BMJ Open  Risk factors for mental illness in adults with atopic eczema or psoriasis: protocol for a systematic review

Elizabeth I Adesanya 1, Yochai Schonmann 2,3, Joseph F Hayes 4, Rohini Mathur 1, Amy R Mulick 1, Lauren Rayner 5, Liam Smeeth 1, Catherine H Smith 6, Sinéad M Langan 1,7, Kathryn E Mansfield 1

ABSTRACT

Introduction Evidence indicates that people with the common inflammatory skin diseases atopic eczema or psoriasis are at increased risk of mental illness. However, the reasons for the relationship between skin disease and common mental disorders (ie, depression and anxiety) or severe mental illnesses (ie, schizophrenia, bipolar disorder and other psychoses) are unclear. Therefore, we aim to synthesise the available evidence regarding the risk factors for mental illness in adults with atopic eczema or psoriasis.

Methods and analysis We will conduct a systematic review of randomised controlled trials, cohort, case–control and cross-sectional studies. We will search the following databases from inception to March 2020: Medline, Embase, Global Health, Scopus, the Cochrane Library, Web of Science, Base, Psycinfo, the Global Resource of Eczema Trials, and the grey literature databases Open Grey, PsyfExtra and the New York Academy of Medicine Grey Literature Report. We will also search the bibliographies of eligible studies and relevant systematic reviews to identify additional relevant studies. Citation searching of large summary papers will be used to further identify relevant publications. Two reviewers will initially review study titles and abstracts for eligibility, followed by full text screening. We will extract data using a standardised data extraction form. We will assess the risk of bias of included studies using the Quality in Prognosis Studies tool. We will synthesise data narratively, and if studies are sufficiently homogenous, we will consider a meta-analysis. We will assess the quality of the evidence using the Grading of Recommendations, Assessment, Development and Evaluation framework.

Ethics and dissemination Ethical approval is not required for a systematic review. Results of the review will be published in a peer-reviewed journal and disseminated through conferences.

PROSPERO registration number CRD42020163941.

INTRODUCTION

Psoriasis and atopic eczema are inflammatory skin conditions associated with considerable morbidity and reduced quality of life for both sufferers and their families. Atopic eczema and psoriasis are common in the UK population—psoriasis affects between 1.3% and 2.6% of adults, and the prevalence of atopic eczema in adults is approximately 2.5%. Similarly, mental illness is common. According to the 2017 Global Burden of Disease Study, mental illness is one of the leading causes of years lived with disability worldwide. In England, 17% of adults have common mental disorders (CMD—including depression or anxiety), severe mental illness (SMI—including schizophrenia, bipolar affective disorder and other psychoses) affects nearly 1% of the UK population. Individuals with SMI experience substantial health inequalities; they are at increased risk of serious health problems (eg, diabetes mellitus and cardiovascular disease) and die up to 20 years earlier than the general population.

Associations between atopic eczema or psoriasis and mental illness are well established. Evidence suggests that people with atopic eczema or psoriasis are at increased risk of mental illness. The temporal sequence of the associations between skin disease and mental illness is also well recognised, with evidence suggesting that atopic eczema or
Psoriasis precedes mental illness diagnosis. However, the reasons for the relationship between inflammatory skin disease and mental illness are unclear. To the best of our knowledge, there are no existing systematic reviews addressing risk factors for the relationship between atopic eczema or psoriasis and mental illness in adults. Previous systematic reviews have aimed to establish summary measure of effects for the association between either atopic eczema or psoriasis and specific mental illnesses (e.g., depression); the majority have focused on the relationship between atopic eczema or psoriasis and CMDs and SMIs. One systematic review has investigated the risk factors that mediate the association between atopic eczema and mental illness in children and adolescents only. The majority of studies in this review of children were conducted in European countries or territories. Meta-analysis of the 35 studies included in the review found that although demographic factors such as age, sex, and socioeconomic status did not moderate the risk of developing mental illness in children with atopic eczema, children from predominantly minority ethnic backgrounds were more likely to be diagnosed with a mental illness in comparison with their Caucasian counterparts.

The primary aim of this systematic review will be to explore, synthesise and critically evaluate the strength and quality of all available evidence on the risk factors associated with the development of mental illness (CMDs and SMIs) in adults with atopic eczema or psoriasis. If possible, we will also compare and contrast the risk factors associated with the development of mental illness in adults with atopic eczema to the risk factors in psoriasis.

**METHODS**

This study protocol adheres to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P).

**Patient and public involvement**

Patients and/or the public were not involved in this systematic review protocol.

**Eligibility criteria**

We will screen studies for potential inclusion in our review according to the eligibility criteria presented in table 1.

**Information sources**

We will search the following databases for relevant articles from inception to March 2020: Medline, Embase, Global Health, Scopus, the Cochrane Library (which includes Cochrane Reviews, Cochrane Protocols, Trials, Editorials, Special Collections, Clinical Answers and Other Reviews).

<table>
<thead>
<tr>
<th><strong>Table 1</strong> Eligibility criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inclusion criteria</strong></td>
</tr>
<tr>
<td>Study design and characteristics</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Participants</td>
</tr>
<tr>
<td>Human participants aged 18 and over with atopic eczema or psoriasis.</td>
</tr>
<tr>
<td>Studies including both adults and children where data for adults is reported separately.</td>
</tr>
<tr>
<td>Exposure</td>
</tr>
<tr>
<td>Risk factors for mental illness (CMD or SMI).</td>
</tr>
<tr>
<td>Comparators</td>
</tr>
<tr>
<td>Studies must compare adults with atopic eczema or psoriasis with the risk factors of interest with adults with atopic eczema or psoriasis without the risk factors of interest.</td>
</tr>
<tr>
<td>Outcomes</td>
</tr>
<tr>
<td>Study outcomes must be a CMD or SMI, either clinically diagnosed or self-reported with or without validated tools.</td>
</tr>
</tbody>
</table>

CMD, common mental disorder; RCT, randomised controlled trial; SMI, severe mental illness.
Web of Science (which includes the Science Citation Index Expanded, the Social Sciences Citation Index, the Arts & Humanities Citation Index, the Conference Proceedings Citation Index-Science, the Conference Proceedings Citation Index—Social Science & Humanities and the Emerging Sources Citation Index), Base, PsycInfo and the Global Resource of Eczema Trials. Both Medline and Embase capture a large amount of published literature—Medline indexes more than 5200 journals, and Embase indexes almost 8500 journals22 23—while the other databases are likely to contain appropriate papers for this review. To ensure that all relevant literature is included in the review, we will also search for grey literature in Open Grey, the New York Academy of Medicine Grey Literature Report and PsycExtra. Finally, we will search the five largest clinical trial registries—ClinicalTrials.gov, the EU Clinical Trials Register, the Japan Primary Registry Network, International standard Randomised Controlled Trial Number (ISRCTN) and the Australian New Zealand Clinical Trials Registry—to identify relevant trials.

**Search strategy**

We will search medical subject headings and free text (in titles, abstracts and keywords) for synonyms relating to three key concepts: (1) ‘risk factors’, (2) ‘atopic eczema or psoriasis’ and (3) ‘mental illness’ (table 2). We will combine the three key concepts in the search strategy using the Boolean logic operator ‘AND’. We have developed and piloted an initial search strategy in the Medline database that has been peer reviewed by a librarian (online supplemental table 1), and we will adapt it appropriately for other databases. We will also manually scrutinise the reference lists and bibliographies of relevant systematic reviews to identify additional papers for inclusion. Finally, we will use citation searching on large summary papers to identify any further relevant publications.

**Table 2** Keywords included in the search strategy for all databases

<table>
<thead>
<tr>
<th>Search term</th>
<th>Keywords</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factor terms</td>
<td>risk OR risk factor* OR protective factor OR predict* OR correlat* OR associat* OR aetiol* OR etiol* OR relationship OR mediat* OR mechanism* OR caus* OR path*</td>
</tr>
<tr>
<td>Atopic eczema or psoriasis terms</td>
<td>atopic dermatitis OR eczema OR atopy OR psoriasis OR psoria* OR (pustulo* AND palmopl* OR palmar* OR palmar)</td>
</tr>
<tr>
<td>Mental illness terms</td>
<td>mental health OR mental* ill* OR mental disorder* OR psychiatr* ill* OR psychiatr* disorder OR psychiatr* disease* OR psychological* ill* OR psychological* disorder* OR psychological* disease* OR affective* OR anxi* OR depress* OR phobi* OR panic OR bipolar* OR schizophrenia OR schizo* OR delusion* OR psychotic* OR psychos#s OR psychological* distress</td>
</tr>
</tbody>
</table>

**Study records**

**Data management**

A single reviewer (EA) will import all results returned from the electronic database searches into the reference management tool EndNote V.X9 (Clarivate Analytics, V.9.2/2019). After identifying and removing duplicate records, we will import the search results into Rayyan (a web application for systematic reviews),25 where the integrated deduplication function will be used to identify any previously missed duplicates.

**Study selection**

Two reviewers (EA and YS) will independently screen the titles and abstracts of the search results for potentially relevant studies. Both reviewers will then screen the full text of all potentially relevant studies for inclusion using the eligibility criteria. Any disagreements during this process will be discussed by EA and YS, with consultation from a third reviewer (KM) if necessary. We will record and report in a flowchart the reasons for study rejection following full text screening.

**Data extraction**

We will develop a standardised data extraction form (to extract information described below), which will be piloted by two reviewers (EA and YS) who will extract data from the larger of either 10% or five of the eligible studies. Any disagreements between the two reviewers will be discussed, with a third reviewer (KM) available to arbitrate if required, and changes made to the data extraction form if necessary. A single reviewer (EA) will complete the extraction of data for the remaining studies. We will use a modified version of the Population, Intervention, Comparator(s), Outcome(s) and Study Design (PICOS) framework to summarise data for extraction.26 However, due to the inclusion of observational studies in our review, we will replace the term ‘intervention’ with ‘exposure’, and ‘study design’ will be replaced by ‘study characteristics’. We will extract information for each component of the PICOS framework, in addition to study results for each study included in the review (table 3).

**Exposures**

Our exposures of interest will be risk factors for mental illness in people with atopic eczema or psoriasis. We will consider any variable that authors of included papers have conducted analyses to assess whether they are associated with mental illness in people with atopic eczema or psoriasis as potential risk factors. These may include sociodemographic factors (eg, sex, ethnicity and deprivation), lifestyle factors (eg, level of physical activity, diet and alcohol consumption) or environmental factors.

**Outcomes**

Our primary outcome of interest will be mental illness in individuals with atopic eczema or psoriasis. Mental
risk factor pair.28 If more than one study are identified for each broad outcome (CMD or SMI) and for a specific subtype of a CMD or SMI (such as depression or schizophrenia), we will categorise the strength of evidence into four qualitative categories: ‘high’, ‘moderate’, ‘low’ or ‘very low’. The quality of evidence for included studies will be upgraded if there is a large magnitude of effect or a dose-response gradient.28 The quality of evidence will be rated down if there is a high risk of bias, imprecision in the study estimate, a high probability of publication bias or inconsistent results.28 We will present the judgement made during this process in a ‘Summary of Findings’ table.

Confidence in cumulative evidence
We will use the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework to evaluate and summarise the quality of cumulative evidence for each broad outcome (CMD or SMI) and risk factor pair.29 If more than one study are identified for a specific subtype of a CMD or SMI (such as depression or schizophrenia) and a specific risk factor, we will use GRADE to summarise the quality of evidence for that subtype. We will categorise the strength of evidence into four qualitative categories: ‘high’, ‘moderate’, ‘low’ or ‘very low’. The quality of evidence for included studies will be upgraded if there is a large magnitude of effect or a dose-response gradient.28 The quality of evidence will be rated down if there is a high risk of bias, imprecision in the study estimate, a high probability of publication bias or inconsistent results.28 We will present the judgements made during this process in a ‘Summary of Findings’ table.

Ethics and dissemination
As this study is a systematic review that does not involve human participation, we do not require ethical approval. We will disseminate the results of this review by publishing...
in an open access, peer-reviewed journal and presenting at conferences. We will document any important amendments and protocol deviations, along with justifications, and publish them as an appendix in the final review.

Author affiliations
1Department of Non-Communicable Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK
2Gisal Research Center for Family Medicine and Primary Care, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel
3Department of Quality Measurements and Research, Clalit Health Services, Tel Aviv, Israel
4Division of Psychiatry, University College London, London, UK
5Department of Psychological Medicine, Institute of Psychiatry, Psychology, and Neuroscience, King’s College London, London, UK
6St John’s Institute of Dermatology, Guys and St Thomas’ Foundation Trust and King’s College London, London, UK
7Health Data Research UK, London, UK

Contributors EA, SL and KM had the original idea for the review. All authors (EA, YS, JH, RM, AM, LR, LS, CHS and KM) were involved in the design of the study. EA wrote the first draft of the protocol. All authors (EA, YS, JH, RM, AM, LR, LS, CHS, SL and KM) contributed to further drafts and approved the final manuscript. Kate Perris peer reviewed the search strategy.

Funding EA was funded by a British Skin Foundation (BSF) PhD studentship (Reference: 024/S/18). SL was funded by a Wellcome Trust Senior Clinical Fellowship (Reference: 205039/Z/16/2).

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access
This is an open access article distributed in accordance with the Creative Commons Attribution 4.0 Unported (CC BY 4.0) license, which permits usage, distribution, and reproduction in any medium, provided the original work is properly cited, a link to the licence is given, and any translated material is included. BMJ does not warrant the accuracy and reliability of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. All information including but not limited to local regulations, clinical guidelines, and terminology is the responsibility of the author(s).

Supplemental material

This is an open access article distributed in accordance with the Creative Commons Attribution 4.0 Unported (CC BY 4.0) license, which permits usage, distribution, and reproduction in any medium, provided the original work is properly cited, a link to the licence is given, and any translated material is included. BMJ does not warrant the accuracy and reliability of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. All information including but not limited to local regulations, clinical guidelines, and terminology is the responsibility of the author(s).

REFERENCES


5
# Supplementary Material

## Supplementary Table 1: Search strategy in MEDLINE database

<table>
<thead>
<tr>
<th>Item number</th>
<th>Searches</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk factor terms</strong></td>
<td>risk OR risk factor* OR protective factor OR predict* OR correlat* OR associate* OR aetiol* OR etiol* OR relationship OR mediat* OR mechanism* OR caus* OR path*</td>
</tr>
<tr>
<td>1</td>
<td>exp Risk/</td>
</tr>
<tr>
<td>2</td>
<td>1 OR 2</td>
</tr>
<tr>
<td><strong>Atopic eczema terms</strong></td>
<td>atopic dermatitis OR atopic eczema OR atopy</td>
</tr>
<tr>
<td>3</td>
<td>Dermatitis, Atopic/</td>
</tr>
<tr>
<td>4</td>
<td>exp Eczema/</td>
</tr>
<tr>
<td>5</td>
<td>4 OR 5 OR 6</td>
</tr>
<tr>
<td><strong>Psoriasis terms</strong></td>
<td>psoriasis OR psoria*</td>
</tr>
<tr>
<td>6</td>
<td>pustulo* AND (palmopl* OR palmari* OR palmar)</td>
</tr>
<tr>
<td>7</td>
<td>exp Psoriasis/</td>
</tr>
<tr>
<td>8</td>
<td>8 OR 9 OR 10</td>
</tr>
<tr>
<td><strong>Combining atopic eczema and psoriasis terms with ‘OR’</strong></td>
<td>7 OR 11</td>
</tr>
<tr>
<td><strong>Mental illness terms</strong></td>
<td>mental health OR mental* ill* OR mental disorder* OR affective OR anxi* OR depress* OR phobi* OR panic OR bipolar* OR schizo* OR schizophrenia OR delusion* OR psychotic* OR psychos#s</td>
</tr>
<tr>
<td>9</td>
<td>psychiatr* AND (ill* OR disorder OR disease*)</td>
</tr>
<tr>
<td>10</td>
<td>psychological* AND (ill* OR disorder OR disease* OR distress)</td>
</tr>
<tr>
<td><strong>Combining key concepts with ‘AND’</strong></td>
<td>3 AND 12 AND 18</td>
</tr>
</tbody>
</table>