Short Report

Novel clusters of multimorbidity in people with asthma and atopic eczema: a UK population-based study

Authors: Alasdair Henderson[1],* Amy Mulick[1],* David Prieto-Merino[1],* Julian Matthewman[1], Jennifer Quint[2], Ronan Lyons[3,4], Aziz Sheikh[5], David McAllister[6], Dorothea Nitsch[1], Kathryn E Mansfield[1],** Sinéad M Langan[1,7]**

* Contributed equally as joint first authors

** Contributed equally as joint senior authors

Affiliations:

[1] Department of Non-Communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT, United Kingdom
[2] National Heart and Lung Institute, Imperial College London, London, United Kingdom
[3] National Centre for Population Health and Wellbeing Research, Swansea University Medical School, Swansea, United Kingdom
[4] Administrative Data Research UK, Swansea University Medical School, Swansea, United Kingdom
[5] Usher Institute, University of Edinburgh, 30 West Richmond Street, Edinburgh, EH8 9DX, UK
[6] Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK
[7] Health Data Research UK, Gibbs Building, 215 Euston Road, London, NW1 2BE, United Kingdom

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INTRODUCTION

Common allergic diseases, including asthma and atopic eczema, affect twenty percent of the UK population,[1] and are themselves distressing and costly. Allergic conditions are also associated with substantial morbidity beyond associations with other allergic diseases. Most of the recent research has focussed on specific comorbidities, which describes an additional health conditions (mental or physical) co-existing with an index condition (e.g., asthma).[2] Multimorbidity, by contrast, identifies the coexistence of multiple health conditions without determining a single index condition.

Previous research has highlighted that many people - at least one fifth - of the population are multimorbid.[3] Traditionally, multimorbidity has not been perceived as a problem in allergic diseases, beyond known allergic comorbidities. However, we and others have found increased risks of comorbidity and multimorbidity in those with allergic diseases, ranging from cardiovascular outcomes to fractures.[4]–[6] There is a need to better characterise how mental and physical diseases cluster with common allergic conditions, to prevent the development of multimorbidity and reduce its impact.

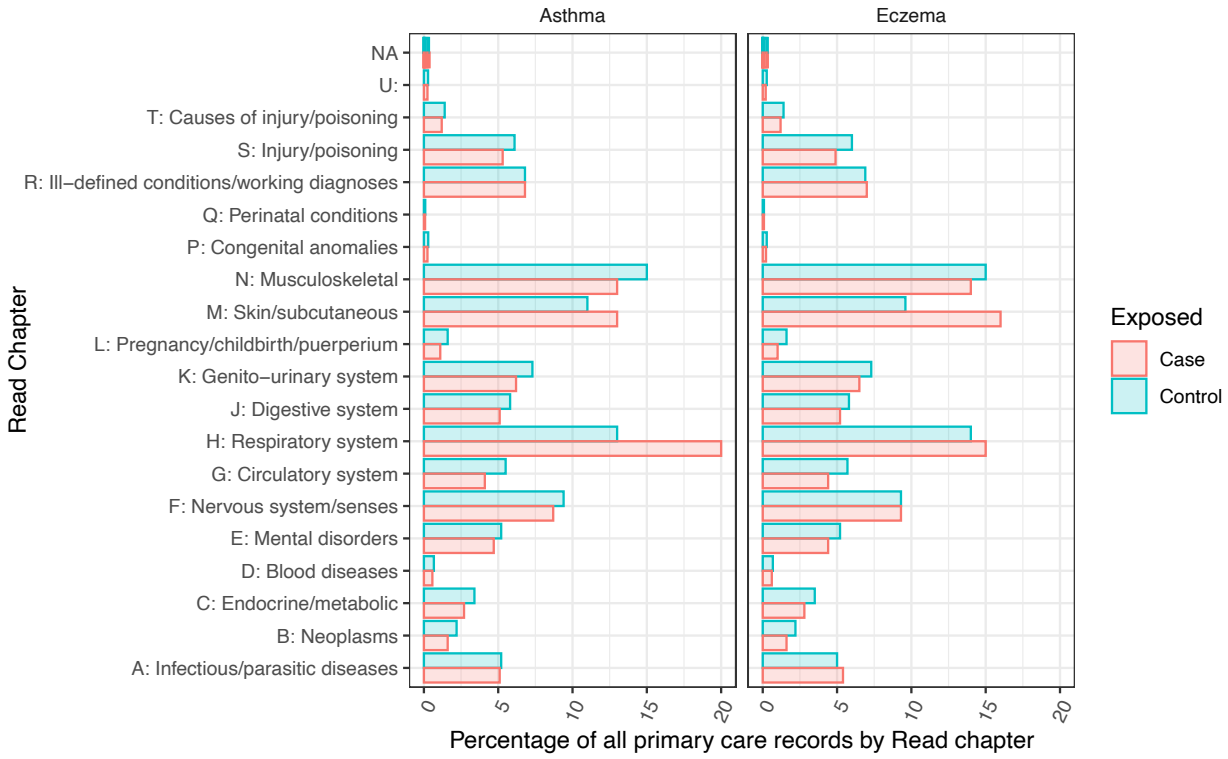
We used routinely-collected electronic health records from UK primary care to conduct an exploratory analysis identifying and comparing clusters of multimorbidity in people with either atopic eczema or asthma to comparison groups matched of people matched by age, sex and primary care practice without eczema or asthma. We then analysed patterns of disease clusters (multimorbidity) in these groups by recording every event in the electronic health records by Read code chapters A to W. The Read code chapters that start with alphabetic characters cover broad diagnoses categorised by body systems. For example, Chapter A includes infectious disease, and Chapter B cancers.

We then performed statistical analyses to identify clusters of multimorbidity. We applied a disease-driven approach by clustering comorbidities rather than clustering individuals. We used mixed-effects logistic regressions to estimate how closely related two Read code chapters were in our study. We used these models to predict the probability of having both morbidities, given the presence of one. We then visualise the results with a dendrogram highlighting groups of Read chapters that have at least a 30% probability of co-occurence given that you already have one event recorded from the same group.

RESULTS

We identified 434,422 individuals with atopic eczema and 1,333,281 matched controls. We also identified 460,052 individuals with asthma and 1,523,963 matched controls without asthma. The most common recorded Read chapter codes in our study were chapters M (skin/subcutaneous), H (respiratory system) and N (musculoskeletal) (**Figure 1**).

Figure 1. Study population: bar chart illustrating the relative proportion of events by Read code chapter for cases and matched controls in the asthma and eczema cohort



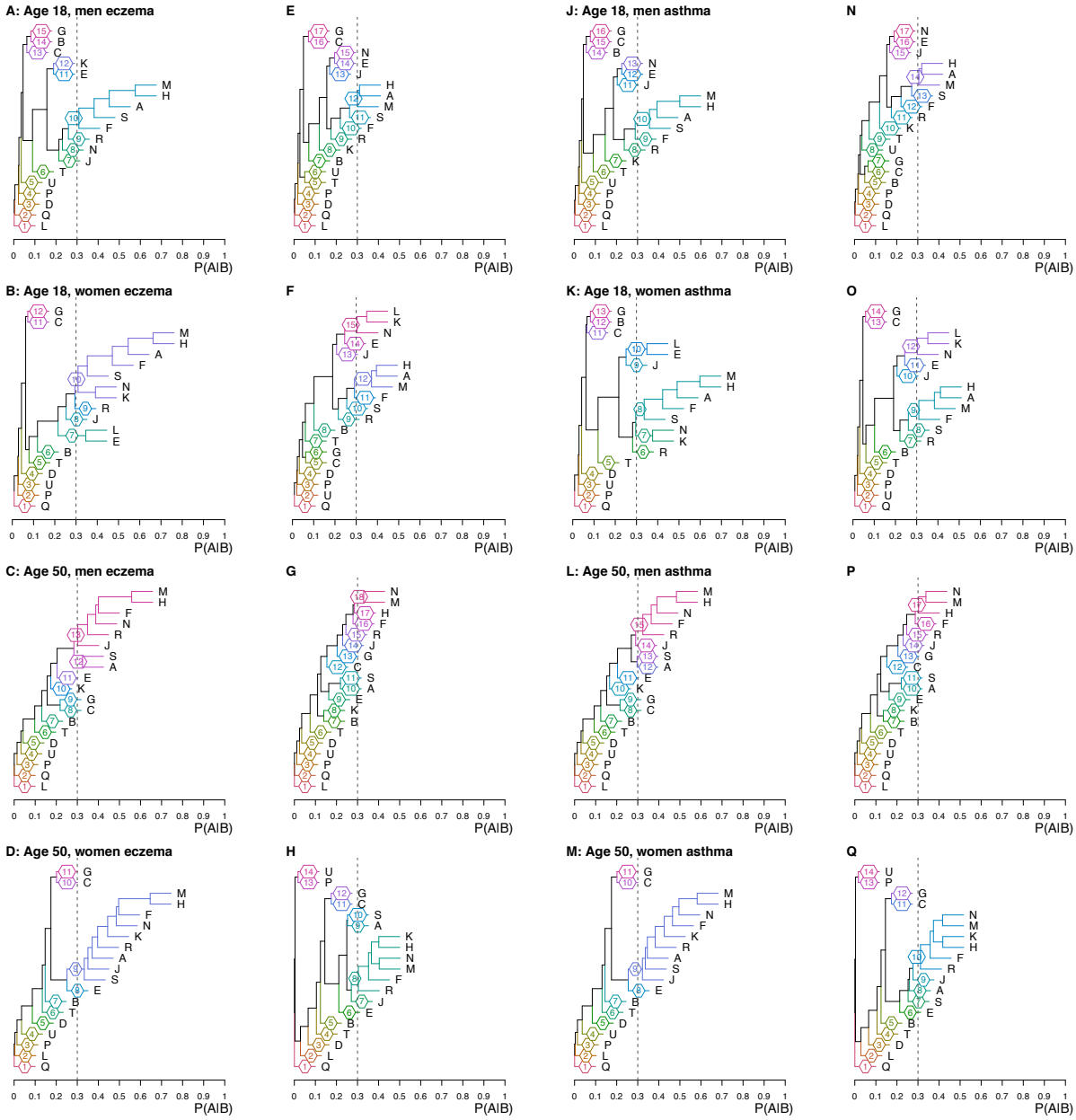
Multimorbidity in people with atopic eczema or asthma

Men

We found larger and stronger clusters of disease morbidity in people with common allergic conditions - atopic eczema or asthma - than in matched controls without these conditions. We used dendrograms to visualise clusters of Read chapters of disease for two sexes (male and female) at two age points (18 and 50 years old) (**Figure 2**). In the dendrogram, if two chapters join to the right of the dotted line (which shows 30%) then there is a >30% probability of having a record from the second chapter within 5 years if you have recorded an event from the first chapter. For example, in Figure 2A, chapters M (skin conditions) and H (respiratory conditions) join together at approximately a probability of 57% in men with eczema aged 18 years old.

Therefore, if an 18 year old man has eczema (part of chapter M) by age 18, there is an approximately 57% chance they will also record a disease from chapter H within 5 years. **Figure 2** shows that for people with common allergic conditions (**A-D** for atopic eczema and **J-M** for asthma) the clusters of chapters with a >30% probability are larger and stronger than they are for people without these conditions (**E-H** and **N-Q** respectively).

Figure 2. Dendrograms of Read chapter clustering for people with common allergic conditions: atopic eczema (A-D), matched controls (E-H), with asthma (J-M) and matched controls (N-Q)



The largest cluster we identified was in women aged 50 with atopic eczema (**Figure 2D**) or asthma (**Figure 2M**). This single large cluster contained nine Read chapters; skin (M), respiratory (H), neurological (F), musculoskeletal (N), genito-urinary (K), ill-defined conditions (R), infectious diseases (A), digestive system (J) and injury/poisoning (S).

We also constructed undirected networks of disease co-occurrence within 5 years with probabilities greater than 30% for all groups in our study. **Figure 3** shows that people with common allergic conditions are more likely to have two diseases co-occur within 5 years than the matched controls without asthma or atopic eczema. We see that women aged 50 with atopic eczema (37 connections) or asthma (36 connections) (**Figure 3, panels D and M**) have the most connectivity between Read chapters and therefore the highest probability of disease co-occurrence. Women aged 18 with common allergic conditions also have a large number of connections (33 and 28 for those with eczema and asthma respectively) that could result in multimorbidity (**Figure 3, panels B and K**). We see from these networks that there is a higher chance of multimorbidity in women than in men. Even in those without atopic eczema or asthma, women have a much higher probability of multiple diseases at age 18 (**Figure 3, panels F and O**) or age 50 (**Figure 3, panels H and Q**) than their male counterparts (**Figure 3, panels E, N, G and P**).

DISCUSSION

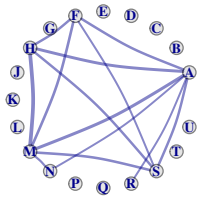
This is to our knowledge the first hypothesis free exploration of clusters of multimorbidity in asthma and eczema using UK routine health data. In our study we found unique clusters of neurological and musculoskeletal disease in people with eczema/asthma which were not observed in age- and sex-matched controls.

As this was a cross-sectional study it reflects contemporary health needs in people with and without asthma/eczema across all age groups. Due to the design we cannot draw any causal conclusions and we used broad chapters of diseases so our conclusions are limited by a lack of detail. However, our identification of novel clusters of multimorbidity at a Read chapter level can motivate and direct further investigation.

In conclusion, we used a hypothesis free design and have found a new cluster of neurological and musculoskeletal disease in people with eczema and asthma which was not observed in controls. Our work highlights that allergic disease is not an isolated entity and documents the extensive and unique additional health needs of people with allergic disease.

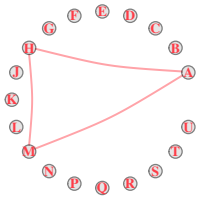
Figure 4. Undirected networks of Read code comorbidities in people with atopic eczema (A-D), matched controls without atopic eczema (E-H), people with asthma (J-M) and matched controls without asthma (N-Q).

A: Age 18, men eczema



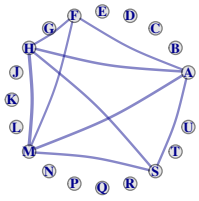
Connections: 13
Max prob: H – M: 0.58

E



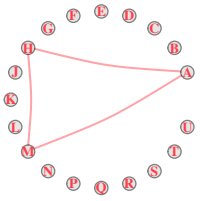
Connections: 3
Max prob: A – H: 0.31

J: Age 18, men asthma



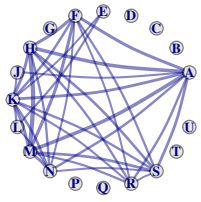
Connections: 9
Max prob: H – M: 0.5

N



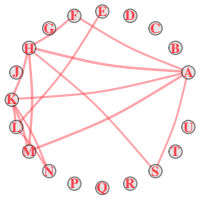
Connections: 3
Max prob: A – H: 0.32

B: Age 18, women eczema



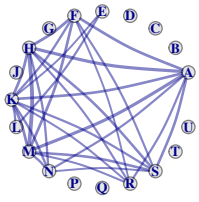
Connections: 33
Max prob: H – M: 0.66

F



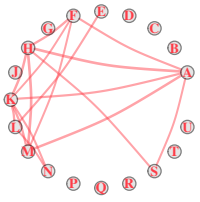
Connections: 14
Max prob: A – H: 0.4

K: Age 18, women asthma



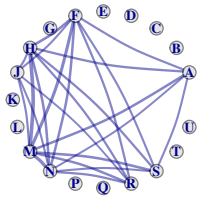
Connections: 28
Max prob: H – M: 0.6

O



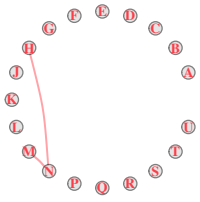
Connections: 16
Max prob: A – H: 0.41

C: Age 50, men eczema



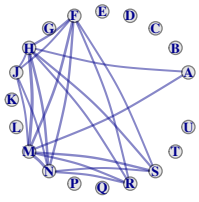
Connections: 24
Max prob: H – M: 0.56

G



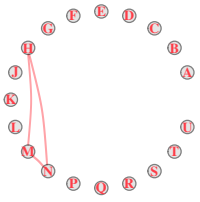
Connections: 2
Max prob: M – N: 0.33

L: Age 50, men asthma



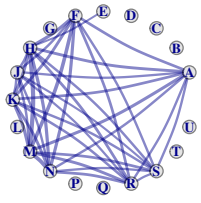
Connections: 20
Max prob: H – M: 0.48

P



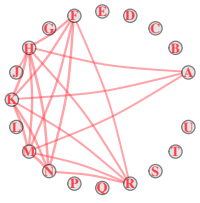
Connections: 3
Max prob: M – N: 0.34

D: Age 50, women eczema



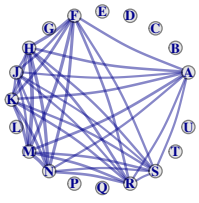
Connections: 37
Max prob: H – M: 0.65

H



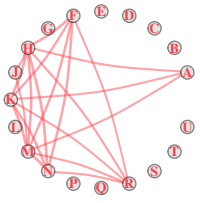
Connections: 19
Max prob: M – N: 0.4

M: Age 50, women asthma



Connections: 36
Max prob: H – M: 0.58

Q



Connections: 20
Max prob: H – K: 0.42

DECLARATIONS AND ACKNOWLEDGEMENTS

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Ethical approval

The study was approved by the London School of Hygiene and Tropical Medicine Research Ethics Committee and by the CPRD Independent Scientific Advisory Committee (ISAC Protocol Number: 20_000259).

Data sharing

No additional unpublished data are available as this study used existing data from the UK CPRD electronic health record database that is only accessible to researchers with protocols approved by the CPRD's Independent Scientific Advisory Committee.

All data management and analysis computer code is available via GitHub (https://github.com/a-henderson91/2020_multimorbidity). All code is shared without investigator support.

Declaration of interests

All authors have completed the ICMJE uniform disclosure form (www.icmje.org/coi_disclosure.pdf).

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