or almost clear skin after 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response after 16 weeks of treatment. Some patients with initial partial response may subsequently improve further with continued treatment every other week beyond 16 weeks. Tralokinumab can be used with or without topical corticosteroids. The use of topical corticosteroids, when appropriate, may provide an additional effect to the overall efficacy of tralokinumab. Topical calcineurin inhibitors may be used, but should be reserved for problem areas only, such as the face, neck, intertriginous and genital areas. If a dose is missed, the dose should be administered as soon as possible and then dosing should be resumed at the regular scheduled time. No dose adjustment is recommended for elderly patients, patients with renal impairment or patients with hepatic impairment. For patients with high body weight (>100 kg), who achieve clear or almost clear skin after 16 weeks of treatment, reducing the dosage to every fourth week might not be appropriate. The safety and efficacy of tralokinumab in children below the age of 18 years have not yet been established. *Method of administration:* Subcutaneous use. The pre-filled syringe should be not shaken. After removing the pre-filled syringes from the refrigerator, they should be allowed to reach room temperature by waiting for 30 minutes before injecting. Tralokinumab is administered by subcutaneous injection into the thigh or abdomen, except the 5 cm around the navel. If somebody else administers the injection, the upper arm can also be used. For the initial 600 mg dose, four 150 mg tralokinumab injections should be administered consecutively in different injection sites. It is recommended to rotate the injection site with each dose. Tralokinumab should not be injected into skin that is tender, damaged or has bruises or scars. A patient may self inject tralokinumab or the patient's caregiver may administer tralokinumab if their healthcare professional determines that this is appropriate. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Precautions and warnings:** If a systemic hypersensitivity reaction (immediate or delayed) occurs, administration of tralokinumab should be discontinued and appropriate therapy initiated. Patients treated with tralokinumab who develop conjunctivitis that does not resolve following standard treatment should undergo ophthalmological examination. Patients with pre-existing helminth infections should be treated before initiating treatment with tralokinumab. If patients become infected while receiving tralokinumab and do not respond to antihelminth treatment, treatment with tralokinumab should be discontinued until infection resolves. Live and live attenuated vaccines should not be given concurrently with tralokinumab. **Fertility, pregnancy and lactation:** There is limited data from the use of tralokinumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of tralokinumab during pregnancy. It is unknown whether tralokinumab is excreted in human milk or absorbed systemically after ingestion. Animal studies did not show any effects on male and female reproductive organs and on sperm count, motility and morphology. **Side effects:** *Very common (≥1/10):* Upper respiratory tract infections. *Common (≥1/100 to <1/10):* conjunctivitis, conjunctivitis allergic, eosinophilia, injection site reaction. *Uncommon (≥1/1,000 to <1/100):* keratitis. **Precautions for storage:** Store in a refrigerator (2°C-8°C). Do not freeze. Store in the original package in order to protect from light. **Legal category:** POM **Marketing authorisation number and holder:** PLGB 05293/0182, EU/1/21/1554/002. LEO Pharma A/S, Ballerup, Denmark. **Basic NHS price:** 4 pre-filled syringes: £1,070 (each syringe contains 150 mg/mL). **Last revised:** July 2021. **Reference number:** REF-19086(2)

Reporting of Suspected Adverse Reactions
Adverse events should be reported.
Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
Adverse events should also be reported to Drug Safety at LEO Pharma by calling +44 (0)1844 347333 or e-mail: medical-info.uk@leo-pharma.com

References: 1. Adtralza® SPC. **2.** Duggan S. Drugs 2021;81(14):1657–1663. **3.** Bieber T. Allergy 2020;75:54–62. **4.** Data on file, LEO Pharma (002-TRA-APR 2022, REF-21352). **5.** Blauvelt A, *et al.* Poster presented at the American Academy of Dermatology Association Annual Meeting, March 25-29, 2022.

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Concise report

CED
Clinical and Experimental Dermatology

Where are we with developing diagnostic criteria for skin diseases? Mapping the evidence in 2021

Jessie Luke[1] and **Esther Burden-Teh**[1]

[1]*Centre of Evidence Based Dermatology, School of Medicine, University of Nottingham, Nottingham, UK*

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Abstract

The breadth and scope of dermatological diagnostic criteria is currently unknown. We created a map of diagnostic criteria to provide a panoramic view of past and ongoing research to develop dermatological diagnostic criteria. We analysed studies for which the primary research aim was to develop, validate or critically appraise diagnostic criteria for dermatological conditions identified with a PubMed search conducted in July 2021. The researched skin diseases were grouped based on similarities in pathogenesis. In total, 166 studies covering 104 skin diseases were included in the data extraction. The two largest disease categories were autoimmune diseases (17%) and rare disorders and genetic syndromes (17%). Of the total studies analysed, 28% included a type of validation and 64% provided diagnostic accuracy data. This map of diagnostic criteria covers a vast range of dermatological conditions, but many common skin diseases were under-represented. We plan to update the map and make it available for all health professionals and researchers.

Diagnostic criteria provide some guidance for clinical diagnosis and are essential for any research that compares populations.[1] In dermatology, the breadth and scope of diagnostic criteria for skin diseases is not currently known, and the activity of dermatological diagnostic criteria research has not been recorded. We wanted to pioneer an analysis of what diagnostic criteria have been proposed in dermatology and the evidence-based methods used to generate them. We aimed to create a map of diagnostic criteria to form a central repository of tools for clinicians and researchers to use. Our map also provides a panoramic view of past and ongoing research activity to develop diagnostic criteria, essential for understanding where the current gaps are and what stage of development the diagnostic criteria have reached.

Report

To identify where the gaps in diagnostic criteria research are a PubMed search was conducted in July 2021. The search strategy was developed with an information specialist, and built around key words for dermatological disease and diagnostic criteria. The project protocol and search strategy are available on the Centre of Evidence Based Dermatology (CEBD) website.[2] Studies for which the primary research aim was to develop, validate or critically appraise diagnostic criteria for a skin disease were included. Skin diseases were included if they were listed in the British Association of Dermatologists Index and would be reviewed in a dermatology clinic. Diagnostic criteria were defined as a group of features (which may include clinical, imaging, histopathological, biochemical or genetic items) that collectively are used to diagnose a condition. No restrictions were placed on the stage of diagnostic criteria development, study type or publication status. Studies before 1990 were excluded because of low availability of electronic papers and resource limitations. Papers underwent single reviewer assessment for citation screening, full text eligibility review and data extraction (JL). Queries were discussed with a second reviewer. Skin diseases were categorized into groups based on similarities in pathogenesis. Limited core details were extracted from non-English papers. Data were analysed descriptively, presenting

Correspondence: Dr Esther Burden-Teh, Centre of Evidence Based Dermatology, School of Medicine, University of Nottingham, Nottingham, NG7 2NR, UK
E-mail: esther.burden-teh@nottingham.ac.uk

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percentages for the frequency of different categories of characteristics. An infographic (Fig. 1) was created to show the results.

The search identified 788 citations, of which 412 full-text papers were reviewed; of these, 166 studies covering 104 skin diseases were included for data extraction. A full list of included studies is available on the open data sharing repository Figshare[2] and the CEBD website.[3] The two largest disease categories were autoimmune disorders (17%) and rare disorders and genetic syndromes (17%), and the next five largest disease categories were atopic dermatitis (14%), vascular disease and vasculitis (10%), other inflammatory diseases (8%), cancer (7%) and infectious diseases (5%) (Table 1). Nearly a third (31%) of studies were published in the past 5 years, and since 1990, the number of published studies has increased each year. Studies were conducted in 38 countries, most frequently in the USA, Japan and Canada. There were few published studies from countries in Africa and South America. The mean number of study participants was 676. Cross-sectional studies accounted for 43% of included studies, while 28% were case series, 13% were publications based on expert opinion, 12% were consensus studies and 4% were systematic reviews. Only studies that are cross-sectional in design are able to evaluate diagnostic accuracy. Of the included studies, 93% proposed predominantly clinical diagnostic criteria. Overall, 64% of included studies provided diagnostic accuracy data such as sensitivity, specificity, positive predictive value or negative predictive value results. In addition, 28% of studies included a type of validation, testing the diagnostic accuracy of criteria in either a separate dataset (other than the one from which the criteria were derived) or using a special statistical technique such as bootstrapping.

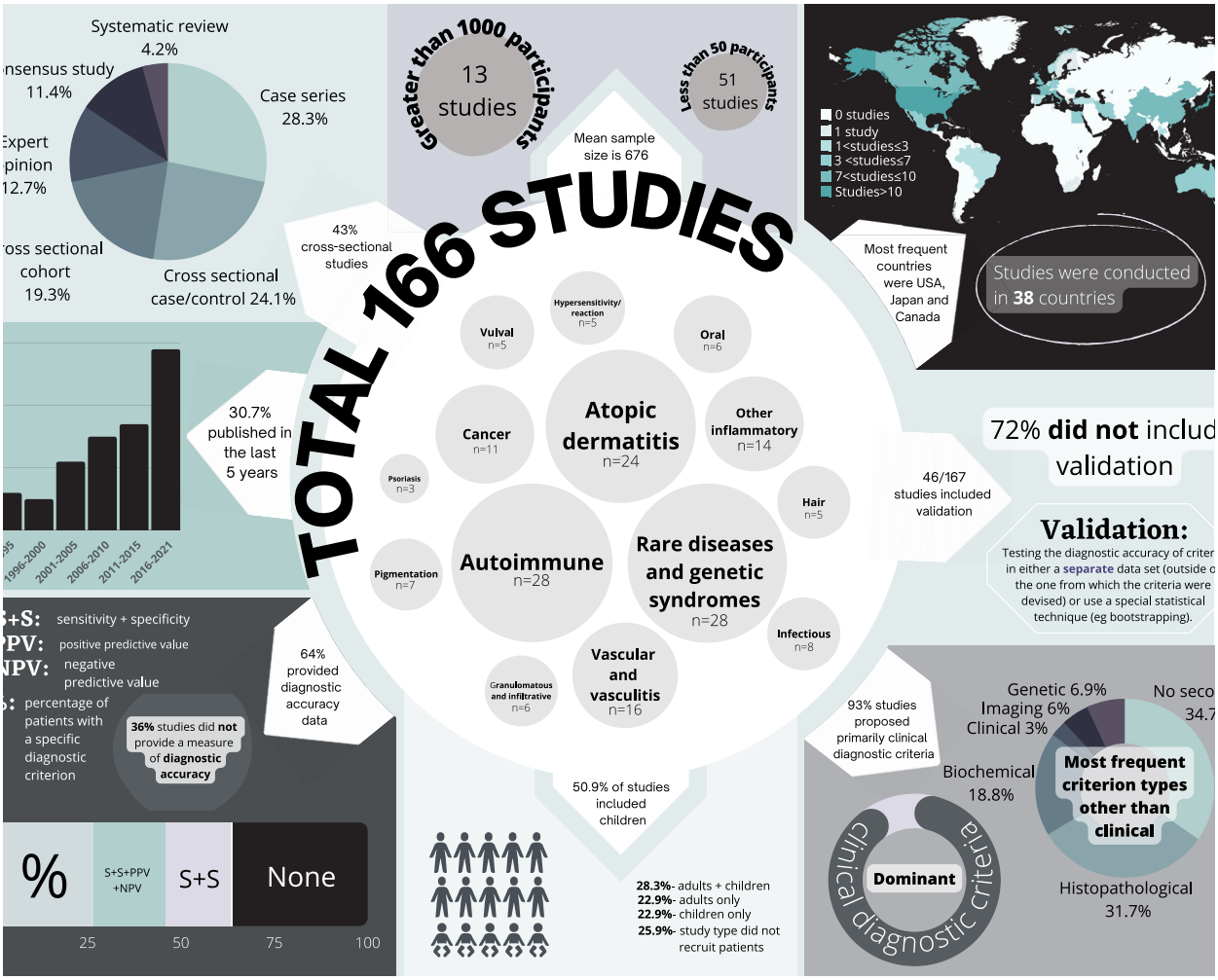

Figure 1 Infographic depicting the results from the project to map diagnostic criteria for dermatological diseases.

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Table 1 Study characteristics for the 14 disease categories.

Disease area	Studies, *n*	Year of publication: range (median)	Study countries, *n*	Total sample size, *n*	Proportion of cross-sectional diagnostic accuracy studies;[a] *n/N* (%)	Main type of diagnostic data (%)	Main type of diagnostic criteria proposed	Proportion of studies that included children; *n/N* (%)	Proportion of studies including validation; *n/N* (%)
Inflammatory									
Atopic dermatitis	24	1994–2021 (2007)	15	40 382	21/24 (87.5)	Se + Sp + PPV + NP (62.5)	Clinical	21/24 (87.5)	19/24 (79.2)
Psoriasis	3	2017–2021 (2019)	1	114	2/3 (66.7)	None (66.7)	Clinical	2/3 (66.7)	0/3 (0)
Hypersensitivity/reaction	5	2010–2019 (2013)	1	170	1/5 (20.0)	None (80.0)	Clinical	1/5 (20.0)	0/5 (0)
Hair	5	2002–2018 (2009)	3	134	2/5 (40.0)	None (80.0)	Clinical	2/5 (40.0)	0/5 (0)
Vulval	5	2013–2020 (2015)	2	551	0/5 (0.0)	Percentage (60.0)	Clinical	0/5 (0.0)	1/5 (20.0)
Oral	6	2003–2018 (2013.5)	4	439	4/6 (66.7)	Percentage (66.7)	Clinical	4/6 (66.7)	1/6 (16.7)
Other inflammatory	14	2004–2021 (2017)	6	1716	4/14 (28.6)	None (42.9)	Clinical	4/14 (28.6)	2/14 (14.3)
Rare disorders and genetic syndromes	28	1995–2021 (2013)	12	4665	6/28 (21.4)	None (42.9)	Clinical	22/28 (78.6)	3/28 (10.7)
Cancer	11	1997–2021 (2019)	4	479	0/11 (0.0)	None (54.5)	Clinical	0/11 (0.0)	2/11 (18.2)
Autoimmune	28	1995–2021 (2010.5)	12	6047	7/28 (25.0)	Se + Sp (39.3)	Clinical	7/28 (25.0)	10/28 (35.7)
Pigmentation	7	1992–2020 (2015)	7	619	6/7 (85.7)	Percentage (42.9)	Clinical	6/7 (85.7)	1/7 (14.3)
Infectious	8	1998–2016 (2004.5)	5	925	6/8 (75.0)	Se + Sp + PPV + NPV (37.5)	Clinical	6/8 (75.0)	4/8 (50.0)
Vascular and vasculitis	16	1990–2019 (2002.5)	9	39 575	12/16 (75.0)	Percentage (37.5)	Clinical	12/16 (75.0)	3/16 (18.8)
Granulomatous and infiltrative	6	2001–2020 (2015)	4	138	1/6 (16.7)	None (83.3)	Clinical	1/6 (16.7)	0/6 (0)
Total	166	1990–2021 (2013)	38	95 954	72/166 (43.3)	None (36.1)	Clinical	88/166 (53.0)	46/166 (27.7)

NPV, negative predictive value; PPV, positive predictive value; Se, sensitivity; Sp, specificity. [a]Case/control or cohort.

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From our evidence map, it is clear that a vast range of dermatological conditions are covered. There is notable crossover with diseases also reviewed under rheumatology and numerous rare genetic disorders. However, many common skin diseases such as acne, rosacea and psoriasis, were under-represented. It is encouraging that research to develop diagnostic criteria is increasing with time, but to date only a relatively small number of studies are testing their diagnostic accuracy and validating them, which means that data are not available on how well the criteria work at identifying people with the condition.

A strength of this project is the broad search strategy inclusive of all dermatological diseases and the systematic method used to extract and categorize the data. An important limitation is that only one electronic database was searched.

The project has created an easy-to-understand infographic to share key findings with the public, researchers and clinicians. A list of dermatological diseases and citation references are available on the CEBD website as a repository of tools for future use by researchers.[2] Future research studies should address important gaps identified by this mapping project and aim to further develop and test existing criteria.

Learning points

- Diagnostic criteria are important for clinical diagnosis in dermatology and for comparing populations in clinical research.
- To date, the activity of dermatological diagnostic criteria has not been investigated or recorded.
- Understanding where there are evidence gaps in dermatological diagnostic criteria can direct future research.
- In the current study, the categories of autoimmune disorders and rare diseases and genetic syndromes constituted 34% of the diagnostic criteria proposed.
- Only 43% of study designs were cross-sectional studies and 72% of studies did not include validation.

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Conflict of interest

The authors declare that they have no conflict of interest.

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None.

Ethics statement

Ethics approval and informed consent not applicable.

Data availability

The data that support the findings of this study are openly available online.[2]

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