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BAD Elective Prize/Project Grant Report: Dermatoepidemiology at the LSHTM

Prevalence and disease associations of eczema:

Eczema is an inflammatory skin disease, traditionally considered a disease of childhood. However, eczema may affect around 10% of adults(1, 2) and the global prevalence of eczema is increasing(3). There is good evidence that eczema is associated with asthma and hayfever(4), and increasing evidence that eczema may be associated with other systemic diseases (5).

Recent studies have reported increasing evidence of associations between chronic inflammatory skin conditions such as eczema, and non-allergic diseases such as cardiovascular disease, autoimmune diseases, and malignancy.

Chronic inflammatory conditions of varying aetiologies, from psoriasis and rheumatoid arthritis to HIV, have been linked to cardiovascular disease(6-8). Cardiovascular disease is a significant and increasing cause of mortality and morbidity in both high and low and middle income countries. A range of evidence supports an association between eczema and cardiovascular disease. Mechanistic studies suggest that platelet dysfunction and decreased fibrinolysis may contribute to increased clotting in eczema(9, 10), whilst severe eczema has been associated with increased incidence of coronary artery disease using cardiac computed tomography angiography (CCTA)(11). The association between *psoriasis* and cardiovascular risk factors and outcomes is well established. In eczema, studies have reported associations between eczema and cardiovascular risk factors including raised BMI(12), and type 1 diabetes(13). Some studies have reported associations between eczema and proxies for cardiovascular disease including erectile dysfunction(14). However, epidemiological studies have inconsistently linked eczema to cardiovascular outcomes e.g. myocardial infarction (MI) and stroke across different populations(15-18). Potentially important confounders are often unavailable in administrative databases, or may be difficult to quantify. Possible confounders or effect mediators could include the contribution of smoking, raised BMI, the effect of decreased sleep, increased stress, or the contribution of treatments used for eczema, all of which may increase cardiovascular risk(19, 20).

Dermatoepidemiology describes the study of causes, prevention, health services research, and evaluation of interventions of skin diseases. Considering different biases and confounding factors is one of the most challenging and exciting aspects of dermatology. Information bias from increased health seeking behaviour may lead to artefactual associations; however adjusting for all health seeking behaviour may remove the effect of exposures and outcomes that are of interest(22). Theories from basic science are also involved in informing scientific ideas and interpretation of research findings. For example altered immune profiles in eczema may explain the reduced incidence of malignancies such as pancreatic tumours, childhood leukaemia, glioma and other brain

tumours, but an increased incidence of meningioma(21). Possible explanations which have been proposed to explain these associations include the activation of natural killer cells in allergic diseases, which could provide surveillance against malignant cells, although definitive explanations are lacking(23).

Dermatoepidemiology at the LSHTM:

I have spent my elective time at the London School of Hygiene and Tropical Medicine (LSHTM), in the Faculty of Epidemiology and Population Health, where I have developed my interest in dermatoepidemiology. I am extremely grateful to the British Association of Dermatologists for supporting my endeavours with an Elective Prize. In dermatoepidemiology research we consider all factors which may affect associations between exposures and outcomes, including factors such as health seeking behaviour, health systems, data types and data collection methods; in analysing the associations we use a range of epidemiological and statistical methods to generate and appraise evidence in order to improve skin health at a population level. This approach requires collaboration from different disciplines, including clinical dermatology, epidemiology, and statistics, in order to produce high quality and clinically relevant research. Being part of the collaboration between academics from different disciplines has been one of the most exciting and rewarding experiences of my elective.

During the first week, I attended the first dedicated dermatoepidemiology conference in Europe, the European Dermato-Epidemiology Network (EDEN) Forum (<http://www.dermepi.eu/>), which introduced me to the spectrum of dermatoepidemiology work in the EU and beyond. I was able to meet researchers in the field from all backgrounds and partake in stimulating discussions with experienced academics. The aim of the EDEN Forum was to facilitate collaboration and I found it a very welcoming atmosphere for someone at my career stage. I also had the opportunity to write the meeting report for the British Journal of Dermatology, which introduced me to the history of dermatoepidemiology organisations, its increasingly recognised importance in dermatology research, and gave me the opportunity to become familiar with new and exciting research in the field. The abstract book of the forum is freely available to everyone at http://www.dermepi.eu/?page_id=270.

Back at the LSHTM, I thoroughly enjoyed joining the meetings of the eczema working group, where epidemiologists and statisticians collaborate under the leadership of Sinéad Langan, a Wellcome Senior Clinical Fellow leading a programme of work on population health research in eczema. Their research network extends to other researchers at the university, and in universities across the world. One of the team's current projects is a study of the association between eczema and cardiovascular disease. It was a privilege to join their meetings and to observe the challenges and successes of their epidemiological study using routinely collected electronic health data in the UK. I was surprised that I was able to contribute at all to the discussions; however I quickly found that my medical training was a useful contribution to the different disciplines.

Within this project, I have been leading a systematic review study investigating the association between eczema and cardiovascular outcomes (specifically angina, myocardial infarction, coronary revascularisation, heart failure, cardiac arrhythmias, stroke, and cardiovascular death) in population based studies, which has been an opportunity to challenge myself to lead research. The review is needed in order increase our understanding of the comorbidities of eczema, to inform management and prevention strategies at an individual and population level, and to highlight research gaps. I have had the opportunity to work with researchers in Canada, USA, Denmark and at the LSHTM to produce a protocol for the study, which I have registered on PROSPERO International prospective

register of systematic reviews (registration number: CRD42017060359) and submitted the protocol to a journal for publication. Through this experience, I have developed my skills in research management, literature searching, academic writing and the journal submission process, and will further develop my critical appraisal skills as I continue with the review. Critical appraisal of included studies will be academically challenging due to the likely strong collinearity between eczema severity and level of treatment, as factors such as confounding by severity could contribute to an observed increase in cardiovascular disease and stroke in eczema.

The group at the LSHTM primarily use routinely collected electronic health data, which provides large datasets with good external validity to answer important research questions. Whilst at the LSHTM I have been learning about the uses of these datasets, for example the Clinical Practice Research Datalink, by completing the training exercise developed by the research group and observing how CPRD data are used in practice. I have gained data management skills using STATA, which is the gateway to exciting possibilities for me to be able to do my own analysis in future research. In the environment of LSHTM it has been clear to me how important it is to understand medical statistics and the software used in order to contribute meaningfully to dermatoeidemiology projects. I have also realised how important it is to maintain the regular use of statistical software, which presents yet another challenge for finding the time to combine clinical and academic duties, whilst maintaining and developing skills in both!

Spending an extended period of time in the academic environment of the LSHTM has been inspiring, and confirmed my commitment to a career as an academic dermatologist, with the aim of having a positive impact on population skin health. I intend to continue working with Sinéad Langan at the LSHTM and to keep developing my skills in the field of dermatoeidemiology research throughout my foundation years, and I hope to complete a PhD in the near future.

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