BJD
British Journal of Dermatology

The global state of psoriasis disease epidemiology: a workshop report

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Summary

The International Psoriasis Council, a global nonprofit organization dedicated to innovation across the full spectrum of psoriasis, led a symposium to discuss the current state of psoriasis epidemiology and to introduce the vision and development of a Global Psoriasis Atlas. The symposium was held on 9 September 2015 at the 45th annual meeting of the European Society for Dermatological Research, Rotterdam, the Netherlands. Collectively, these presentations highlighted challenges associated with assessing psoriasis epidemiology and emphasized the urgent need for an authoritative resource to clarify psoriasis disease burden on a global scale.

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Accepted for publication
4 April 2017

Funding sources
C.E.M.G. is funded in part by the Medical Research Council grant MR/1011808/1 and is a National Institute for Health Research Senior Investigator.

Conflicts of interest
None declared.

DOI 10.1111/bjd.15610

Psoriasis represents a significant public heath challenge, affecting approximately 125 million people globally.[1] Prevalence estimates within adult populations range from 0·91% in the U.S.A. to 8·5% in Norway.[2] Currently, our knowledge of psoriasis epidemiology is fragmented into pockets of estimates worldwide without a standardized method for collecting data.[3] This fragmentation creates challenges to researchers wishing to make comparisons across populations and ultimately to draw conclusions regarding the impact of disease on a global level. The majority of data collected on psoriasis prevalence and incidence are from European countries, the U.K. and the U.S.A., thus there is still a demand for a leading, unified, global epidemiological resource on psoriasis epidemiology.

The International Psoriasis Council (IPC) assembled a panel of experts in dermatology and epidemiology to present on a variety of topics including temporal trends of psoriasis epidemiology, use of multisource data to determine psoriasis epidemiology, lessons from epidemiological studies of atopic eczema, insights into psoriasis epidemiology through registry data, and the potential for epidemiological studies to elucidate the link between psoriasis and cardiovascular comorbidities. The goals of the symposium were to identify key needs in the epidemiological study of psoriasis and to describe the development and current milestones of a web-based Global Psoriasis Atlas (GPA).

Darren Ashcroft (Manchester, U.K.) reviewed global estimates of psoriasis prevalence and incidence and described the multitude of challenges that complicate accurate assessments of psoriasis disease burden. In some instances, variation of prevalence estimates may be caused by a lack of standardized definitions for an incident case (patient reported vs. physician diagnosis) and also for the prevalence estimate (point estimate, period or lifetime estimate). Methodological differences in study design may also be a source of variation between countries, while estimates derived from small population samples leave uncertainty as to the validity of extrapolated estimates. The key to harmonizing global data will be a standardized approach to its collection and analysis.

Geographical variation in psoriasis prevalence may also be attributed to differences in climate, genetic background and

antigen exposure (pathogenic and environmental). Higher prevalence rates for psoriasis have been reported in countries at higher latitudes and, in contrast, lower rates have been observed in African and Asian countries that are closer to the equator. This observation is complex, and similar findings have also been reported for other autoimmune disorders. The 'equator effect' is not well understood and may be due to genetic and environmental factors such as vitamin D levels and exposure to pathogens.[2]

Professor Ashcroft also presented new findings examining psoriasis epidemiology in the U.K. using the Clinical Practice Research Datalink (CPRD). A cohort study was conducted using CPRD data from 1999 to 2013 derived from approximately 104 000 patients with psoriasis and 500 000 controls.[4] This comprehensive, longitudinal study was powered to investigate mortality rates using data collected over a 15-year period. The data suggest that there is an increasing population living longer with psoriasis in the U.K.; however, there was no evidence of any change in the premature mortality gap compared against people without psoriasis. Alongside this, striking evidence from the study demonstrated a bimodal age distribution of psoriasis incidence for 'early-onset' psoriasis, with women being more likely to be diagnosed at an earlier age. In addition, the study also identified an increase in prevalence and incidence with increasing latitude across the U.K. It is anticipated that the findings from this study will have important implications on the delivery of healthcare and resource allocation within the U.K.

Epidemiological studies can be used to understand the causes and patterns of psoriasis, describe quality of life, identify trends in health care, prioritize research needs, quantify the risk of major adverse cardiovascular events and risk of solid tumours and lymphoma, estimate the risk of tuberculosis in patients treated with biologics, investigate the natural history of psoriasis, and identify environmental factors influencing psoriasis and its comorbidities. Together, the information gained from these studies can be positioned to quantify the financial burden to society and ultimately to shape policy decisions.

Although country-specific databases offer rich resources and are essential for accurate assessments of psoriasis prevalence within each country, Matthias Augustin (Hamburg, Germany) described the need for multisource data and elaborated that each source has strengths and weaknesses. For example, large, prospective databases are extremely powerful tools to provide cohort data, which, if sufficient, can be stratified into datasets according to sex, age, genotype and ethnic background. However, developing and maintaining this type of resource is costly, and access could be restricted to specific research groups, thus limiting general use. In contrast, public polls and population surveys have the potential to compile valuable data cost-effectively within a geographical setting; however, biases could arise due to variation of patient-reported diagnosis, methodology and cultural differences.[5]

Currently, prevalence and incidence data in Germany are derived from claims databases, public health data, hospital records, public polls, population surveys and patient registries. Population surveys and electronic databases are also used in the U.S.A.; however, a centralized data resource is lacking, and multiple databases operate in isolation. In this type of scenario, researchers may struggle to define the best approach to combine data in order to estimate prevalence. As mentioned previously, prevalence rates can differ depending on the data source, therefore it is vital that homogeneous data are collected in order to reduce bias.

Registry cohorts are also important sources for epidemiological study of psoriasis, and provide real-world data collection for analysis. Luigi Naldi (Bergamo, Italy) described several examples of studies that have used registry data to investigate research questions including drug survival, using a prospective pharmacovigilance cohort from the British Association of Dermatologists Biologic Interventions Register;[6] identification of cardiovascular events in a Danish real-world cohort;[7] and diagnosis of latent tuberculosis infection from the Italian PsoCare registry.[8] These reports demonstrate the ability of registry data to track drug efficacy over time, as well as to monitor adverse events and patient comorbidities. On a larger scale, registry consortia, such as the European PSONET, can be linked, thereby increasing statistical power to investigate the effectiveness and safety of medicines used in the treatment of psoriasis. The challenges of extracting meaningful data from a network of population-based registries are to reduce variations in data collection and develop methods to adjust for confounders in combined datasets.[9]

In order to establish the true burden of psoriasis, the need for an accurate determination has to be driven by patient data so as not to provide an underestimate. A case in point is the Global Burden of Disease 2010 Study, which estimated the burden of diseases, including 15 skin disorders, in 187 countries.[10] Loss of health per country was defined by the disability-adjusted life year (DALY) score, which equates to the number of years lived with disability. The DALY scores for skin disorders were weighted according to symptoms that affect only the skin (itch, disfigurement) and did not factor in the impact of other debilitating comorbidities such as depression.[11] Psoriasis received a 2010 DALY ranking of 144 out of 176 conditions.[12] Given the fact that psoriasis is a systemic disease associated with psychosocial, cardiovascular and metabolic comorbidities, it is likely that the global disease burden is far greater than reported.

The panel emphasized the need to view the health burden of psoriasis at the patient level in a comprehensive (systemic) manner, not only at the level of the skin. Epidemiological studies in psoriasis have reported a significantly increased risk of inflammatory comorbid conditions[13] including psoriatic arthritis, depression, obesity, diabetes, liver disease, metabolic syndrome and cardiovascular disease (CVD). The association between psoriasis and major CVD events was discussed by Tamar Nijsten (Rotterdam, the Netherlands) as a prime example of the need for more evidence to decipher this relationship as either a causal association or an indirect outcome. He emphasized that thousands (perhaps tens of thousands) of

incident cases would be required to discern the true link between psoriasis and CVD.

He also stressed that genetic and environmental factors should be assessed in the association analyses in order to characterize possible interactions and contributions to the pathophysiology of psoriasis and CVD. From a richly powered dataset, the temporal trajectory of psoriasis could be clarified further, whether it may be a straight 'psoriatic march' or wayward maze, in order for the course to be stopped at the optimal time point and to reduce the risk of comorbidities. The concept of 'psoriatic march' describes the initiation of cutaneous inflammation leading to systemic inflammation and subsequent triggering of a cascade of events that may increase the risk of CVD in patients with severe psoriasis.[14,15] Although it is unclear whether psoriasis pathology proceeds linearly, it will be important to understand how early drug treatment and lifestyle changes (e.g. weight loss) could affect morbidity.

Insight into disease best practices in epidemiological studies and lessons learned can be translated from research in other skin disorders, such as atopic eczema (AE). Carsten Flohr (London, U.K.) presented the global state of AE epidemiology and highlighted the genetic and environmental factors that underlie its aetiology. AE is a relapsing inflammatory disorder prevalent in 20% of children and 5% of adults living within developed countries.[16] Common to many other chronic diseases, the complex interaction of genetic and environmental factors contributes to the pathogenesis of AE. Approximately 40–50% of patients with AE with moderate-to-severe disease carry a filaggrin loss-of-function mutation, which predisposes to skin barrier impairment, elevated transepidermal water loss and skin dryness.[17,18] Through interaction with environmental factors, such as water hardness (high domestic water calcium carbonate levels), and hygiene practices that damage the skin barrier further, the typical immunological phenotype of AE evolves.[19,20]

As a secondary phenomenon, environmental food and aeroallergens are recognized by antigen-presenting cells in the epidermis, leading to allergic sensitization and thus contributing to the development of clinical food and respiratory allergy and AE disease flares and chronicity. Much like psoriasis, AE has a detrimental impact on patient quality of life and is associated with anxiety and clinical depression in addition to the allergic comorbidities. However, the so-called 'atopic march' has recently been questioned, as less than one-third of children with early-onset AE develop food and respiratory allergies later.[21,22] Future epidemiological studies of AE will expand the current knowledge of disease pathology and comorbidity and will be used to prevent, treat and control disease burden in children and adults.

Accordingly, to move the epidemiological study of psoriasis forward, a rigorous, consistent and transparent approach for estimating global psoriasis prevalence is required. Chris Griffiths (Manchester, U.K.) described the development and current milestones of the web-based GPA, which has been initiated with the intention of being the leading resource on psoriasis epidemiology. Under the auspices of the International League of Dermatological Societies (ILDS), the International Federation of Psoriasis Associations (IFPA) and the IPC, the GPA is envisioned to inform research, policy and healthcare delivery. The goals of this long-term initiative are to provide a common benchmark on the complete burden of psoriasis in all countries and global regions, to leverage existing data through publications and registries, and to enhance the understanding of psoriasis and its comorbidities.

The GPA will operate through two work streams: (i) an extensive systematic review and update of published psoriasis epidemiology including in the grey literature; and (ii) the development of a core set of rigorous methods for data collection. A GPA prototype will be launched based on findings from a systematic review of current incidence and prevalence data in general populations. It will complete three large-scale epidemiological studies using electronic healthcare datasets, establish criteria for the design of future studies, and develop research tools to support future international field studies examining epidemiological studies of psoriasis. The GPA was recently launched at a reception hosted by the IPC, ILDS and IFPA on 30 September 2016 in Vienna, Austria at the 25th congress of the European Academy for Dermatology and Venereology. Phase 1 of the GPA is set to began in early 2017.

In conclusion, patients with psoriasis, as with many people with immune-mediated inflammatory diseases, experience a high degree of morbidity and, unlike their autoimmune counterparts who are marked by 'invisible inflammation', patients with psoriasis have a highly visible condition and sometimes endure social stigma due to these characteristics. The World Health Organization (WHO) has recently declared and recognized psoriasis as a serious, chronic, disfiguring, disabling, noncommunicable disease.[3] The WHO report highlights the need for data collection documenting prevalence and incidence of psoriasis in order to estimate accurately the social and economic burden of the disease worldwide.[3] Despite advances in effective psoriasis care, individual patients and countries are still managing the complex financial and social costs associated with disease burden in a suboptimal fashion. The GPA will provide data to help identify disease burden in hard-to-reach populations within resource-poor settings, as well as in developed nations. Ultimately, this resource is expected to drive improvement and equality of healthcare planning for psoriasis globally.

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