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DR WILLIAM W Y HAW (Orcid ID : 0000-0003-1526-7202)

DR ALI AL-JANABI (Orcid ID : 0000-0002-2094-0556)

MR BERND WM ARENTS (Orcid ID : 0000-0001-6884-8014)

DR LEILA ASFOUR (Orcid ID : 0000-0002-0049-8377)

DR LESLEY S EXTON (Orcid ID : 0000-0003-0073-1885)

DR DOUGLAS GRINDLAY (Orcid ID : 0000-0002-0992-7182)

DR SIDRA SALEEM KHAN (Orcid ID : 0000-0003-4996-9106)

MISS LINA MANOUNAH (Orcid ID : 0000-0001-6129-6624)

PROFESSOR CHING-CHI CHI (Orcid ID : 0000-0001-5699-0283)

MRS ESTHER J VAN ZUUREN (Orcid ID : 0000-0002-4780-0182)

PROFESSOR CARSTEN FLOHR (Orcid ID : 0000-0003-4884-6286)

DR ZENAS ZEE NGAI YIU (Orcid ID : 0000-0002-1831-074X)

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Global Guidelines in Dermatology Mapping Project (GUIDEMAP): a scoping review of dermatology clinical practice guidelines

W.Y. Haw,[1,2] A. Al-Janabi,[1,2] B.W.M. Arents,[3] L. Asfour,[1] L.S. Exton,[4] D. Grindlay,[5] S.S. Khan,[1] L. Manounah,[4] H. Yen,[6] C.-C. Chi,[6,7] E.J. van Zuuren,[8] C. Flohr[9] and Z.Z.N. Yiu[1,2]

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1) The Dermatology Centre, Salford Royal NHS Foundation Trust, Manchester NIHR Biomedical Research Centre, Manchester Academic Health Science Centre, Manchester, UK
2) Division of Musculoskeletal and Dermatological Sciences, School of Biological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK
3) Skin Patients Netherlands, Nieuwerkerk a/d IJssel, the Netherlands
4) Clinical Standards Unit, British Association of Dermatologists, London, UK
5) Centre of Evidence Based Dermatology, University of Nottingham, UK
6) Department of Dermatology, Chang Gung Memorial Hospital, Linkou, Taoyuan, Taiwan;
7) College of Medicine, Chang Gung University, Taoyuan, Taiwan.
8) Department of Dermatology, Leiden University Medical Centre, Leiden, the Netherlands
9) Unit for Population-Based Dermatology Research, St John's Institute of Dermatology, King's College London and Guy's & St Thomas' Hospital NHS Foundation Trust, London, UK

Corresponding author: Zenas Z.N. Yiu

Email: zenas.yiu@manchester.ac.uk.

ORCID: WYH - 0000-0003-1526-7202

AA-J - 0000-0002-2094-0556

BWMA - 0000-0001-6884-8014

LA - 0000-0002-0049-8377

LSE - 0000-0003-0073-1885

DG - 0000-0002-0992-7182

SSK - 0000-0003-4996-9106

LM - 0000-0001-6129-6624

HY –

C-CC - 0000-0001-5699-0283

EJvZ - 0000-0002-4780-0182

CF - 0000-0003-4884-6286

ZZN - 0000-0002-1831-074X

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Conflicts of interest:

BWMA was a member in the guidelines development group (GDG) for Atopic Dermatitis and Hand Eczema of the Dutch Society of Dermatology and Venereology (NVDV).LM was a member in the GDG for the British Association of Dermatologists (BAD) guidelines for biologic therapy for psoriasis

LSE was a member in the GDG for the BAD guidelines on contact dermatitis (2017), SCC (2020, early view) actinic keratosis (2017), PDT (2018), PUVA (2015) & Ciclosporin (2018), member of the GDG on the BAD guidelines biologic therapy for psoriasis (2017 & 2020), BCC (just submitted) & urticaria (about to be submitted). Involved in the finalisation of BAD guidelines SCC in situ (2014), cutaneous warts (2014) & tinea capitis (2014).

CF led the British guidelines on the use of oral propranolol in complex haemangiomas. He also leads the European Dermatology Forum/European Academy of Allergy and Clinical Immunology guideline on the management of atopic dermatitis and is a member of the British Association of Dermatologists chronic urticaria GDG. He is Chief Investigator of the UK National Institute for Health Research-funded TREAT (ISRCTN15837754) and SOFTER (clinicaltrials.gov: NCT03270566) trials as well as the UK-Irish Atopic eczema Systemic Therapy Register (A-STAR; ISRCTN11210918) and a Principal Investigator in the European Union Horizon 2020-funded BIOMAP Consortium (http://www.biomap-imi.eu/). His department has also received funding from Sanofi-Genzyme.

ZZNY was a member in the GDG for the BAD guidelines for biologic therapy for psoriasis.

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What is already known about this topic?

- Skin-related diseases are leading causes of disability and disease burden globally.
- Clinical practice guidelines (CPGs) are important to ensure appropriate standards of care for skin conditions. However, the number, distribution, accessibility, and quality of dermatological CPGs available globally is unknown.

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What does this study add?

- This is the first scoping review describing the distribution of CPGs for common dermatological conditions of highest burden available internationally.
- Inflammatory skin conditions and skin cancers represent a higher proportion in the number of CPGs produced, largely driven by high-income countries.
- Further studies to evaluate the quality of CPGs in dermatology, and development of CPGs in skin diseases predominantly affecting resource-poor countries, are needed.

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Summary

Introduction

Clinical practice guidelines (CPGs), statements that include recommendations intended to optimise patient care, play a critical role in standardising and improving treatment outcomes based on best evidence. It is currently unclear how many CPGs are available globally to assist clinicians in the management of patients with skin disease.

Objective

Our aim was to search for and identify CPGs for dermatological conditions with the highest burden globally.

Methods

We adapted a list of 12 dermatological conditions with the highest burden from the Global Burden of Disease (GBD) study 2019. A broad systematic literature search was conducted to identify CPGs published between October 2014 to October 2019. The scoping review was conducted and reported in accordance with the PRISMA framework.

Results

A total of 226 CPGs were included. Melanoma had the greatest representation in the CPGs, followed by dermatitis and psoriasis. Skin cancers had the highest CPGs representation overall but with lower GBD disease burden ranking. There was an uneven distribution by geographical region, with resource-poor settings being under-represented. The CPGs' skin disease categories correlated weakly with the GBD disability-adjusted life-years metrics. 89 CPGs did not have funding disclosures and 34 CPGs were behind a paywall.

Conclusion

The global production of dermatology CPGs showed wide variation in geographical representation, article accessibility and funding reporting. The number of skin disease CPGs were not commensurate with its disease burden. Future work will critically appraise the methodology and quality of dermatology CPGs and lead to the production of an accessible online resource summarising these findings.

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Main text

Introduction

Clinical practice guidelines (CPGs) can be defined as statements that include recommendations intended to optimise patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options.[1] CPGs have the potential to improve healthcare quality by synthesising and translating evidence into recommendations; identifying appropriate evidence-to-practice gaps; decreasing costly and preventable adverse events; optimising patient outcomes; and facilitating shared decision-making processes.[2,3] The production of CPGs is a resource-intensive process. Research waste continues to be a problem in biomedical research,[4] with poor design, conduct and reporting of medical research being a common problem for the production of CPGs in dermatology.[4,5]

There are few resources available that comprehensively document the number and the quality of CPGs worldwide, and none dedicated to dermatological diseases. We previously conducted a survey of the *BJD* readership about CPGs and found that a key concern was how CPGs were accessed, with many readers suggesting that an internet hosted comprehensive dermatology guideline repository would be helpful for quick access and reference in the clinic.[6]

There is therefore a need to collate CPGs in common dermatological diseases internationally.[7] Firstly, this may help reduce research waste and identify high quality CPGs and systematic reviews for future guideline development groups (GDGs) to reference from, avoiding duplication of work. Secondly, it will provide patients and clinicians with a summary of critically appraised dermatology CPGs, also highlighting areas for improvement in CPG reporting and development standards. Thirdly, a resource that clinicians, including those from developing countries, can freely access from anywhere in the world would be an important contribution for education and reference purposes in dermatology.

With this mind, we performed a global scoping review as a first step to collate and describe the state of current CPGs within dermatology. The review questions are:

1. How many CPGs are produced for the dermatological conditions of the highest burden globally in a period of five years?

2. Is the number of international clinical guidelines of skin diseases commensurate with their disease burden?

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Methods

We performed a systematic search for guidelines of common skin conditions following a pre-specified protocol in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement,[8] focusing on the skin conditions with the highest burden as listed in the Global Burden of Disease (GBD) Study 2019[9,10]: acne, alopecia areata, atopic and contact dermatitis, cellulitis, keratinocyte carcinoma, cutaneous malignant melanoma, psoriasis, scabies, urticaria, tinea capitis, venous ulcers, viral warts and molluscum contagiosum. All records were screened by at least two independent appraisers. Disagreements at any stage were reconciled by discussion with a third appraiser.

Searches were performed in MEDLINE, Embase, National Institute for Health and Care Excellence (NICE) Evidence Search, Guidelines International Network, ECRI guidelines trust, Australian CPGs, TRIP database, and DynaMed. Appropriate disease search terms were combined with a guidelines search filter (e.g. Canadian Agency for Drugs and Technologies in Health (CADTH) filter). Our full search strategy is presented in the supplementary materials (Appendix S1). The search was conducted in October 2019, we included CPGs published between October 2014 to October 2019.

We supplemented the online search by manual searches for guidelines produced by dermatological societies listed under the International League for Dermatological Societies. We also contacted CPG-producing dermatological societies directly to solicit copies of their current guidelines. Where we did not receive a response, we searched for CPGs produced by the dermatology societies through Google and the society websites.

To capture the full range of guidelines, we used a broad definition of CPGs, inclusive of consensus agreement guidelines informed by reviews of the evidence that were systematic or structured, developed by local, regional, national or international groups or affiliated governmental organisations. All CPGs involving the diagnosis, screening, management, drug/treatment and prevention of the included skin conditions were eligible. Records that lack systematic search protocols or explicit criteria for appraising evidence, secondary publications derived from CPGs, consensus statements or consensus conferences based on the opinion of expert panel, editorials, clinical trials, single-author documents were excluded. On consensus after discussion with the study group, we excluded CPGs which were directed predominantly for policy makers, such as health technology assessments; or were focussed on treatment-related side effects. Where multiple or updated versions of the same guideline and organisation was found, we selected the latest full or long version, and subsequently the English version which was

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often used in peer-reviewed publications. We included guidelines from any country and in any language; Google Translate was used to translate the abstracts and full-texts of non-English CPGs, with the exception of Thai CPGs where a translator was used. The inclusion and exclusion criteria can be found under supplementary materials (Appendix S2).

The titles and abstracts were screened using the website and the application *Rayyan*.[11] If no abstract was available, full-text articles were obtained and screened in order to be considered for inclusion. In addition, CPG depositories from ILDS-members, GIN, Dynamed, NICE and TRIP were hand-searched to identify additional relevant CPGs. We extracted the following items from the full-text records for analysis: skin disease subtypes, organisation producing the CPG; year of publication; geographical region; language; keyword in title; topics covered, publication source; funding source and whether the CPG was behind a paywall. We also evaluated the distribution of CPGs by socio-demographic index (SDI), an indicator of a location's socio-demographic development, based on the country and geographical region where the CPGs were produced[10]. The SDI, which combines information on income per capita, education and fertility, was used to categorise all GBD geographies into five SDI quintiles (high, high-medium, medium, low-medium, and low quintile). We further calculated the correlation between the number of CPGs published for each skin disease to the GBD 2019 disability-adjusted life-years (DALYs) estimates.

We registered our study protocol with OSF registries (https://osf.io/fuj3h) on 30 October 2019. Data were collected, summarised, and tabulated in a standardised Excel spreadsheet for descriptive analysis.

Results

Identification and selection of CPGs

The PRISMA flowchart of the guideline selection is summarised in Figure 1. Our search yielded 17,211 potential citations. After removal of duplicates, 14,914 were screened by title and abstract. Of the 576 full-text articles screened, 137 CPGs met the inclusion criteria. In addition, a further 89 articles were identified through manual searching and local dermatological society websites. In total, 226 CPGs were included in the final analysis. A list of the included articles and detailed summary at full-text screening stage are provided in supplementary materials (Table S1).

Trends in dermatological CPGs

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The included CPGs were published between October 2014 and October 2019. Across the 12 skin diseases, the top five number of CPGs produced were melanoma (41 CPGs), atopic (30) and contact (12) dermatitis, psoriasis (29), venous ulcer (25), and urticaria (24); as shown in Figure 2. Melanoma comprised of 15.2% (7 out of 46) dermatological CPGs in 2015, with a steady rise in the past five years to 22.2% (12 out of 54) in 2019. Venous ulcer was the one of the most prevalent (15.2%, 7 out of 46) dermatological CPGs in 2015, but dropped to 5.6% (3 out of 54) in 2019. The frequency of atopic and contact dermatitis, psoriasis and urticaria CPGs trended upwards from 2014 to 2019. The apparent increase in CPGs could in part be explained by the fact that only the latest version of any CPG was included in the database. Overall, low representation was observed for cellulitis (7), scabies (5), viral warts and molluscum contagiosum (4), alopecia areata (3) as well as tinea capitis (1).

Characteristics of dermatological CPGs

The top three journals with the highest frequencies of dermatology CPGs were the *Journal of* the *European Academy of Dermatology and Venereology* (11), the *Journal of the American Academy of Dermatology* (9) and the *British Journal of Dermatology* (8). Skin diseases CPGs were published in dermatology journals (89, 39.4%), in non-dermatology journals (73, 32.3%), and some were available online only (64, 28.3%). The majority (120, 53.1%) of skin disease CPGs were multi-disciplinary collaborative efforts between different specialties, with a significant minority (84, 37.2%) solely written by GDGs from the dermatology community. For example, there was involvement of paediatricians and allergists in atopic dermatitis CPGs, whereas for melanoma and keratinocytes carcinomas CPGs often consisted of a multi-disciplinary team of dermatologists, surgeons, oncologists, and pathologists. We also found 88.1% (199) of CPGs were developed by national or regional GDG members, whilst 11.9% (27) were part of a collaborative effort consisting of internationally recognised experts.

The majority (163, 72.1%) of dermatological CPGs were developed by countries with a high socio-demographic index (SDI) in comparison to high-middle (18, 8.0%), middle (12, 5.3%) and low-SDI countries (4, 1.8%). The geographic distribution included Europe (117, 51.8%), North America (48, 21.2%), Asia (35, 15.5%), Latin America (11, 4.9%), Australasia (10, 4.4%), as well as international collaboration across these regions (5, 2.2%) (Figure 3). The countries with the highest number of dermatological CPGs are the United States (34, 15.0%) and the United Kingdom (24, 10.6%), together representing about 25% of all CPGs. The majority of dermatological CPGs were written or available in English (173, 76.5%), whereas some were published only in their native languages, i.e. Dutch (12, 5.3%), Spanish and Danish (5, 2.2%

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respectively). There were also some inconsistencies in the keyword nomenclature, only 11.5% (26) were titled as “clinical practice guidelines”. Furthermore, 88.5% (200) of included article had at least one keyword in the title, most frequently “guideline” (145, 64.2%), “consensus” (33, 14.6%) and “recommendation” (22, 9.7%).

Most CPGs focussed on treatment/management recommendations (97, 42.9%), while other CPGs were broader in scopes and covered diagnostic/treatment (69, 30.5%) and diagnostic/treatment/prevention (46, 20.4%) (Figure 4). Specifically, a significant proportion of CPGs on psoriasis (24, 10.6%), melanoma (23, 10.2%), atopic and contact dermatitis (17, 7.5%), and acne (5, 2.2%) focus on drug and treatment recommendations; while CPGs on venous ulcers (19, 8.4%) and keratinocyte carcinoma (10, 4.4%) included additional aspects on prevention and long-term management. There were also drug/treatment-specific CPGs (8, 3.5%), for example photodynamic therapy and systemic treatments, which provided recommendations spanning a range of skin diseases.

Funding source and open access

All 226 guidelines were assessed for inclusion of a funding statement and accessibility (Table S1). Approximately 40% (89) of CPGs failed to provide a funding statement. In CPGs with a funding statement, dermatology/ medical societies were the most common source (36, 15.9%), followed by government/public funding (25, 11.1%). 8.0% (18) CPGs declared funding from pharmaceutical companies, including topics such as acne, atopic and contact dermatitis, keratinocytes carcinomas and psoriasis. Furthermore, 85.0% (192) of CPGs were open access, whilst many of the CPGs that were behind a paywall originated from high-middle (3, 1.3%) and high SDI (30, 13.3%) countries.

Comparison of disability-adjusted life year outcomes for specific skin disease CPGs

Comparing the total number of CPGs representing skin diseases mapped to the GBD DALYs estimates, we found that the coefficient of determination (R^2) was 0.167, indicating overall poor correlation between these variables (Figure 5). Melanoma and keratinocyte cancers had disproportionately greater CPGs representation compared to its disease burden as measured by DALYs, particularly predominance by high-income countries (e.g. Australasia, Europe and North America). CPGs representation of urticaria, atopic and contact dermatitis appeared proportionately aligned with their DALYs metrics. Acne, alopecia areata, cellulitis and scabies were under-represented in the number of CPGs in comparison to their corresponding DALY metrics.

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Discussion

To the authors' knowledge, this is the first scoping review to provide a comprehensive global overview of the number and characteristics of CPGs for common dermatological conditions. We define dermatology as the study of diseases affecting the skin, hair and nails, including venereology and tropical skin diseases to represent global skin health needs. Our systematic search, each screened by two independent reviewers, found 226 CPGs on skin conditions during the period from October 2014 to October 2019 with lack of correlation to the disease burden according to the GBD 2019 study.[9,10] A number of research gaps that require future investigation have arisen as a consequence thereof.

Inflammatory skin conditions (e.g. atopic and contact dermatitis, psoriasis and urticaria) and skin cancers (keratinocyte carcinomas and melanoma) cause the greatest disease burden in high-income countries,[12,13] and together they have seen the greatest increase in the number of CPGs in the past five years. The sharp rise in treatment-related CPGs may be partly explained by the availability of new, effective treatments for these conditions, for example targeted immunotherapy for psoriasis and melanoma. On the other hand, the treatment landscape for scabies, tinea capitis and viral skin diseases, which are more common in low-income countries, remained almost unchanged.[12,13] Newer insights into chronic skin conditions, such as prevention of venous leg ulcer recurrence and skin cancer screening, have led to the incorporation of preventative recommendations into CPGs for the management of these long-term conditions.

During the search process for this review, we noticed that a significant number of local CPGs (64, 28.3%) were not indexed in electronic library databases and only found on websites, rendering them difficult to find for clinicians and guideline developers.[14] Particularly those on societies' websites were hard to find (e.g. archived in non-intuitive subsections of the website). As a result, the website searches relied heavily on supplementary hand searches, which might hamper reproducibility efforts in a biomedical database. Our review found that 85% of the CPGs were freely available online; making guidelines easier to locate and open access could help improve their uptake in clinical practice further.

This review also found a range of terms being used to describe skin disease CPGs. Although over half of the identified guidelines used the term "guideline" in their title, only a relatively small number were titled as 'clinical practice guideline'. A number of CPGs were expert recommendations that might not intend to be a CPG, even if they could be interpreted and used

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as a guideline. This highlights the need for a more precise definition of what constitutes a recommendation statement versus a CPG.

There was also an uneven distribution and substantial variation of skin disease CPGs by geographical region. The high number of CPGs developed in North American and European countries may reflect the healthcare environment in which CPGs were used to evaluate treatment cost-effectiveness, allocation of resources and healthcare priorities.[15] Furthermore, the review showed significant under-representation of CPGs from regions like Asia (35, 15.5%), South America (11, 4.9%) and none from the African continent. Low-income countries usually have fewer resources to develop and implement locally written CPGs, or research capacity to explore local context issues.[16] To address this gap, they often adopt or adapt CPGs from high-income countries, especially where high-quality guidance already exists.[17] However, these CPGs are sometimes written with different health systems in mind, leading to under-representation of considerations around skin of colour, resource and workforce availability. As a result, the guidance in CPGs might not be directly appropriate for local implementation.[16] The generalisability of CPGs in some skin diseases could also be improved by increasing international collaborations during guideline development.[2] CPGs produced in collaboration with other countries were more frequently of higher methodological standards and conform with the internationally accepted quality criteria.[5]

Regular monitoring of existing CPGs and timely dissemination of updated ones are essential ways of ensuring that CPGs remain useful in improving health care quality and patient outcome.[18] For example, the AWMF (Association of the Scientific Medical Societies) in Germany and the National Institute for Health and Care Excellence (NICE) in the UK requires CPGs to be checked or updated every 3 to 5 years. This is particularly important in disease areas where there are significant evidence gaps or where numerous new effective treatments have been introduced. In the hand search, we found a number of skin disease CPGs, in particular from dermatological societies in low-income countries, which were updated less regularly compared to high-income countries and excluded during the screening process, as they were outside the study timeframe.

The process of writing a guideline is time- and resource-consuming. We propose that further collaboration between guideline developers on quality assessment could limit the workload and that sharing of knowledge and expertise might also increase the overall quality of individual local guidelines. The concept of "living guidelines" could potentially make this more feasible, with the promise to provide timely, up-to-date and high quality guidance to target users.[19] Therefore, our team have developed a centralised repository of current dermatological CPGs available

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internationally. The free online resource, which can be found at https://sites.manchester.ac.uk/guidemap/, is a work in progress and will be updated over time as "living guidelines".

The source of funding for CPGs may create conflicts of interest, especially for CPGs involving treatment recommendations, and may introduce bias in the development of CPGs. Over one third (105, 37.8%) of GDGs failed to declare their source of funding, if any. Approximately 7% (18) of GDGs received financial funding from pharmaceutical industry; although most claimed to have maintained editorial independence. The influence of industry sponsorship or GDG members' conflicts of interest may be particularly important where evidence is lacking or of poor quality.[20] This level of participation can affect readers' opinions regarding the integrity of these CPGs, and some studies have even documented that disclosure of industry funding may lead clinicians to downgrade the quality of the guideline content.[21]

A number of CPGs (34, 15.0%) were published behind paywalls that restrict access to research findings, also limiting the dissemination and clinical benefit of CPGs to clinicians and patients. They also exacerbate the substantial inequalities in scholarly resources between developed and developing countries, creating a barrier to access important medical knowledge.[22]

The concept of 'disease burden' can be expressed in terms of DALYs, calculated as sum of years of life lost plus the years of productive life lost due to ill-health, disability or premature death. The global burden of skin and subcutaneous diseases have been steadily increasing; total DALYs from 1.21% in 1990 to 1.76% in 2017.[9,23] Our study showed poor association between DALYs and the representation of CPGs according to their skin disease categories. The findings are consistent with reports of weak association between global burden of disease and the number of published randomised trials[24] and moderate correlation between systematic reviews and DALYs across the entire Cochrane Database of Systematic Reviews.[25] Furthermore, a study in 2015 comparing research funding by the US National Institutes of Health demonstrated that skin cancer research was generally overfunded, whereas dermatitis, decubitus ulcer, fungal skin diseases, and cellulitis received substantially less financial support.[15] Besides, although skin cancers are represented by lower DALYs according to GBD metrics, their true burden are thought to be significantly underestimated, and might still be deemed important because of the associated morbidity and mortality. We recognise that many variables play a part in research prioritisation and development of CPGs including disease prevalence, therapeutic options, geographic and clinical settings, cost constraints and local resource availability, healthcare priority setting, pharmaceutical suppliers, as well as public interest.[26,27]

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Our systematic search strategy aimed to identify all available skin diseases CPGs from October 2014 to October 2019. However, some guidelines have a built-in 'expiry date' and are renewed according to a fixed schedule. We cannot exclude that some relevant CPGs may have fallen beyond the search scope and time limits of this review. We may also have missed CPGs that are inaccessible to the public and some dermatological societies did not respond to us contacting them about soliciting their CPGs. If a CPG did not clearly identify itself as a guideline or if the meaning was lost during translation of non-English CPG, it might have been missed in this review despite measures taken to limit such omissions. In addition, we did not formally assess the quality of individual CPGs with a validated tool, as this will be the focus of future work.

Conclusion

In the first global scoping collation of CPGs for common dermatological conditions, we found numerous internationally available CPGs for the diagnosis, treatment, and prevention of these diseases. By highlighting the current state and numbers of CPGs in dermatology, we provide insight into the potential mismatch between the resources used to develop certain dermatological diseases and the corresponding disease burden worldwide. For the next stage of this project, we will perform critical appraisal to assess the quality of each of the included CPG, with the overarching objective to establish an accessible online resource indexing current and future CPGs in dermatology ranked by guideline quality.

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Figures

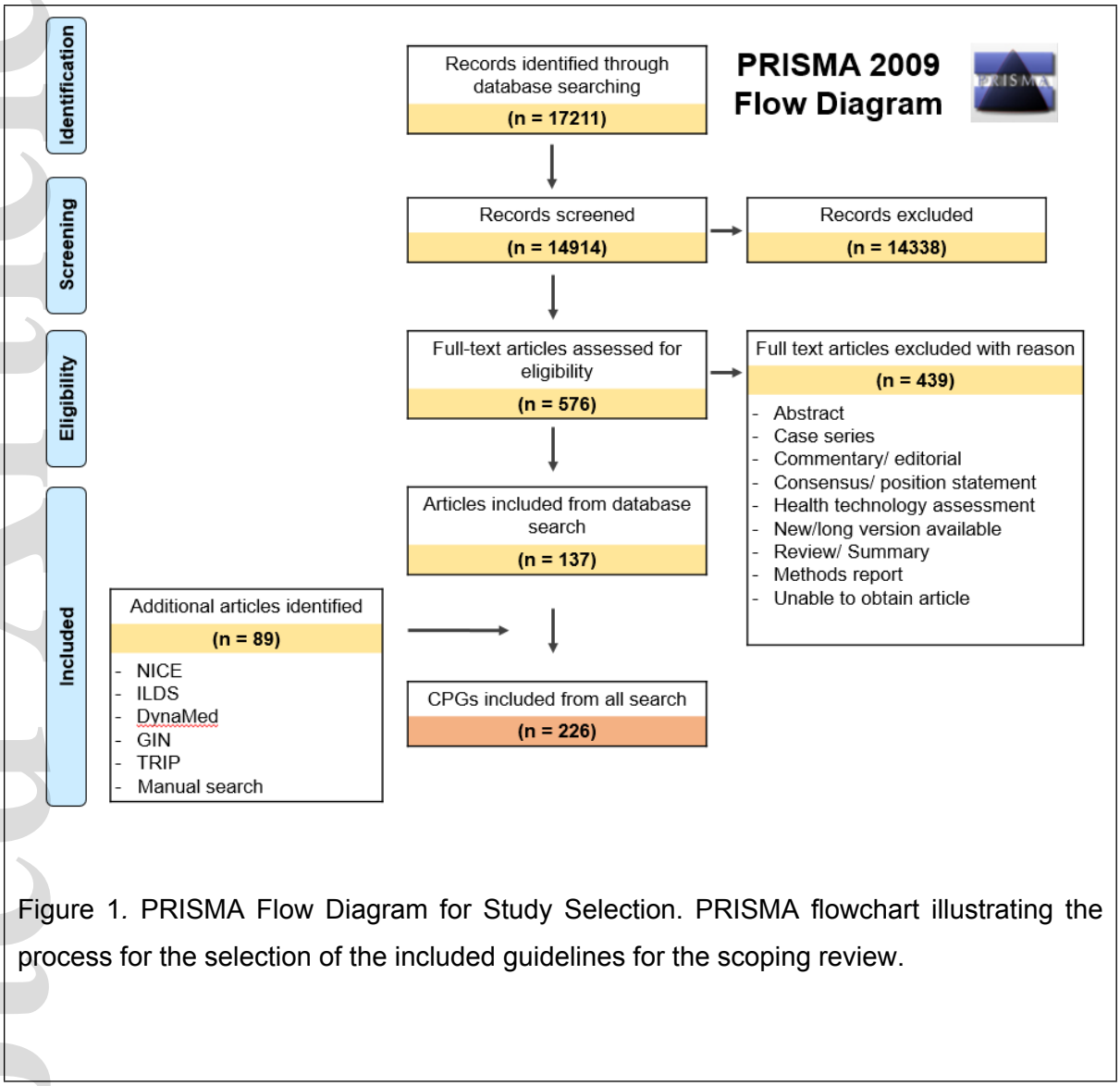

Figure 1. PRISMA Flow Diagram for Study Selection. PRISMA flowchart illustrating the process for the selection of the included guidelines for the scoping review.

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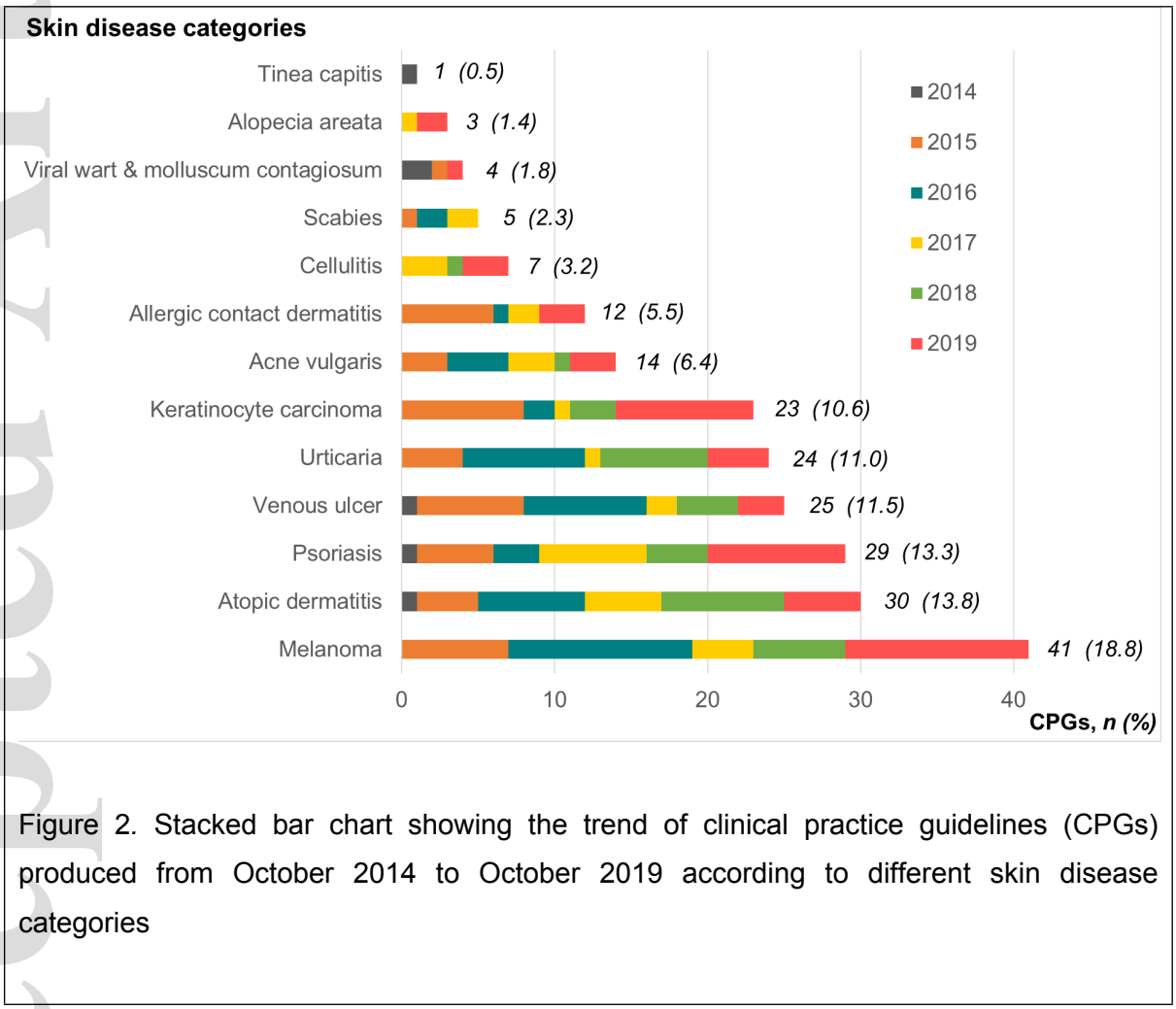

Figure 2. Stacked bar chart showing the trend of clinical practice guidelines (CPGs) produced from October 2014 to October 2019 according to different skin disease categories

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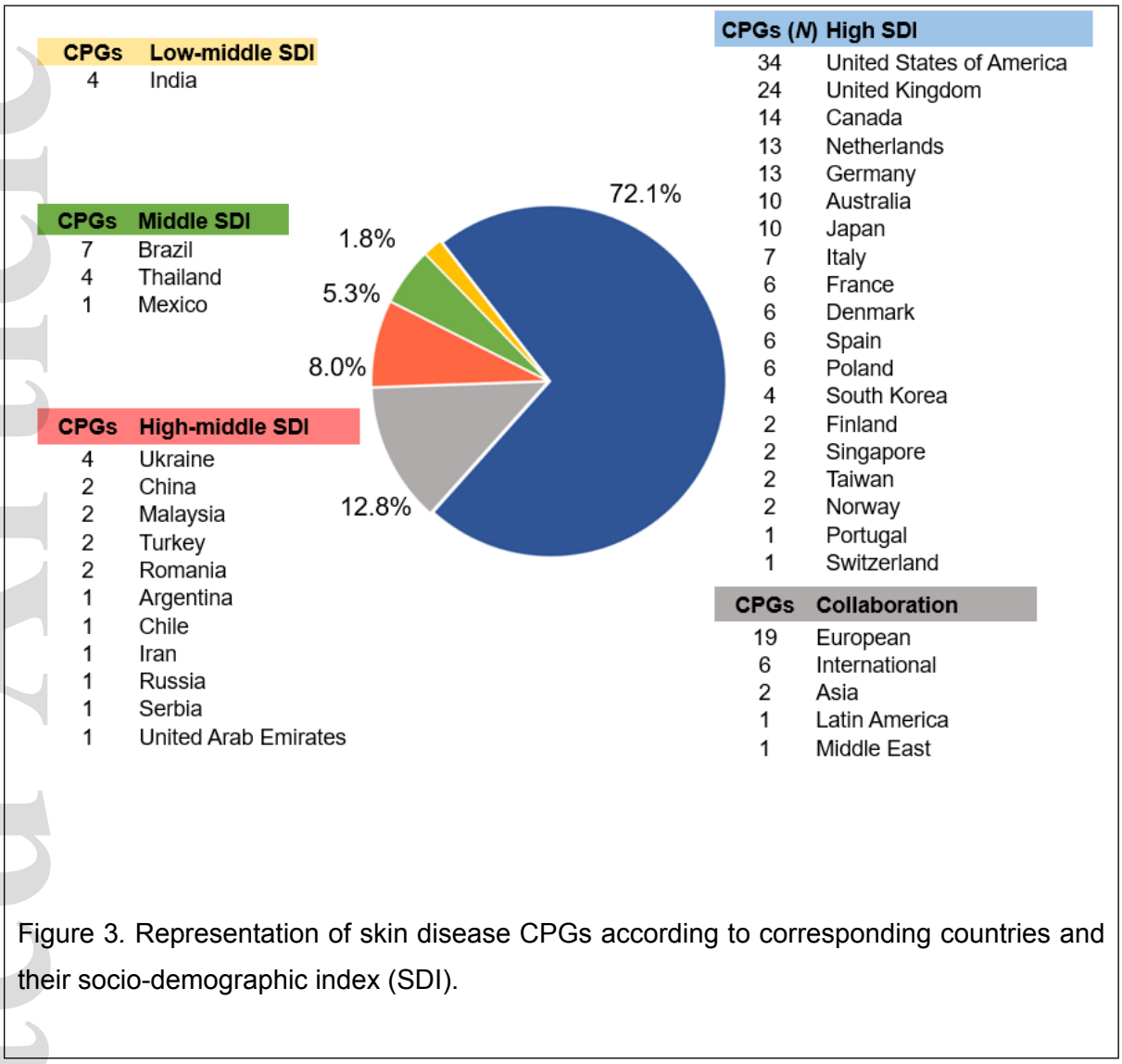

Figure 3. Representation of skin disease CPGs according to corresponding countries and their socio-demographic index (SDI).

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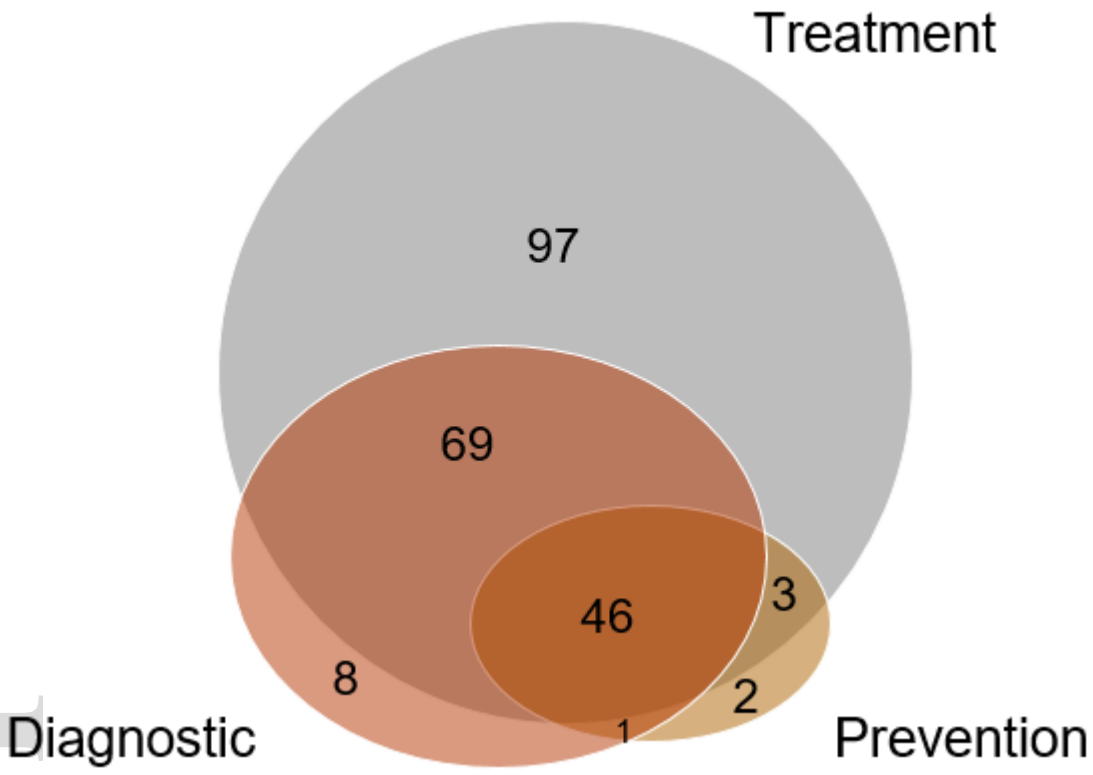

Figure 4. Venn diagram showing distribution of topics covered in skin disease CPGs.

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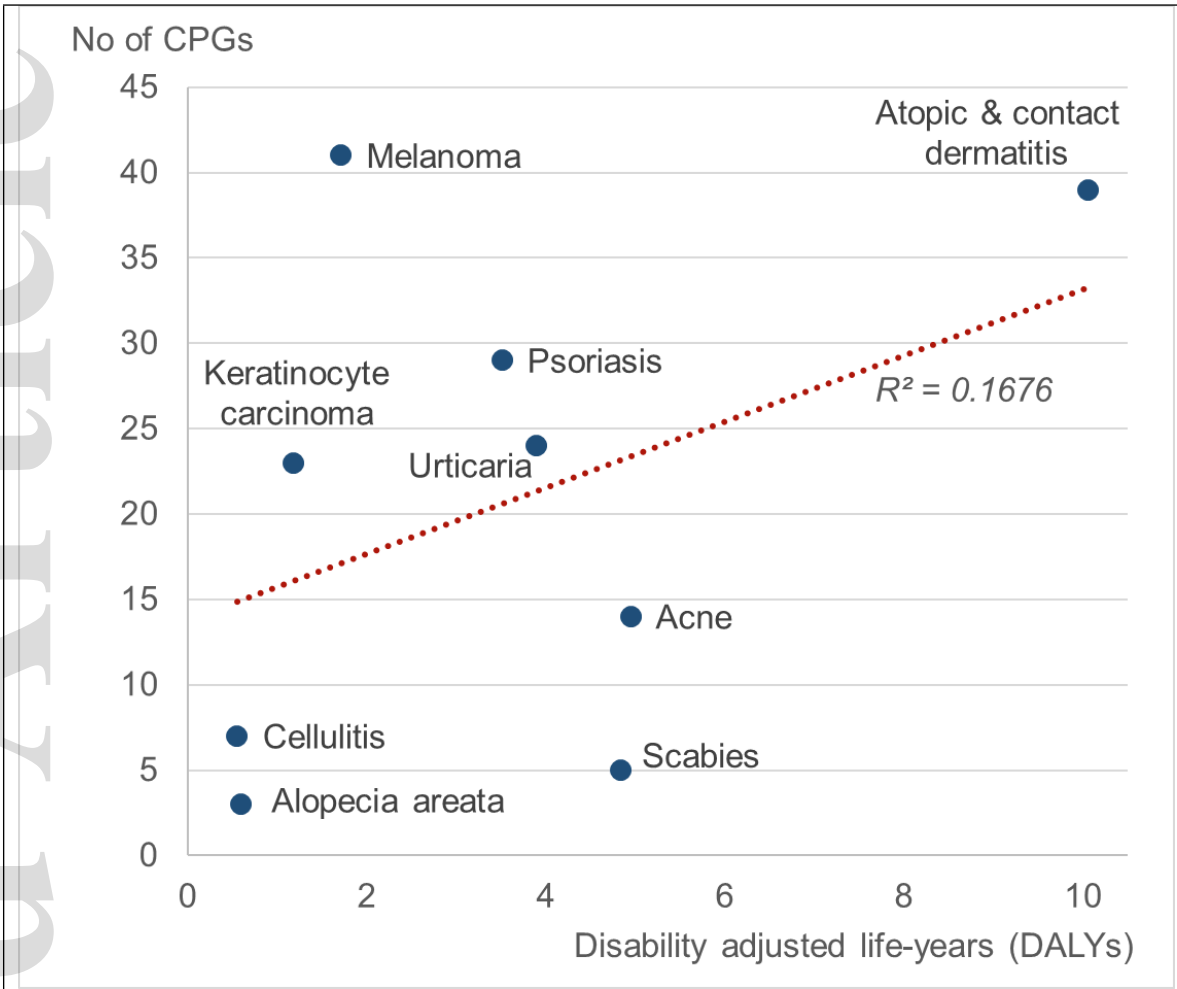

Figure 5. Scattered chart comparing correlation between 9 skin disease CPGs and the corresponding disability adjusted life-years (DALYs) as measured in the Global Disease Burden (GBD) 2019. 3 of the 12 skin diseases (tinea capitis, viral warts and molluscum contagiosum and venous ulcers) were used as representative conditions in the review for which there were no DALYs data available from the GBD study. These 3 groups were therefore excluded in the correlation analysis

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