The burden of asthma, hay fever and eczema in adults in 17 countries: GAN Phase I study (r2)

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Take home message (a 256-character (including spaces) summary)

There is a substantial global burden of asthma, hay fever and eczema in adults representing a major global public health problem. Accessible, affordable, equitable and effective strategies are needed to reduce this burden across the life-course.

ABSTRACT

Asthma, hay fever and eczema are three common chronic conditions. There are no recent multi-country data on the burden of these three conditions in adults; the aims of this study are to fill this evidence gap.

The Global Asthma Network (GAN) Phase I is a multi-country cross-sectional population-based study using the same core methodology as the International Study of Asthma and Allergies in Childhood (ISAAC) Phase III. It provides data on the burden of asthma, hay fever, and eczema not only in children and adolescents but also for the first time in their parents/guardians.

Data were available from 193,912 adults (104,061 female; mean age 38 (SD 7·5)) in 43 centres in 17 countries. The overall prevalences (range) of symptoms of current wheeze, asthma ever, hay fever ever and eczema ever were 6·6% (0·9% -32·7%), 4·4%(0·9% -29·0%), 14·4%(2·8%-45·7%), and 9·9%(1.6%-29.5%), respectively. Centre prevalence varied considerably both between countries and within countries. There was a moderate correlation between hay fever ever and asthma ever, and between eczema ever and hay fever ever at the centre level. There were moderate to strong correlations between indicators of the burden of disease reported in adults and the two younger age groups.

We found evidence for a substantial burden of asthma, hay fever ever and eczema ever in countries examined highlighting the major public health importance of these diseases. Prevention strategies and equitable access to effective and affordable treatments for these three conditions would help mitigate the avoidable morbidity they cause.

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INTRODUCTION

Asthma, hay fever and eczema are three common chronic conditions that typically start in childhood and often continue across the life-course [1]. All three conditions cause considerable morbidity globally especially when basic effective treatments are unavailable [2]. Asthma is an important cause of avoidable mortality [3].

The International Study of Asthma and Allergies in Childhood (ISAAC) investigated the symptom prevalence and determinants of asthma, rhinoconjunctivitis and eczema in school children on two previous occasions (ISAAC Phase I in 1993-5 and ISAAC Phase III in 2001-3) [4-15]. The Global Asthma Network (GAN) subsequently continued the work of ISAAC through the centres of ISAAC and new centres that are interested in GAN Phase I, which is a multi-country population-based cross-sectional study designed to assess the three conditions, as well as severity, management and risk factors in 13-14-year-old adolescents, 6-7-year-old children, and their parents/guardians using the same methods of ISAAC Phase III [16].

There has been no large survey on the prevalence of asthma in adults since WHO implemented the World Health Survey (WHS) in 2002 and 2003 [17], and no such surveys for hay fever ever or eczema ever. In this paper we report data on the prevalence of asthma symptoms, hay fever ever and eczema ever in adults in GAN Phase I. We compare their global patterns, and contrast with those observed in children in the same populations.

METHODS

The GAN methodology has previously been published [16,18], and will only be briefly summarized here.

Participants

The adult participants were the parents (or guardians) of children and adolescents in GAN Phase I. Cluster sampling was applied to randomly select at least 10 schools from a geographically defined sampling frame. All schools were included if there were < 10 schools in the sampling frame. The compulsory age group was adolescents, who self-completed written questionnaires at school. Additional inclusion of 6-7-year-olds was optional. Optionally parents/guardians were also asked to complete similar questionnaires on their own health (the adult group), and the linkage between adults and children and adolescents was documented.

Questionnaires

Questionnaires for the adults were developed building on questionnaires used in ISAAC and the European Community Respiratory Health Survey [19,20]. The original questionnaire was in English; with translation to local languages and back-translation to English completed using a specific methodology common to ISAAC and GAN [16].

Definitions

Asthma:

"Current wheeze" was defined by a positive answer to the question "Have you had wheezing or whistling in the chest in the past 12 months?". "Severe asthma symptoms" were defined as those with current wheeze who, in the past 12 months, reported having had ≥4 attacks of wheeze, or >1 night per week sleep disturbance from wheeze, or wheeze affecting speech.

143 ‘‘Asthma ever’’ was defined as a positive answer to the question ‘‘Have you ever had
144 asthma?’’
145 Hay fever:
146 “Hay fever ever” was defined by a positive answer to the question: “Have you ever had hay
147 fever?”
148 Eczema:
149 “Eczema ever” was defined as a positive answer to the question: “Have you ever had
150 eczema?”
151
152 **Sample size and study power**
153 Sample sizes of at least 1000 and preferably 3000 were sought for the adolescents and
154 children within each centre [17]. A participation rate of at least 80% for the adolescents and
155 70% for the children was aimed for [21]. The actual response rate was 90% for adolescents
156 and 79% for children [22]. We were unable to calculate a conventional response rate for the
157 adults because some schoolchildren have only one parent or guardian and the number of
158 adults that received the questionnaire was not known. The estimated median participation
159 rate of adults, by using a “per child” approach [21], was 82·9%, range 30·2% - 100%, with 4
160 centres unable to be calculated due to insufficient information.
161
162 **Data handling and analysis**
163 All centres submitted their datasets and a Centre Report documenting the methodology
164 used to the GAN Global Centre in Auckland (New Zealand) [16]. A first quality control check
165 was performed together with a careful review of the Centre Report for adherence to
166 protocol. Depending on the language used locally, the dataset was then sent to one of the
167 two GAN data centres in either Murcia (Spain) (Spanish and Portuguese speaking centres) or
168 London (United Kingdom) (all other languages), for a standardised and coordinated data

check. Centres reported in this analysis are any centres that were included in the analysis of data from children and adolescents [18] that also collected data from adults. For prevalence estimations, positive answers to a specific symptom in the centre was divided by the number of completed questionnaires.

Global national income (GNI) category for each country was calculated using cut-off points provided by the World Bank in June 2020 [23], and countries were classified into high income country (HIC), upper middle income country (U-MIC) and, lower middle/low income country (L-MIC/LIC). The Spearman correlation coefficient was used to estimate the correlation between symptoms of different conditions and between age groups using centre level data. The correlation was defined as strong if correlation coefficient ≥0.7, moderate if ≥0.4 but <0.7, and weak if <0.4. Multilevel log-binomial regression was used to estimate how much of the variability of each symptom's prevalence was dependent on centre-level variation, additional to within-centre binomial sampling error. As the intraclass correlation coefficient was higher than 5% (ICC>0.05) in the null model in all instances, multilevel models fitting centre as a random effect were used to estimate the effect of sex and GNI in the prevalence of symptoms of the three conditions. A uniform approach to data processing, checking and analysis was used, using Stata versions 13–15 (Stata Corp LLC, College Station, Texas, USA).

Centre funding and ethics

All centres in GAN Phase I obtained their own funding and applied for ethics approval from their local ethics committee before starting the study.

Role of the funding source

The funding sources had no role in study design; collection, analysis, and interpretation of data; writing of the report; or the decision to submit the paper for publication.

RESULTS

Data were collected from 193,912 adults (104,061 female; mean (SD) age 38 (7·5); 5·0% >50 year-old; 16·8% current smokers; 47.2% parents of adolescents) in 43 centres (including 12 ISAAC Phase I and 19 ISAAC Phase III centres) in 17 countries between 2015 and 2020 (Web Tables 1-2). The prevalence of current wheeze was highest (10·6%, 95% Confidence Interval (CI): [10·2%, 10·9%]) among participants from HICs, followed by 8·4% [8·2%, 8·6%] among participants from U-MICs, and 3·6% [3·5%, 3·8%] among participants from L-MICs/LICs (Table 1). Similar trends across GNI categories were noted for asthma ever, severe asthma symptoms and hay fever ever with the exception of eczema ever which was lowest in U-MICs.

Asthma

The prevalence of asthma ever was 4·4%, ranging from 0·9% in Gjilan and Ferizaj, Kosovo to 29·0% in Costa Rica. Heterogeneity was high both between countries and between centres within countries (Figure 1, Web Table 1, and Web Figures 1-2). Centre level variation explained 21·8% of the variability of the prevalence in the multilevel analysis. Adult females had a higher prevalence of asthma ever than males (4·8% vs 3·9%; aRR for males 0·85, 95% CI: [0·82, 0·89]).

The overall prevalence of current wheeze was 6·6%, ranging from 0·9% in New Delhi, India to 32·7% in Tegucigalpa, Honduras. Heterogeneity of the prevalence of current wheeze was high (Figure 2, Web Table 1, and Web Figures 1-2). Centre level variation explained 13·1% of the variability of the prevalence of current wheeze in the multilevel analysis. Adult females had a higher prevalence of current wheeze than males (6·8% vs 6·2%; aRR for males 0·97, 95% CI: [0·94, 1·00]).

The prevalence of severe asthma symptoms was 2·6%, ranging from 0·2% in Bikaner, India to 20·9% in Tegucigalpa, Honduras. The prevalence of severe asthma symptoms among those who reported current wheeze was 39·0%, ranging from 15·0% in Bikaner, India to 63·9% in Tegucigalpa, Honduras (Web Table 1, and Web Figures 1-2). Centre level variation accounted for 17·0% of the variability of the prevalence of severe asthma symptoms. Adult females had a higher prevalence of severe asthma symptoms than males (2·9% vs 2·2%; aRR for males 0·83, 95% CI: [0·82, 0·90]).

Hay fever

The prevalence of hay fever ever was 14·4%, ranging from 2·8% in Ibadan, Nigeria to 45·7% in Bangkok, Thailand (Figure 3, Web Table 1, and Web Figures 1-2). Centre level variation explained 21·8% of the variability of the prevalence of hay fever ever. The prevalence of hay fever ever was higher in females than males (14·7% vs 14·0%; aRR for males 0·92, 95% CI: [0·90, 0·93]).

Eczema

The prevalence of eczema ever was 9·9%, ranging from 1·6% in Tijuana, Mexico to 29·5% in Bangkok, Thailand (Figure 4, Web Table 1, and Web Figures 1-2). Centre level variation explained 19·6% of the variability of the prevalence of eczema ever. The prevalence of eczema ever was higher in females than males (10·0% vs 9·9%; aRR for males 0·90, 95% CI: [0·88, 0·93]).

Correlations of prevalence between the three conditions

There was moderate correlation between the prevalence of hay fever ever and asthma ever (Rho: 0·54, 95% CI: [0·32, 0·76]), and between eczema ever and hay fever ever (0·66 [0·48,

0·83]), but no significant correlation between asthma ever and eczema ever (0·13 [-0·19, 0·45]) at the centre level (Figure 5). The correlation between the prevalence of hay fever ever and asthma ever and between the prevalence of eczema ever and hay fever ever remained after stratification by sex (Web Figure 3).

Relationship between age groups

There was strong correlation between the prevalence of asthma ever in adults vs adolescents (Rho: 0·87, 95%CI: [0·79, 0·95]), between asthma ever in adults vs children (0·83 [0·66, 1.00]), between current wheeze in adults vs adolescents (0·81 [0·68,0.94]), between severe asthma symptoms in adults vs adolescents (0·79 [0·67, 0·92]), between severe asthma symptoms in adults vs children (0·82 [0·65, 0·98]) between hay fever ever in adults vs adolescents (0·75 [0·57, 0·92]), between eczema ever in adults vs adolescents (0·87 [0·78, 0·95]), and between eczema ever in adults vs children (0·71 [0·51, 0.91]). There was moderate correlation between current wheeze in adults vs children, and between hay fever ever in adults vs children (Web Figure 4).

DISCUSSION

The major findings of GAN Phase I were: 1) the overall prevalence of symptoms of current wheeze, asthma ever, hay fever ever and eczema ever was 6·6%, 4·4%, 14·4%, and 9·9%, respectively; 2) centre prevalence varied considerably both between countries and within countries; 3) the burden of all three conditions was higher in females and in higher income countries; 4) there was a moderate correlation between hay fever ever and asthma ever, and between eczema ever and hay fever ever at the centre level; 5) there were moderate to strong correlations between the prevalence of asthma symptoms, hay fever ever and eczema ever reported in adults and the two younger age groups.

A multi-country survey on the prevalence of asthma in adults has been conducted previously by the European Community Respiratory Health Survey (ECRHS) in the 1990s [24]. The questions used in the ECRHS were “Have you had wheezing or whistling in your chest at any time in the last 12 months?” and “Have you had an attack of asthma in the last 12 months?” [25] The ECRHS reported large geographical variations in the prevalence of asthma [25]. The median prevalence of current asthma was 4·5% (range 2·0% -11·9%) in ECRHS stage one and 5·2% (range 1·2% – 13·0%) in ECRHS stage two [26]. Females had a higher prevalence of current asthma than males and the prevalence of wheeze was negatively associated with age. The ECRHS concluded that the geographical variations in the prevalence of asthma were most likely due to environmental factors [26]. The WHS enrolled 308,218 adults aged ≥18 years from 64 countries [17]. The WHS defined current wheeze symptoms as a positive response to any of the symptom questions: “during the last 12 months, have you experienced any of the following: 1) attacks of wheezing or whistling breathing? (yes/no); or 2) attacks of wheezing that came on after you stopped exercising or some other physical activity? (yes/no)”. The WHS reported that global prevalence of current wheeze symptoms

289 was 9·2%, ranging from 2·4% in Vietnam to 24·0% in Brazil. The prevalence of current
290 wheeze symptoms increased with age, was higher among male than female, more common
291 in smokers than nonsmokers, and was relatively high in HICs and LICs, and relatively low in
292 MICs [17]. In our survey, the prevalence of asthma ever varied markedly between centres as
293 did the prevalence of current wheeze symptoms with less variability within countries than
294 seen in children and adolescents. Current severe asthma symptoms were commonly
295 reported (range: 15·0% – 63·9%) amongst participants reporting wheeze in the past 12
296 months across all centres suggesting a concerning level of poor asthma control [27]. There
297 was a clear association between GNI category and the prevalence of current wheeze was
298 highest in HICs and lowest in L-MICs/LICs, similar to the pattern seen of a lower prevalence
299 of current wheeze symptoms in children and adolescents in L-MICs/LICs [18]. Asthma
300 symptoms were more common in females as seen in the adolescent group and other studies
301 of older children [4,28] and the ECRHS. The WHS reported that males were more likely to
302 report current wheeze symptoms, perhaps because its study population was older (34%
303 aged >50 years), and 30% were smokers, thus may have wheeze due to chronic obstructive
304 pulmonary disease. Whether the difference between our findings and that of WHS with
305 regards to GNI was attributable to differences in definitions (e.g. of symptoms), study
306 population, different prevalence of environmental risk factors and genetic backgrounds
307 requires further investigation.
308
309 The ECRHS reported that the median prevalence of nasal allergy and hay fever was 20·9%
310 (range 9·5% - 40·9%) [26]. Subjects with perennial rhinitis were more likely to have current
311 asthma. In our study, the prevalence of hay fever ever was 14·4% but was variable (from
312 2·8% in Ibadan, Nigeria, to 45·7% in Bangkok, Thailand) with less variability within countries.
313 This was also seen in children and adolescents as was an association between hay fever and
314 GNI categories with the greatest burden seen in HICs [18]. Consistent with the ECRHS, our

study shows moderate correlation between the prevalence of hay fever ever and asthma ever.

The overall prevalence of eczema ever was 9·9% but varied from 1·6% in Tijuana, Mexico, to 29·5% in Bangkok, Thailand, with less variability within countries. We did find an association between eczema ever and GNI categories with the greatest burden seen in HICs, which was also seen in children and adolescents in GAN Phase I [18]. In previous ISAAC surveys, the adolescents in GAN Phase I, as well as in other cohort studies, a difference between sexes (more prevalent in females) was found [7,18,29,30] and we found the same in this study of adults. No significant correlation between the prevalence of asthma ever and eczema ever in adults was identified. As eczema tends to occur in early stage of life and decreases with age [31], whether this was in part due to recall bias was unknown.

There was considerable variation in prevalence of all three conditions in adults, which is partly accounted for by centre level variation. We speculate that the difference in the prevalence of risk factors may contribute to the difference in observed prevalence between centres and countries; risk factors associated with the three conditions collected as part of GAN Phase I will be analysed and reported separately, which should provide more insight into this issue. We found moderate to strong correlations between the prevalence of asthma symptoms, hay fever ever and eczema ever reported in adults and the two younger age groups, likely indicating that parents/guardians and the two younger age groups have similar environmental and genetic risk factors of the three conditions.

The strengths and weaknesses of the ISAAC and GAN Phase I methodology have been discussed in depth [4] and have been previously summarised elsewhere [16,18]. We acknowledge limitations of the small number of GAN Phase I centres vs ISAAC Phase I and III,

the self-selection of centres potentially limiting representativeness, challenges of inferring clinical diagnoses from self-reporting via questionnaires (e.g. risk of recall bias and lack of direct physician diagnoses), difficulties around the translation of concepts such as "wheezing" into different languages. Furthermore, we did not collect information on current symptoms of hay fever and eczema, but only information of hay fever ever and eczema ever, which may not represent current prevalences of hay fever and eczema because both conditions may remit during adolescence. Moreover, it is possible that parents of children with hay fever or eczema may be more aware of these two conditions and more likely to report having hay fever ever or eczema ever than parents of children with no hay fever or eczema; such potential recall bias may affect the correlation of the prevalence of hay fever ever and eczema ever between children and adults. There was difficulty in obtaining a high response rate for some centres [22]. The correlation analysis is an ecologic analysis (at centre level) and these correlations may not hold at the individual level. Key additional strengths are the linkages between the child, adolescent and adult participants that have enabled additional analyses including exploring the relationship between symptoms reported by the different age groups. However, recruiting the parents of the child and adolescent participants will have led to a degree of selection bias and the included adult population may not be fully representative of the local population in terms of factors including age and socioeconomic status.

In conclusion, the present study offers a unique picture of current symptoms related to asthma, and lifetime history of asthma, hay fever and eczema. Our findings in adults were largely consistent with our findings in children and adolescents (particularly) [18] and the burden of the three conditions seems to correlate across the three age groups. Further studies are needed to confirm whether findings from one group may be cautiously extrapolated to the others.

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ILLUSTRATIONS

Figure 1

Map of the prevalence of asthma ever. The symbols indicate prevalence values of <5% (blue squares), 5 to <10% (green circle), 10 to <20% (yellow diamonds) and ≥20% (red stars).

Figure 2

Map of the prevalence of current wheeze. The symbols indicate prevalence values of <5% (blue squares), 5 to <10% (green circle), 10 to <20% (yellow diamonds) and ≥20% (red stars).

Figure 3

Map of the prevalence of hay fever ever. The symbols indicate prevalence values of <5% (blue squares), 5 to <10% (green circle), 10 to <20% (yellow diamonds) and ≥20% (red stars).

Figure 4

Map of the prevalence of eczema ever. The symbols indicate prevalence values of <5% (blue squares), 5 to <10% (green circle), 10 to <20% (yellow diamonds) and ≥20% (red stars).

Figure 5

Rank correlation values and scatter plots of prevalence of the three conditions at the centre level. The dashed line is the identity line. Rank correlation coefficient and 95%CI is shown in each graph.

Web Figure 1

Ranking of centres for the symptom prevalences of current wheeze, asthma ever, hay fever ever and eczema ever.

Web Figure 2

Ranking of centres for the symptom prevalences of current wheeze, asthma ever, hay fever ever and eczema ever by sex (males on left).

Web Figure 3

Rank correlation values and scatter plots of prevalence of the three conditions at the centre level by sex (males on left). The dashed line is the identity line. Rank correlation coefficient and 95%CI is shown in each graph.

Web Figure 4

Rank correlation comparing centre prevalence (%) of reporting current wheeze, asthma ever, severe asthma symptoms, hay fever ever and eczema ever between the three age groups (children, adolescents, adults) included in GAN Phase I. The dashed line is the identity line. Rank correlation coefficient and 95%CI is shown in each graph.

TABLES

Table 1

Symptom prevalence of asthma, hay fever and eczema in centres grouped by Gross National Income (GNI).

Web Table 1

Demographic summary by centre.

Web Table 2

Symptom prevalence of asthma, hay fever and eczema by centre.

Authors individual contributions

The following individual contributions were made: conceptualisation IA, KB, C-YC, AES, PE, LG-M, GM, NP, DS; data curation EE, PE, LG-M, EM, VP-F, CR, SR, RS, ML; verification of the underlying data CR, NP, VP-F, DS; formal analysis ML, NP, CR, DS; investigation IA; methodology IA, C-YC, PE, LG-M, NP, CR, DS, RS; project administration, IA, EE; PE; resources IA; supervision LG-M, NP, DS, RS; validation PE; visualisation EE, PE, CR; writing – original draft KM, C-YC; writing – review/editing IA, GM, AM-T, SR, CR, KB, AES, EE, PE, LG-M, EM, VP-F, NP, DS, RS, ML and the Global Asthma Network Phase I Study Group; the latter contributed original data to the analyses.. All authors shared responsibility for the decision to submit the manuscript.

Declaration of interests

The authors declare that they have no conflict of interest.

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469

470 **Data sharing**

471 The study protocol including a recommended informed consent form and statistical analysis
472 plan are in the public domain (http://globalasthmanetwork.org/surveillance/

surveillance.php). The GAN Phase I data, including de-identified individual participant data, will be password protected and made available on the Global Asthma Network website http://www.globalasthmanetwork.org/ within 12 months of all GAN Phase I analyses being published. Access for non GAN researchers will require a formal request to the GAN Steering Group for consideration, by submission of a written proposal and on acceptance, a signed data access agreement.

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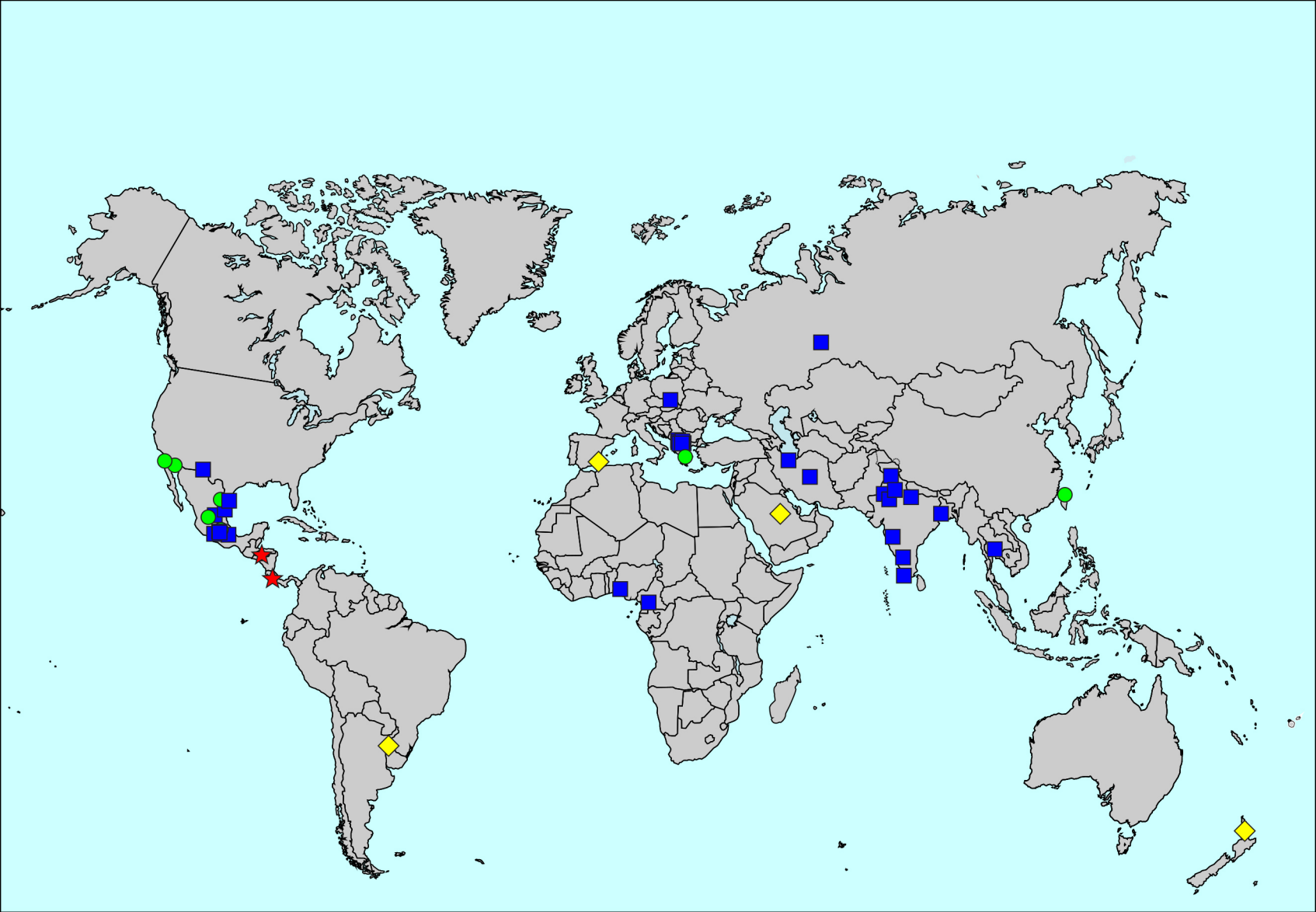
662

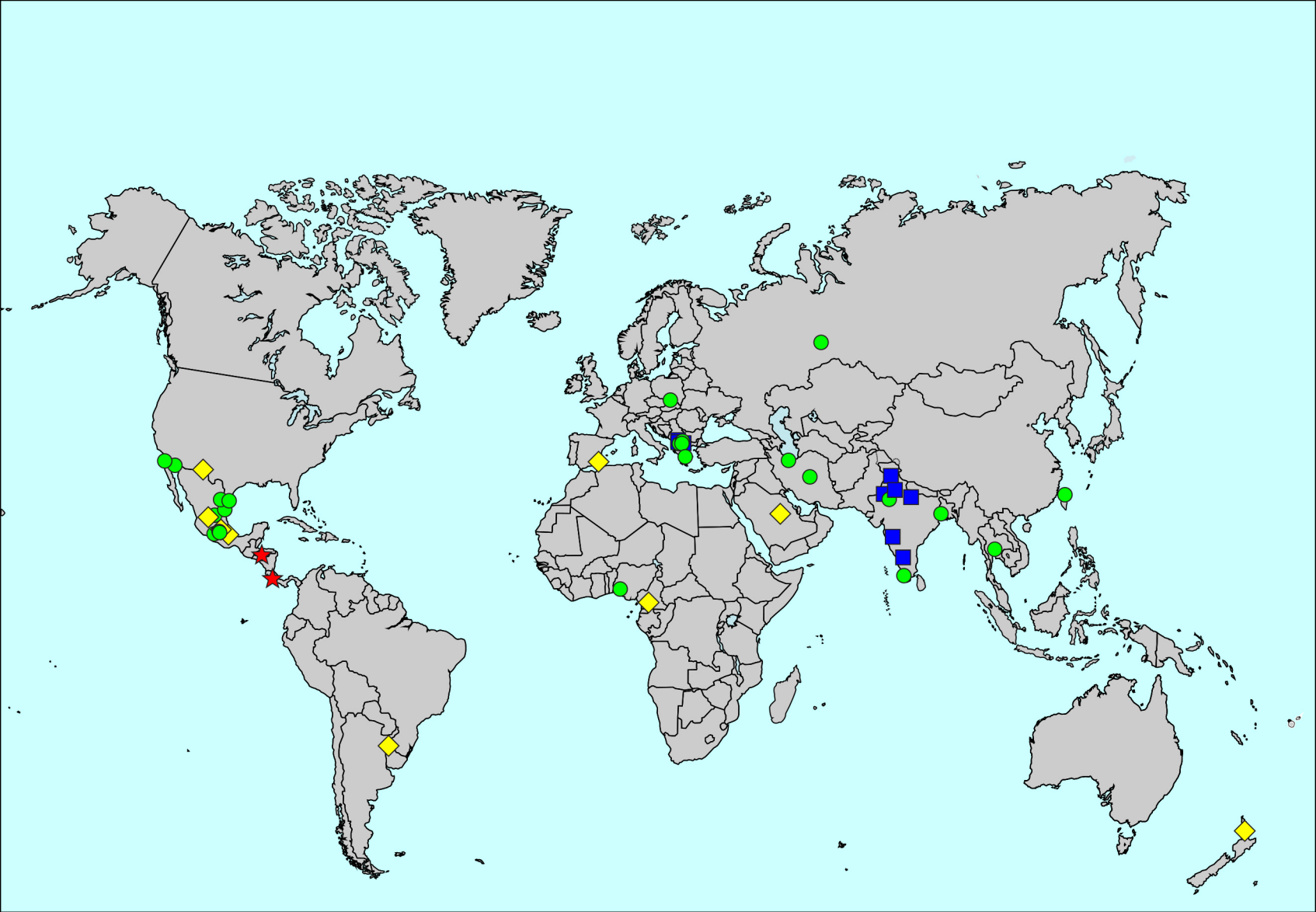
Table 1: Prevalence of asthma, hay fever and eczema in centres grouped by Gross National Income (GNI)

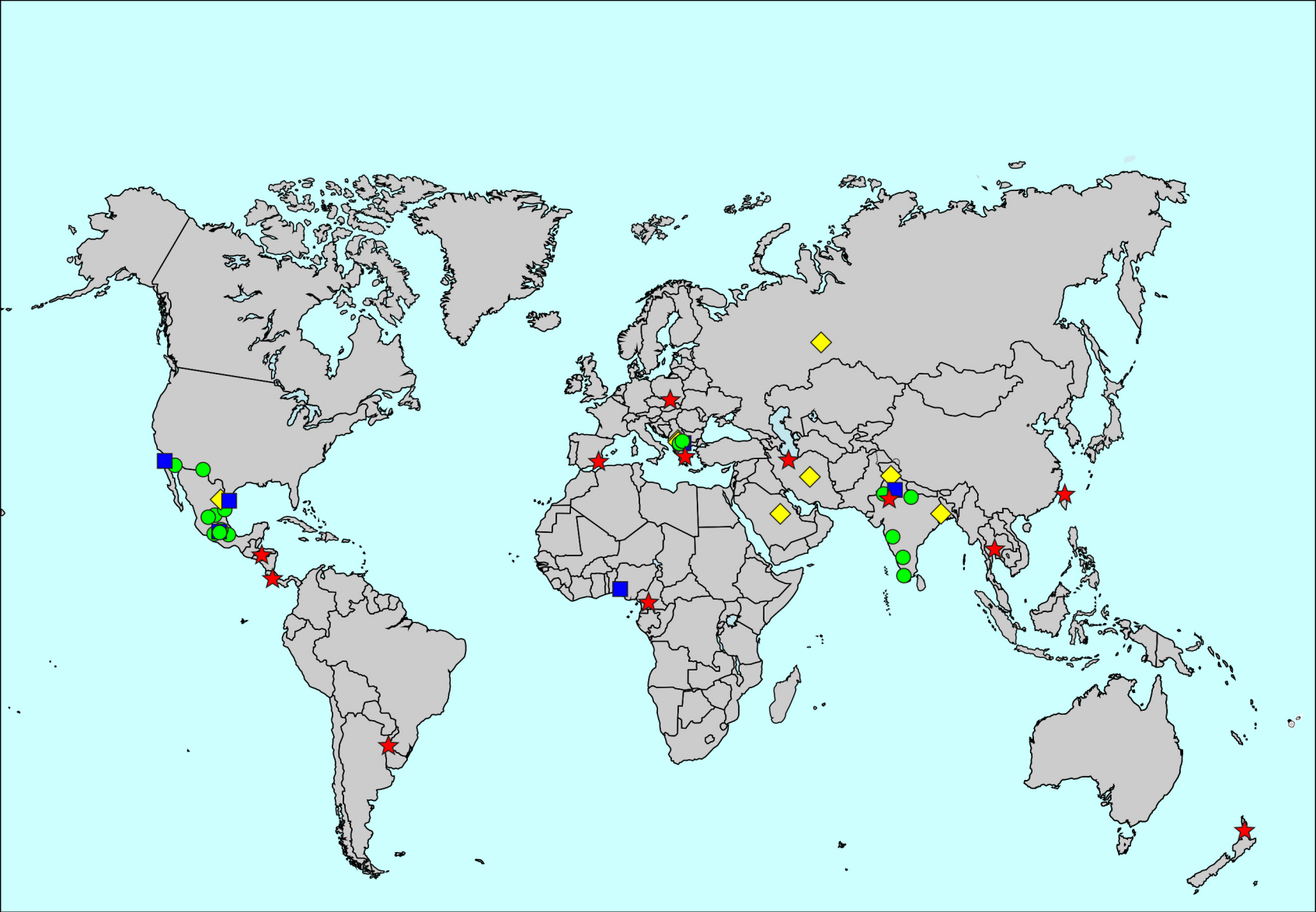
GNI	Years	Centres	No.	Current wheeze	Asthma ever	Severe asthma symptoms*	Severe asthma symptoms* (population denominator)	Eczema ever	Hay fever ever
High	2015-20	6	30556	3231 (10.6%)	3106 (10.2%)	1179 (36.5%)	1179 (3.9%)	5081 (16.6%)	9453 (30.9%)
Upper middle	2015-20	15	74897	6299 (8.4%)	3502 (4.7%)	2669 (42.4%)	2669 (3.6%)	5377 (7.2%)	9736 (13.0%)
Lower middle/Low	2017-19	12	88459	3208 (3.6%)	1926 (2.2%)	1161 (36.2%)	1161 (1.3%)	8791 (9.9%)	8695 (9.8%)
Total		33	193912	12738 (6.6%)	8534 (4.4%)	5009 (39.3%)	5009 (2.6%)	19249 (9.9%)	27884 (14.4%)

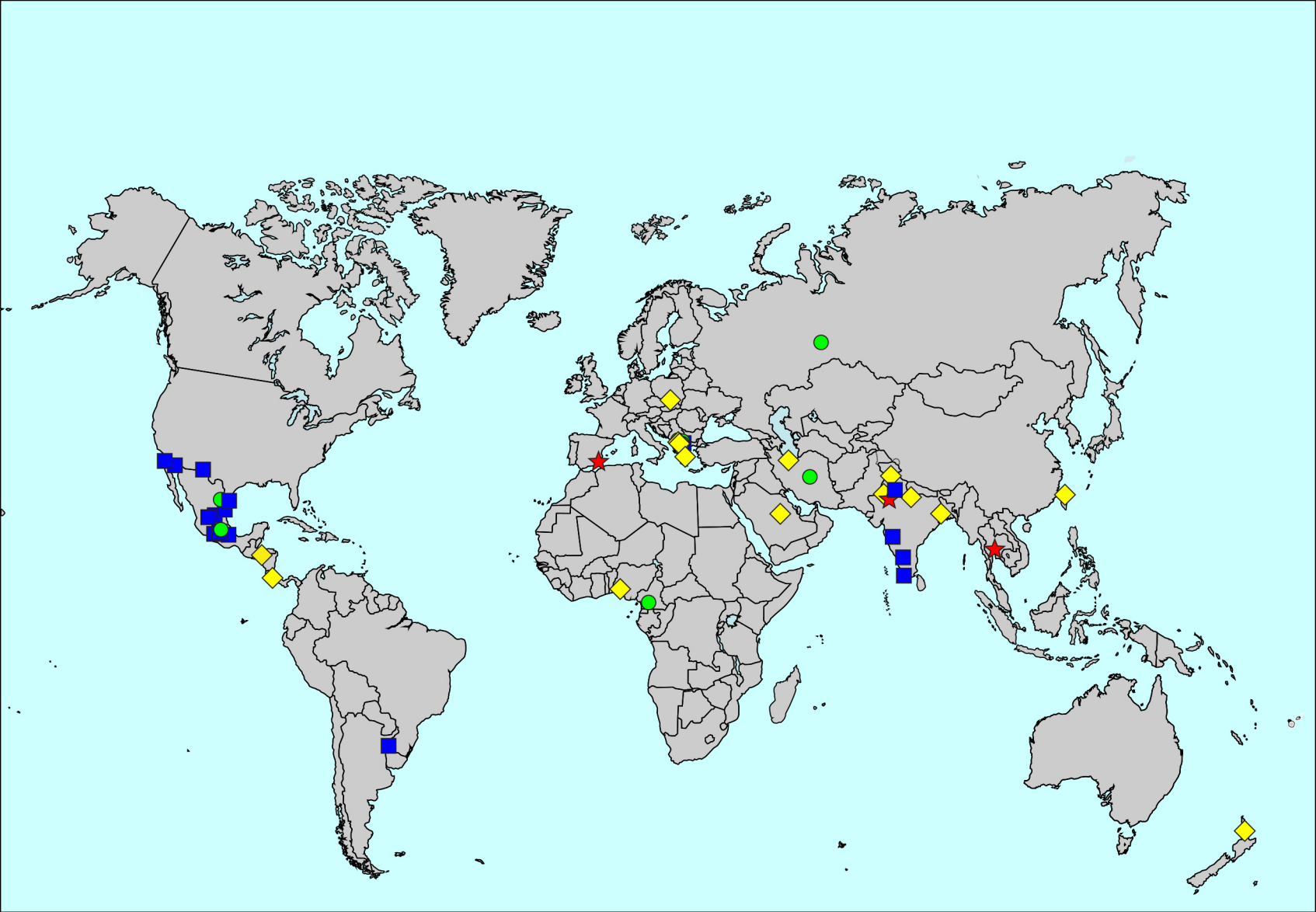
All values as number and (percentage), P-values for comparison between GNI categories: Current wheeze <0.0001, Asthma ever <0.0001, Severe asthma symptoms <0.0001, Severe asthma symptoms (population denominator) <0.0001, eczema ever <0.0001, hay fever ever <0.0001. Test by Chi-square.

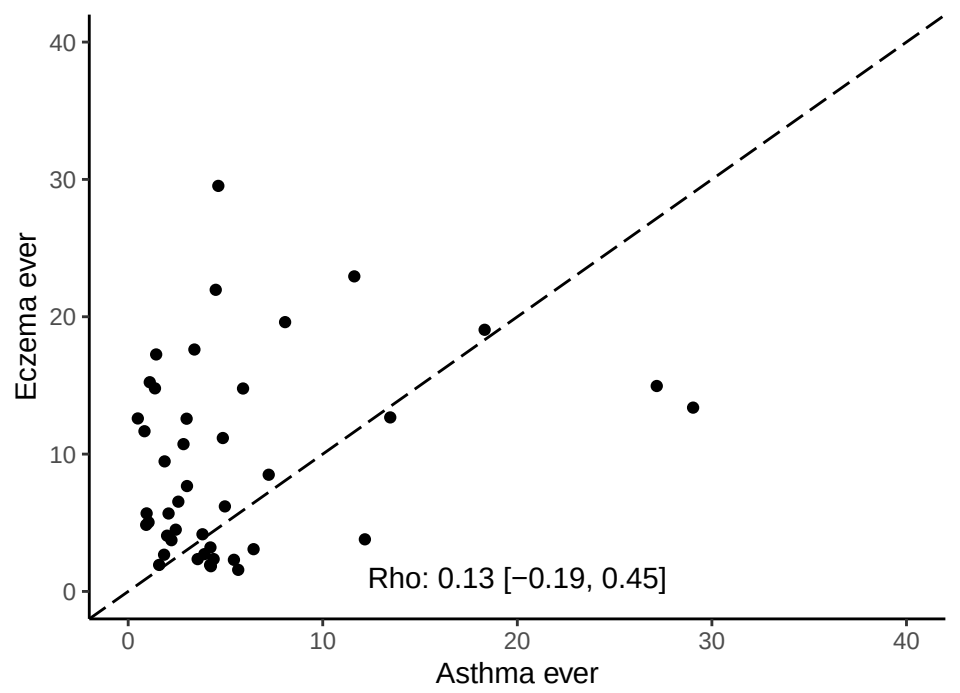
* Current wheeze denominator; †Total participants denominator

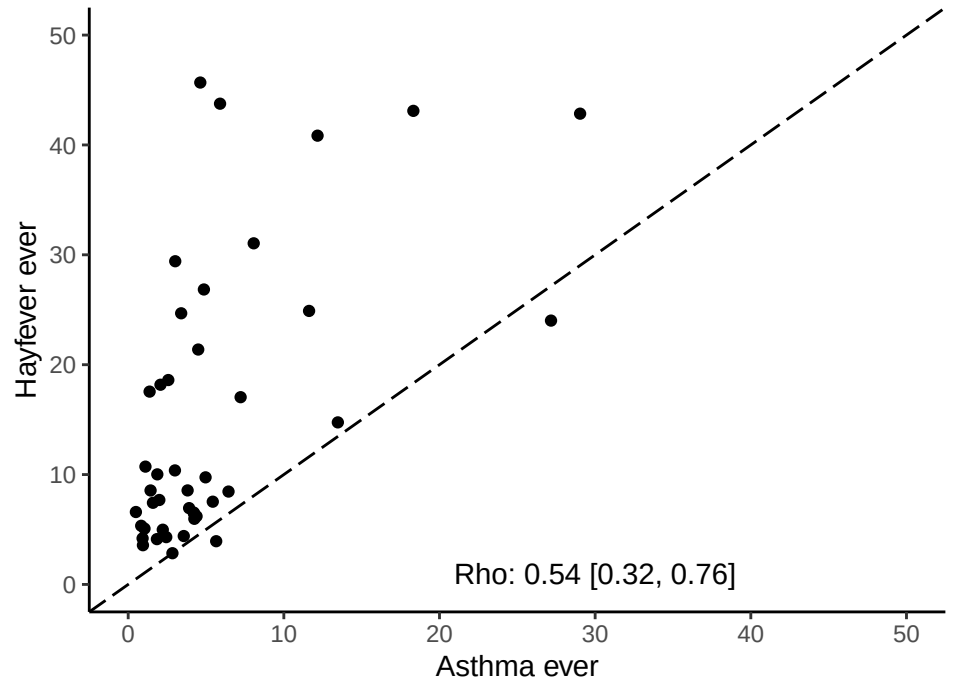


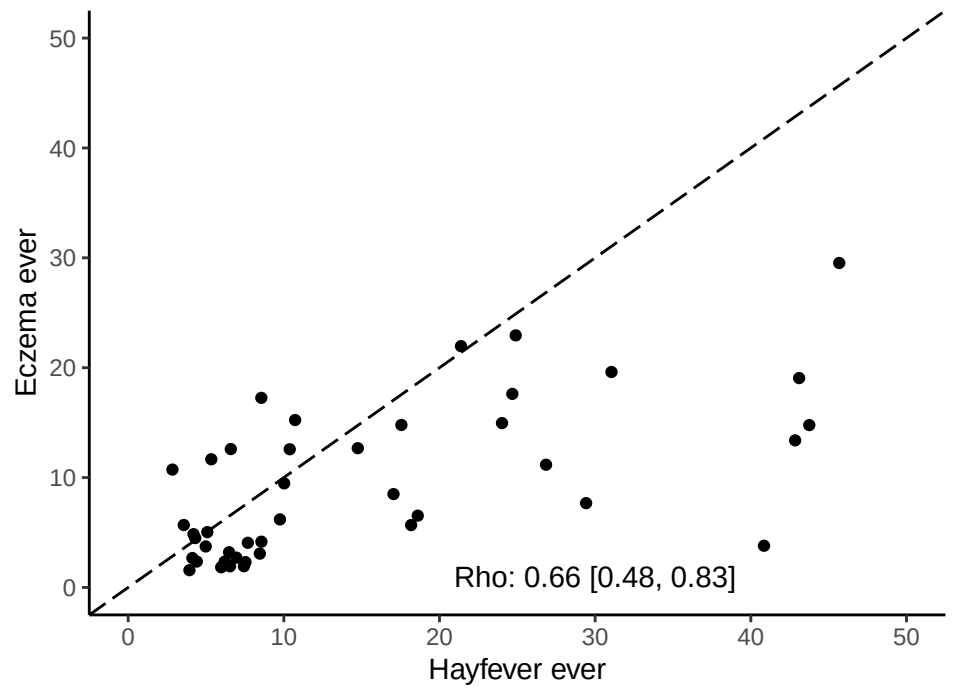







Eczema ever
Asthma ever
Rho: 0.13 [−0.19, 0.45]
0
10
20
30
40


Hayfever ever
Asthma ever
Rho: 0.54 [0.32, 0.76]
0
10
20
30
40
50


Eczema ever
Hayfever ever
Rho: 0.66 [0.48, 0.83]
0
10
20
30
40
50