Title Global Asthma Network Phase I surveillance: geographical coverage and response rates.

Authors Ellwood P^{1*}, Ellwood E¹, Rutter CE², Perez-Fernandez V³, Morales E⁴, Garcia-Marcos L³, Pearce NE^{2,5}, Asher MI¹, Strachan DP⁶ and the GAN Phase I Study Group[#]

* Corresponding author

[#] The GAN Phase I Study Group is listed at the end of the manuscript

¹ Department of Paediatrics: Child and Youth Health, Faculty of Medical and Health Sciences, University of Auckland, New Zealand

² Department of Medical Statistics, London School of Hygiene and Tropical Medicine, London, United Kingdom

³ Pediatric Allergy and Pulmonology Units, 'Virgen de la Arrixaca' University Children's Hospital, University of Murcia, ARADyAL network and Biomedical Research Institute of Murcia (IMIB-Arrixaca), Murcia, Spain

⁴ Biomedical Research Institute of Murcia (IMIB-Arrixaca) and Department of Public Health Sciences, University of Murcia, Murcia, Spain

⁵ Centre for Global NCDs, London School of Hygiene and Tropical Medicine, London, United Kingdom ⁶ Population Health Research Institute, St George's University of London, London, United Kingdom

Author contributions

Study design – PE, EE, MIA, LGM, NEP, DPS, GAN Steering Group Conduct – PE, all study centres Analysis – CR, VPF, EM, EE Writing lead – DPS Review of manuscript – all named authors

Abstract

Background – The Global Asthma Network (GAN) Phase I is surveying school pupils in high-income and low- or middle-income countries using International Study of Asthma and Allergies in Childhood (ISAAC) methodology.

Methods – Cross-sectional surveys of participants in two age groups in randomly selected schools within each centre (2015-2020). 13-14 years (adolescents) are the compulsory age group, optionally including parents or guardians. 6-7 years (children) and their parents are also optional. Adolescents completed questionnaires at school, and took home adult questionnaires for parent/guardian completion. Children took home questionnaires for parent/guardian completion about the child and also adult questionnaires. Questions related to symptoms and risk factors for asthma and allergy, asthma management, school/work absence and hospitalisation.

Results – 53 centres in 20 countries completed quality checks by 31 May 2020. These included 21 centres that previously participated in ISAAC. There were 132,748 adolescents (average response rate 88.8%), 91802 children (average response rate 79.1%), and 177,622 adults, with >97% answering risk factor questions and >98% answering questions on asthma management, school/work absence and hospitalisation.

Conclusion – The high response rates achieved in ISAAC have generally been maintained in GAN. GAN Phase I surveys, partially overlapping with ISAAC centres, will allow within-centre analyses of time-trends in prevalence.

Introduction

The Global Asthma Network (GAN) [1,2] was formed in 2012 as a joint initiative by members of the International Study of Asthma and Allergies in Childhood (ISAAC) and the International Union Against Tuberculosis and Lung Disease, following their co-production of the first Global Asthma Report (GAR), launched in 2011 at the time of the United Nations high-level meeting on non-communicable diseases [3]. Estimates of the worldwide burden of asthma in that report were based very largely on the ISAAC Phase III surveys (2001-2003) of 13-14-year-olds (adolescents) and 6-7-year-olds (children) [4], with time trends from centres which also participated in ISAAC Phase I (1994-1995) [5], plus the World Health Surveys of adults (2002-2003) [6]. The need for updated surveillance of asthma prevalence, severity, diagnosis and management, highlighted in GAR 2011 [3], has become more pressing since then [7], as very few studies anywhere in the world have evaluated trends in asthma prevalence and related risk factors over the last decade [8].

GAN Phase I was developed to address this information gap, with these hypotheses:

- 1) globally, the burden of asthma is changing in adults and children;
- 2) there is large variation in the diagnosis of asthma;
- 3) in many locations, asthma is under-diagnosed and its management is suboptimal; and
- 4) there are potentially modifiable risk factors for asthma.

Its aims were:

- 1) to conduct asthma surveillance around the world in two age groups of school pupils, and their parents, measuring prevalence, severity, management and risk factors, following the methods of ISAAC Phase III;
- 2) to examine time trends in prevalence, severity, management and risk factors from centres which completed ISAAC Phase III; and
- 3) to evaluate the appropriateness of asthma management, especially access to quality-assured essential asthma medicines, as defined by WHO [9].

Although modelled closely on the study design and methodology of ISAAC Phase III, GAN Phase I has extended its scope to include adults, for whom there are limited global data on asthma prevalence [8], severity and risk factors, and to assess asthma management, which is commonly suboptimal in low-income settings [7]. This paper summarises the progress of GAN Phase I at 31 May 2020, when the dataset was temporarily frozen for the first round of analyses including centres which completed the quality checks by this date.

Methods

GAN has collaborators from 383 centres in 137 countries all of whom answered the call for an Expression of Interest (EOI). Of the EOIs, 136 centres in 58 countries registered to participate in GAN Phase I. Of these registered centres some have completed GAN Phase I and provided data to this study, while some, because of timing, will be included in later publications. Other centres have been unable to undertake Phase I at all because of unforeseen circumstances. Many centres in each of these categories have contributed to other published GAN surveys [10-13].

GAN Phase I is a cross-sectional, multi-centre, multi-country study undertaken between 2015-2020. Its methodology has been described and justified elsewhere [2] and detailed in an online manual [14]. Each centre was required to obtain approval from their local ethics committee prior to the start of their study.

Briefly, each GAN centre is based on a defined geographical area, within which a minimum of 10 schools were selected at random (or all schools, if less than ten). All students of a specified age within these schools were studied, selected by grade/level/year, or by chronological age. The sample size estimates of 1000-3000 are stringent because of the number of hypotheses being tested, and high response rates are sought. As in ISAAC, two age groups of school pupils participated: adolescents and children. Centres that undertook ISAAC Phase III and/or ISAAC Phase I were expected to use the same study design and sampling frame in GAN. As in ISAAC Phase III, translations into the local language were required and centres followed the ISAAC protocol for translation, back translation to English, and comparison between the two [15].

The compulsory age group was adolescents, who self-completed written questionnaires at school. Additionally, in some centres, the ISAAC international video questionnaire showing different scenes of asthma in children of a variety of ethnicities was shown [16]. A self-completed risk factor questionnaire, developed for ISAAC Phase III, was strongly recommended in this age group. In ISAAC surveys, there was no contact with the parents of the adolescent age group, but for GAN, it was recommended (but not essential) that the parents/guardians of the adolescents were also surveyed.

This optional parental questionnaire obtained information on the prevalence of asthma, rhinitis and eczema symptoms among adults, plus questions on asthma management and risk factors. The adult symptoms questionnaire combined items from ISAAC and the European Community Respiratory Health Survey (ECRHS) [17] to cover the range of chest symptoms and diagnoses that might be related to asthma in young and middle-aged adults.

Optional was inclusion of children, as with ISAAC Phase III, who took written questionnaires home to be completed by their parents. These included the ISAAC questionnaire on the child's symptoms used in Phases I and III, and the risk factor questionnaire used in Phase III. In GAN it was recommended (but not essential) to add the parental questionnaire to ascertain the prevalence of asthma, rhinitis and eczema symptoms among adults in the household.

Data from each centre were submitted to the GAN Global Centre (Auckland, New Zealand) together with a descriptive centre report. Following initial quality control checks in Auckland, the data were transferred to one of two designated GAN Phase I data centres for checking and analysis: Murcia (Spain) for Spanish- and Portuguese-speaking centres, and London (United Kingdom), for centres using all other languages. A harmonised approach to data processing, checking and analysis was developed, using Stata versions 13-15.

Estimation of participation rates among children and adolescents followed the conventions previously adopted in ISAAC Phase III. High levels of participation are sought as it is a concern that absent school pupils may be away from school due to symptoms of asthma, rhinitis or eczema. A participation rate of at least 80% for the adolescents and 70% for the children is desirable [2,14]. The denominator was the number of pupils in the cluster sample and the numerator was the number of core symptom questionnaires returned with at least some symptom data.

We were unable to calculate a conventional response rate for the adults as it was not known how many adults received questionnaires (because some schoolchildren have only one parent or guardian). Therefore, a "per child" approach was taken to estimate adult response rate, as follows. The denominator was the number of school-aged respondents (index schoolchildren) to whom one or more adult questionnaires were distributed. The numerator was the number of index schoolchildren for whom one or more adult questionnaires were returned. For centres which distributed adult questionnaires to both age groups of schoolchildren, the numerators and denominators were combined to derive a single estimate of "per child" adult response rate.

It was not possible to derive this measure of adult response rate for three centres (Costa Rica (whole country study), Guatemala City, Guatemala; Tegucigalpa, Honduras) where adult responses were not linked to the child identifier.

Results

By 31 May 2020, 53 centres in 20 countries had submitted and completed quality checks of data and methodology. Figure 1 shows the location of these centres, also 84 centres in 38 countries which formally registered an intention to complete GAN Phase I but were unable to do so, and the remaining GAN collaborating centres. Most centres completed their fieldwork before the onset of the COVID-19 pandemic, but surveys were still active in Iran (Yazd and Karaj) and Greece (Athens) in spring 2020, where fieldwork was truncated due to school closures in the pandemic lockdown.

Twenty-one of the 53 centres had previously participated in ISAAC Phase III (including 17 contributing data on both age groups) and 12 had previously participated in ISAAC Phase I (including 9 with data on both age groups). All of the 12 ISAAC Phase I centres except for Athens also participated in ISAAC Phase III. The geographical overlap between ISAAC and GAN centres is shown in Figure 2. Forty of the 53 GAN centres also contributed data on adult symptoms, risk factors and disease management, as summarised in Table 1.

Table 2 summarises the numbers of pupils and number of schools for which responses were received in GAN Phase I, by age group and questionnaire section (symptoms, risk factors, management and morbidity). When deriving the number of valid responses to the asthma management and asthmarelated morbidity questions, respondents who legitimately skipped these sections because they had answered negatively to asthma symptoms were included in the count of responders.

Overall, responses were received for 132,748 adolescents attending 1260 schools (with risk factor information on 99.3% and management/morbidity information on 98.8%) and 91802 children attending 1506 schools (with risk factor information on 99.3% and management/morbidity information on 99.5%). Additionally, there were responses for 177,622 adults, with risk factor information on 97.7% and 98.2% providing information on asthma management, work absence, or hospitalisation. These 177,622 adults relate to 100,011 school pupils that returned adult questionnaires, comprising 50,416 adolescents and 49,595 children.

The stringent response criteria were able to be met by 45 (85%) of the 53 GAN Phase I centres for adolescents, 33 (80%) of the 41 GAN Phase I centres for children and by 24 (65%) of the 37 GAN Phase I centres for adults. Lower rates in some centres occurred due to schools closing because of the COVID-19 pandemic. Table 3 compares the response rates for the core symptom questionnaires by age group for each GAN Phase I centre and the corresponding response rates in earlier ISAAC surveys, where relevant. Across all GAN centres, the mean participation rate was 88.8% for adolescents and 79.1% for children (compared to 88.0% and 84.5%, respectively, in ISAAC Phase III). For GAN Phase I centres which were also ISAAC Phase III centres, mean response rates were 90.0% for adolescents and 79.0% for children in GAN compared with 89.3% and 84.4% respectively in ISAAC Phase III. One or more responses to the adult symptom questionnaire were received from an average of 73.2% of households contacted.

Discussion

GAN Phase I has completed fieldwork with data and methodology quality checks in a large number of centres in both high-income and low- or middle-income countries including representation from all inhabited continents. This broad geographical coverage is expected to expand as a number of centres

have commenced fieldwork but not yet submitted completed data. However, four countries (India, Kosovo, Mexico and Spain) account for two-thirds of the datasets received by 31 May 2020 which may limit the international generalisability of the findings.

Overlap between ISAAC and GAN is less extensive than anticipated, but 21 diverse centres will provide local time-trends in disease prevalence. These within-centre trends can be used, with caution, to inform projections of trends in prevalence among the remaining centres in ISAAC Phase III, which offer a much more widespread international representation than has been achieved so far in GAN.

Careful checks of the methodology used (centre report and data checks), as with ISAAC, ensured clarity on how the study was actually done and any variations encountered. The high levels of responses achieved in ISAAC have generally been maintained in GAN, suggesting that estimates of prevalence and severity of asthma will be representative of the populations surveyed. Sample sizes in most centres achieved the recommended target of 3000 children per age group, leading to precise estimates of disease prevalence, but in a few centres the numbers of respondents are substantially lower (Table 2).

The response rate in both age groups in Guatemala was unusually low (Table 3) and we explored the possible reasons for this. In both age groups, questionnaires were sent home for completion by the parents, whereas in other centres, the adolescents self-completed the questionnaires in class. This probably explains the exceptionally low response rate among 13-14-year-olds in Guatemala.

Extension of ISAAC methodology to include questions about parental symptoms was an attempt to fill gaps in knowledge about the prevalence, severity, diagnosis and management of asthma and related risk factors among young and middle-aged adults. Parents of schoolchildren are not a random or representative sample of the adult population, but the high response rates achieved in many of the study centres suggest that useful results could be obtained in this manner. The total number of adult respondents in GAN (177,622) is comparable with two previous international studies of young and middle-aged adults, discussed below.

The ECRHS, (1991-1993) recruited 137,619 participants aged 20-44 years in 48 centres in 22 countries (including 5 non-European countries: Algeria, Australia, India, New Zealand, USA) [17]. The GAN adult questionnaire incorporates core ECRHS items, but the geographical overlap with ECRHS countries is limited. The World Health Survey (WHS, 2002-2003) interviewed 178,215 adults aged 18-45 years from 70 countries and included a few questions about asthma and related symptoms among a general health questionnaire [6]. Although there is better geographical overlap with GAN, at least at the country level, the WHS questionnaire lacks detail which limits the scope for historical comparisons with GAN data on asthma severity.

Among adolescents and children, ISAAC offered a global perspective on time trends in asthma prevalence from the mid-1990s to the early 2000s [5, 18] but very few ISAAC centres have repeated their local surveys subsequently, prior to GAN. In Brazil, adolescents in Curitiba, Recife and São Paulo were studied in ISAAC Phases I (1994) and III (2003) and again in 2012 [19] and in South Santiago, Chile, ISAAC Phases I and III were completed, and a further survey of asthma in adolescents completed in 2015 [20]. Three GAN Phase I studies with previous ISAAC data have been published: in Bangkok, Thailand, [21] and four Mexican centres [22, 23]. Time trends in these centres have been summarised elsewhere [8].

With the closure of this first round of data in GAN Phase I, these temporal and geographical comparisons can now be extended to a wider and more diverse range of study centres. These results will form the basis of analyses for journal publications in the near future. However, GAN centres that

were unable to meet the criteria for this first data compilation can still contribute results to future analyses and publications.

In summary, GAN Phase I offers, for the first time in nearly two decades, new standardised worldwide data on prevalence and severity of asthma in adolescents, children and adults. This will enable comparisons to be made over time, and contribute a new picture of the global burden of asthma, rhinoconjunctivitis and eczema. Not only will risk factors be examined, but also time trends in these, and global variation, shedding light on causation. The methodology which ISAAC started has a proven track record of over nearly 30 years, and now extends to adults (parents) as well as adolescents and children. The high response rates achieved in a range of settings are testimony to the feasibility of the approach and give confidence in the estimates obtained.

Acknowledgements

The GAN Global Centre in Auckland was funded by The University of Auckland, The International Union Against Tuberculosis and Lung Disease and Boehringer Ingelheim NZ. The London Data Centre was supported by a PhD studentship [to CR] from the UK Medical Research Council (grant number MR/N013638/1) and funding from the European Research Council under the European Union's Seventh Framework Programme (FP7/2007-2013, ERC grant agreement number 668954). The Murcia Data Centre was supported by the University of Murcia and by Instituto de Salud Carlos III, fund PI17/0170.

Individual centres involved in GAN Phase I data collection were funded by the following organisations: Brazil, Uruguaiana, Funded by Dr Marilyn Urrutia Pereira; Cameroon, Yaounde, funded by Elvis Ndikum (95%) and from family, friends (5%); Costa Rica, Guatamala, Honduras and Nicaragua partially funded by an unrestricted grant from Astra Zenica for logistic purposes. India; Kottayam, New Delhi, Chandigarh, Bikaner, Jaipur, Lucknow, Kolkata, Pune, Mysuru, GAN Phase I was undertaken by Asthma Bhawan in India which was supported by Cipla Foundation; Iran: Karaj, funded by the Alborz University of Medical Sciences; Kosovo, Gjakova, Municipality of Gjakova and the Directorate for Health and Education; Mexico, Puerto Vallarta Centro Universitario de la Costa, Universidad de Guadalajara; New Zealand, Auckland Asthma Charitable Trust; Nigeria, Ibadan, funded by National Institute for Health Research (NIHR) (IMPALA grant Ref 16/136/35) using UK aid from the UK Government to support Global Health Research; Poland, Katowice funded by the Medical University of Silesia; South Africa, Cape Town, SA Medical Research Council, Allergy Society of South Africa; Spain, Salamanca, Gerencia Regional de Salud. Junta de Castilla y León. España, Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica. (SEICAP); Sri Lanka; Anuradhapura, Peradeniya, University of Peradeniya, Peradeniya, Sri Lanka; Syria; Damascus, Lattakia, Damascus: Syrian Private University, Lattakia: Lattakia Medical Syndicate.

GAN Phase I Study Group

Global Asthma Network Steering Group: I Asher, University of Auckland, Auckland, New Zealand; N Billo, Joensuu, Finland; K Bissell, School of Population Health, University of Auckland, Auckland, New Zealand; Chiang C-Y, Division of Pulmonary Medicine, Department of Internal Medicine, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan; A El Sony, The Epidemiological Laboratory for Public Health and Research, Khartoum, Sudan; P Ellwood, University of Auckland, Auckland, New Zealand; L García-Marcos, Virgen de la Arrixaca University Children's Hospital, Murcia, Spain; J Mallol, University of Santiago de Chile (USACH), Santiago, Chile; G Marks, University of New South Wales, Sydney, Australia; K Mortimer, Liverpool School of Tropical Medicine and Aintree University Hospital NHS Foundation Trust, Liverpool, United Kingdom; N Pearce, London School of Hygiene and Tropical Medicine, London, United Kingdom; D Strachan, St George's, University of London, London, United Kingdom.

Global Asthma Network International Data Centres: Auckland: P Ellwood, E Ellwood, I Asher, University of Auckland, Auckland, New Zealand; **Murcia:** V Pérez-Fernández, E Morales, University of Murcia, Murcia, Spain; L García-Marcos, Pediatric Allergy and Pulmonology Units, 'Virgen de la Arrixaca' University Children's Hospital, University of Murcia, ARADyAL network and Biomedical Research Institute of Murcia (IMIB-Arrixaca), Murcia, Spain; London: C Rutter, R Silverwood, S Robertson, London School of Hygiene & Tropical Medicine, London, United Kingdom; D Strachan, St George's, University of London, London, United Kingdom.

Global Asthma Network Principal Investigators: Brazil: M Urrutia-Pereira, Federal University of Pampa, UNIPAMPA (Uruguaiana); Cameroon: AE Ndikum, The University of Yaounde 1 (Yaounde); Costa Rica: ME Soto-Quirós, University of Costa Rica (Costa Rica); Greece: K Douros, National and Kapodistrian University of Athens (Athens); Guatemala: L Pérez-Martini, Asociación Guatemalteca de Neumología y Cirugía de Tórax (Guatemala City); Honduras: SM Sosa Ferrari, Instituto Nacional Cardiopulmonar (Tegucigalpa); India: M Sabir, Maharaja Agrasen Medical College Agroha (Bikaner); M Singh, Postgraduate Institute of Medical Education and Research (Chandigarh); V Singh*, Asthma Bhawan (Jaipur); AG Ghoshal, National Allergy Asthma Bronchitis Institute (Kolkata (19)); TU Sukumaran, PIMS Thiruvalla (Kottayam); S Awasthi, King George's Medical University (Lucknow); PA Mahesh, JSS University (Mysuru); SK Kabra, All India Institute of Medical Sciences (New Delhi); S Salvi, Chest Research Foundation (Pune); Iran: M Tavakol, Alborz University of Medical Sciences (Karaj); N Behniafard, Shahid Sadoughi University of Medical Sciences (Yazd); Kosovo: I Bucaliu-Ismajli, The principal center of family care (Ferizaj); L Pajaziti, (Gjakova); V Gashi, American Hospital in Kosovo (Gjilan); LN Ahmetaj*, University Hospital of Prishtina (Prishtina); V Zhjeqi, University of Prishtina (Prizren); Mexico: MG Sanchez Coronel, COMPEDIA (Colegio Mexicano de Pediatras (Aguascalientes); HL Moreno Gardea, Hospital Angeles Chihuahua (Chihuahua); G Ochoa-Lopez, Department of Pediatric Allergology (Ciudad Juárez); R García-Almaráz, Hospital Infantil de Tamaulipas (Ciudad Victoria); JA Sacre Hazouri, Instituto Privado de Alergia, (Córdoba); DD Hernández-Colín, Hospital Civil De Guadalajara Juan I Menchaca (Guadalajara); N Rodriguez-Perez, Instituto de Ciencias y Estudios Superiores de Tamaulipas (Matamoros); JV Mérida-Palacio, Centro de Investigacion de Enfermedades Alergicas y Respiratorias (Mexicali); BE Del Río Navarro*, Service of Allergy and Clinical immunology, Hospital Infantil de México (Mexico City North); LO Hernández-Mondragón, CRIT de Michoacán (Michoacán); Md Juan Pineda, Universidad de Guadalajara (Puerto Vallarta); Bd Ramos García, Instituto Mexicano del Seguro Social (San Luis Potosí); AJ Escalante-Dominguez, Hospital General Tijuana [Isesalud] (Tijuana); EM Navarrete-Rodriguez, Hospital Infantil de Mexico Federico Gomez (Toluca Urban); FJ Linares-Zapién, Centro De Enfermedades Alergicas Y Asma de Toluca (Toluca Rural); J Santos Lozano, Medica san Angel (Xalapa); New Zealand: I Asher, University of Auckland (Auckland); Nicaragua: JF Sánchez, Hospital Infantil Manuel de Jesús Rivera (Managua); Nigeria: AG Falade, University of Ibadan and University College Hospital (Ibadan); Poland: G Brożek, Medical University of Silesia (Katowice); South Africa: HJ Zar, SA MRC Unit on Child & Adolescent Health (Cape Town); Spain: A Bercedo Sanz, Cantabrian Health Service (Cantabria); L García-Marcos*, Pediatric Allergy and Pulmonology Units, 'Virgen de la Arrixaca' University Children's Hospital, University of Murcia, ARADyAL network and Biomedical Research Institute of Murcia (IMIB-Arrixaca), Murcia, Spain (Cartagena); A López-Silvarrey Varela, Fundacion Maria Jose Jove (La Coruña); J Pellegrini Belinchon, Universidad de Salamanca (Salamanca); Sri Lanka: JC Ranasinghe, Teaching Hospital Peradeniya (Anuradhapura); ST Kudagammana, University of Peradeniya (Peradeniya); Syrian Arab Republic: G Alkhayer, Damascus Private University (Damascus); G Dib, Lattakia University (Lattakia 13-14); Y Mohammad*, National Center for research and training for chronic respiratory disease and co morbidities (Lattakia 6-7); Taiwan: J-L Huang, Chang Gung University (Taipei); Thailand: P Vichyanond*, Mahidol University (Bangkok).

* National Coordinators

Global Asthma Network Adult Age Group Principal Investigators not named above:

Cameroon: GA Ajeagah, The University of Yaounde 1 (Yaounde); Costa Rica: M Soto-Martinez, University of Costa Rica (Costa Rica); Greece: K Priftis, National and Kapodistrian University of Athens (Athens); Guatemala: M Cohen-Todd, Asociacion Guatemalteca De Neumologia Y Cirugia De Torax (Guatemala City); Honduras: J Sanchez, Instituto Nacional Cardiopulmonar (Tegucigalpa); India: SK Kochar, Sardar Patel Medical College (Bikaner); N Singh, Asthma Bhawan (Jaipur); N Sit, National Allergy Asthma Bronchitis Institute (Kolkata (19)); S Sinha, All India Institute of Medical Sciences (New Delhi); M Barne, Chest Research Foundation (Pune); Kosovo: B Ajeti, The Principal center of Family Care (Ferizaj); LH Lleshi, (Gjakova); V Lokaj-Berisha, University of Prishtina (Prizren); Mexico: Md Ambriz-Moreno, (Matamoros); OJ Saucedo-Ramirez, Hospital Angeles Pedregal (Mexico City North); CA Jiménez González, Universidad Autonoma of San Luis Potosí (San Luis Potosí); Taiwan: K-W Yeh, (Taipei); Thailand: S Chinratanapisit, Bhumibol Adulyadej Hospital (Bangkok).

Global Asthma Network National Co-ordinators not named above: Brasil: D Solé, Escola Paulista de Medicina, Federal University of São Paulo, São Paulo.

ISAAC Phase III Principal Investigators: Costa Rica: ME Soto-Quirós*, University of Costa Rica (Costa Rica); India: M Sabir, Maharaja Agrasen Medical College Agroha (Bikaner); L Kumart, Department of Pediatrics (Chandigarh); V Singh, Asthma Bhawan (Jaipur); T Sukumaran, PIMS Thiruvalla (Kottayam); S Awasthi, King George's Medical University (Lucknow); SK Sharma, All India Institute of Medical Sciences (New Delhi (7)); NM Hanumante, Ruby Hall Clinic (Pune); Mexico: R García-Almaráz, Hospital Infantil de Tamaulipas (Ciudad Victoria); JV Merida-Palacio, Centro de Investigacion de Enfermedades Alergicas y Respiratorias (Mexicali Valley); BE Del-Río-Navarro, Service of Allergy and Clinical immunology, Hospital Infantil de México (Ciudad de México (1)); FJ Linares-Zapién, Centro De Enfermedades Alergicas Y Asma de Toluca (Toluca); New Zealand: MI Asher*, University of Auckland (Auckland); Nicaragua: JF Sánchez*, Hospital Infantil Manuel de Jesús Rivera (Managua); Nigeria: BO Onadeko, (Ibadan); South Africa: HJ Zar*, University of Cape Town (Cape Town); Spain: L García-Marcos*, Pediatric Allergy and Pulmonology Units, 'Virgen de la Arrixaca' University Children's Hospital, University of Murcia, ARADyAL network and Biomedical Research Institute of Murcia (IMIB-Arrixaca), Murcia, Spain (Cartagena); A López-Silvarrey Varela, Fundacion Maria Jose Jove (A Coruña); Syria: Y Mohammad, National Center for Research and Training in Chronic Respiratory Diseases -Tishreen University (Lattakia); Taiwan: J-L Huang*, Chang Gung University (Taipei); Thailand: P Vichyanond*, Mahidol University (Bangkok).

* National Coordinators

† Deceased

ISAAC Phase III National Co-ordinators not named above: Mexico: M Baeza-Bacab, University Autónoma de Yucatán, Yucatán; Syrian Arab Republic: S Mohammad, Tishreen University, Lattakia.

ISAAC Phase I Principal Investigators: Costa Rica: ME Soto-Quirós*, University of Costa Rica (Costa Rica); Greece: CH Gratziou*, National Kapodistrian University of Athens (Athens); India: L Kumar, Department of Pediatrics (Chandigarh); T Sukumaran, PIMS Thiruvalla (Kottayam); K Chopra, Maulana Azad Medical College (New Delhi (7)); NM Hanumante, Ruby Hall Clinic (Pune); New Zealand: MI Asher*, University of Auckland (Auckland); Nigeria: BO Onadeko, (Ibadan); Spain: L García-Marcos*, Pediatric Allergy and Pulmonology Units, 'Virgen de la Arrixaca' University Children's Hospital, University of Murcia, ARADyAL network and Biomedical Research Institute of Murcia (IMIB-Arrixaca), Murcia, Spain (Cartagena); Taiwan: K-H Hsieh†, Chang Gung Children's Hospital (Taipei); Thailand: P Vichyanond*, Mahidol University (Bangkok); South Africa: R Erlich, University of Cape Town (Cape Town);

* National Coordinators

† Deceased

ISAAC Phase I National Co-ordinators not named above: India: J Shah, Jaslok Hospital & Research Centre, Mumbai.

References

- 1 <u>http://www.globalasthmanetwork.org</u>
- 2 Ellwood P, Asher MI, Billo NE, Bissell K, Chiang CY, Ellwood EM, et al. The Global Asthma Network rationale and methods for Phase I global surveillance: prevalence, severity, management and risk factors. Eur Respir J 2017;49:1601635.
- 3 The Global Asthma Report 2011. Paris, France: The International Union Against Tuberculosis and Lung Disease; 2011. ISBN: 978-2-914365-83-3.
- 4 Lai CKW, Beasley R, Crane J, Foliaki S, Shah J, Weiland S; ISAAC Phase Three Study Group. Global variation in the prevalence and severity of asthma symptoms: Phase Three of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax 2009;64:476–483.
- 5 Pearce N, Aït-Khaled N, Beasley R, Mallol J, Keil U, Mitchell E, et al. Worldwide trends in the prevalence of asthma symptoms: phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax. 2007;62(9):758-66.
- 6 Sembajwe G, Cifuentes M, Tak SW, Kriebel D, Gore R, Punnett L. National income, selfreported wheezing and asthma diagnosis from the World Health Survey. Eur Respir J 2010;35:279-86.
- 7 The Global Asthma Report 2018. Auckland, New Zealand: Global Asthma Network; 2018. ISBN: 978-0-473-46523-0 (PRINT) | 978-0-473-46524-7 (ELECTRONIC).
- 8 Asher I, Garcia-Marcos L, Pearce N, Strachan D. Trends in worldwide asthma prevalence. Eur Respir J 2020 (in press).
- 9 <u>https://www.who.int/medicines/publications/essentialmedicines/en/</u>
- 10 The Global Asthma Report 2014. Auckland, New Zealand: Global Asthma Network; 2014. ISBN: 978-0-473-29125-9 (PRINT) | 978-0-473-29126-6 (ELECTRONIC). Chapters 8-10.
- 11 Asher I, Haahtela T, Selroos O, et al. Global Asthma Network survey suggests more national asthma strategies could reduce burden of asthma. Allergol Immunopathol 2017;45: 105-114.
- 12 Bissell K, Ellwood P, Ellwood E, Chiang CY, Marks GB, El Sony A, et al. Essential medicines at the national level: the Global Asthma Network's essential asthma medicines survey 2014. Int J Environ Res Public Health 2019;16:605.
- 13 Ellwood P, Ellwood E, Asher I. Asthma management guidelines and strategies who has them? Am J Respir Crit Care Med 2014; 189: Abstract issue.
- 14 Ellwood P, Asher MI, Ellwood E and the Global Asthma Network Steering Group. Manual for Global Surveillance: Prevalence, Severity and Risk Factors. Global Asthma Network Data Centre, Auckland, New Zealand, 2015. ISBN 978-0-473-31442-2.
- 15 Ellwood P, Williams H, Ait-Khaled N, Bjorksten B, Robertson C, Group IPIS. Translation of questions: the International Study of Asthma and Allergies in Childhood (ISAAC) experience. Int J Tuberc Lung Dis 2009;13:1174-82.

- 16 Crane J, Mallol J, Beasley R, Stewart A, Asher MI, International Study of A, et al. Agreement between written and video questions for comparing asthma symptoms in ISAAC. Eur Respir J 2003;21:455-61.
- 17 Burney PGJ, Luczynska C, Chinn S, Jarvis D. The European Community Respiratory Health Survey. Eur Respir J 1994;7:954-60.
- 18 Asher MI, Montefort S, Björkstén B, Lai CK, Strachan DP, Weiland SK, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet 2006;368:733-43.
- 19 Sole D, Rosario Filho N, Sarinho EC, Silva AR, Britto M, Riedi C, et al. Prevalence of asthma and related symptoms in adolescents: findings from 3 surveys. J Investig Allergol Clin Immunol 2015;25:73-4.
- 20 Mallol J, Aguirre V, Mallol-Simmonds M, Matamala-Bezmalinovic A, Calderon-Rodriguez L, Osses-Vergara F. Changes in the prevalence of asthma and related risk factors in adolescents: Three surveys between 1994 and 2015. Allergol Immunopathol 2019;47:313-21.
- 21 Chinratanapisit S, Suratannon N, Pacharn P, Sritipsukho P, Vichyanond P. Prevalence and severity of asthma, rhinoconjunctivitis and eczema in children from the Bangkok area: The Global Asthma Network (GAN) Phase I. Asian Pac J Allergy Immunol 2019;37:226-31.
- 22 Del-Rio-Navarro BE, Navarrete Rodríguez EM, Berber A, Reyes-Noriega N, García-Marcos L, et al. The burden of asthma in an inner-city area: A historical review 10 years after ISAAC. World Allergy Org J 2020;13:100092.
- 23 Del-Rio-Navarro BE, Berber A, Noriega NR, Navarrete Rodríguez EM, García Almaráz R, Mérida Palacio JV, et al. What are the time trends in the prevalence of asthma symptoms in Mexico? Allergol Immunopathol 2020 (in press).

Figure legends

Figure 1 Global Asthma Network Centres

Centres registered with GAN identifying those that completed data collection before end of May 2020 (red); registered centres expected to complete GAN Phase I later (green); centres collaborating with GAN but not expected to contribute Phase I data (yellow).

Figure 2 Overlap of GAN and ISAAC Centres

Centres that completed GAN Phase I checks before 31 May 2020 (red); GAN Phase I centres included in ISAAC Phase III but not ISAAC Phase I (blue); GAN Phase I centres included in ISAAC Phase I and ISAAC Phase III (black*); ISAAC Phase III only centres (white).

* Athens, Greece contributed data to GAN and ISAAC Phase I, but not ISAAC Phase III.

	G	AN Phase I cent	res	ISAAC Phase	e III centres*	ISAAC Phas	se I centres*
Questionnaire module	6-7	13-14	Adults	6-7	13-14	6-7	13-14
Symptoms:							
Asthma (written)	41	53	40	144 [17]	233 [21]	91 [9]	155 [12]
Asthma (video)	NA	29	NA	NA	139 [8]	NA	99 [3]
Rhinoconjunctivitis	41	53	NA	144 [17]	233 [21]	91 [9]	155 [12]
Eczema	41	53	40	142 [17]	231 [21]	91 [9]	155 [12]
Risk factors:							
ISAAC Phase 3 questions	40	52	38	75 [17]	122 [21]	ND	ND
Active smoking	NA	52	38	ND	ND	ND	ND
Perinatal questions	39	NA	NA	ND	ND	ND	ND
Indoor environment	39	NA	38	ND	ND	ND	ND
Asthma-related:							
Management (now)	41	53	40	ND	ND	ND	ND
Management (infancy)	39	NA	NA	ND	ND	ND	ND
School absence	41	53	40	ND	ND	ND	ND
Work absence	NA	NA	40	ND	ND	ND	ND
Hospitalisation	41	53	40	ND	ND	ND	ND

Table 1 Number of study centres contributing data for each GAN Phase I module and age-group, with corresponding data for ISAAC Phases I and III

* Numbers of centres also participating in GAN Phase I in parentheses.

NA Not applicable (module not included for that age group)

ND No data (module not included in ISAAC data collection)

			6-7-yea	r-olds					13-14-ye	ar-olds			Adults					
	Symptoms		Risk factors		Management		Symptoms		Risk fac	tors	Manage	ment	Sympt	oms	Risk fa	ctors	Manag	ement
Centre name	Р	S	Р	S	Р	S	Р	S	Р	S	Р	S	Р	S	Р	S	Р	S
Yaounde	722	27	722	27	703	27	1066	22	1066	22	1056	22	860	32	832	32	824	32
Ibadan	0	0	0	0	0	0	2897	23	2894	23	2810	23	2321	23	2321	23	2217	23
Cape Town	0	0	0	0	0	0	3979	29	3976	29	3879	29	0	0	0	0	0	0
Taipei	3036	25	3036	25	3034	25	3474	24	3465	24	3464	24	9689	49	9673	49	9594	49
Bangkok	3067	7	3067	7	3063	7	3206	6	3201	6	3084	6	5418	13	5416	13	5311	13
Yazd	0	0	0	0	0	0	5141	48	5141	48	5141	48	0	0	0	0	0	0
Karaj	572	39	0	0	572	39	754	42	0	0	754	42	1175	75	0	0	1175	75
Lattakia	1115	9	1078	9	1111	9	1215	10	1214	10	1203	10	0	0	0	0	0	0
Damascus	0	0	0	0	0	0	1100	11	1100	11	1100	11	0	0	0	0	0	0
Kottayam	2099	50	2099	50	2085	50	2090	20	2088	20	2050	20	6940	69	6937	69	6743	69
New Delhi	2516	54	2516	54	2516	54	3024	59	3024	59	3024	59	9449	113	9449	113	9010	113
Chandigarh	2473	57	2473	57	2473	57	3000	54	3000	54	2999	54	10386	111	10386	111	10384	111
Bikaner	2600	45	2600	45	2551	45	2702	33	2702	33	2702	33	10495	78	10495	78	10473	78
Jaipur	2296	44	2296	44	2250	44	3060	57	3057	57	2977	57	8933	101	8902	101	8524	101
Lucknow	2969	32	2969	32	2931	32	2968	31	2969	31	2933	31	11820	63	11786	63	11405	63
Kolkata	0	0	0	0	0	0	2998	37	2998	37	2886	37	7823	91	7818	91	7547	91
Pune	2404	26	2404	26	2403	26	3030	34	3030	34	3021	34	8000	60	7994	60	7909	60
Mysuru (Mysore)	2730	30	2730	30	2730	30	3051	29	3051	29	3051	29	11178	59	11178	59	11177	59
Peradeniya	1492	12	1492	12	1455	12	1696	11	1696	11	1547	11	0	0	0	0	0	0
Anuradhapura	2180	10	2180	10	2120	10	2986	10	2989	10	2638	10	0	0	0	0	0	0
Uruguaiana	0	0	0	0	0	0	1058	17	1052	17	1057	17	896	17	896	17	884	17
Costa Rica	1936	34	1936	34	1936	34	1338	33	1338	33	1316	33	3272	67	3272	67	3102	67
Guatemala City	1072	39	1072	39	1071	39	1420	42	1408	42	1400	42	1078	30	1078	30	1055	29
Tegucigalpa	361	22	361	22	359	22	1431	65	1431	65	1415	65	254	10	254	10	252	10
Mexico City North	2515	58	2515	58	2498	58	3375	9	3370	9	3375	9	5231	66	5219	66	5104	66
Guadalajara	2082	21	2082	21	2075	21	2519	13	2518	13	2516	13	489	20	487	20	483	20

 Table 2
 Number of participants (P) and number of schools (S) responding to each GAN module by study centre and age-group.

Mexicali	2001	37	2001	37	1999	37	2479	20	2464	20	2469	20	2436	41	2427	41	2427	41
Ciudad Victoria	2444	20	2444	20	2439	20	2468	8	2465	8	2467	8	6239	28	6202	28	6149	28
San Luis Potosí	2108	28	2108	28	2108	28	2580	19	2580	19	2579	19	2835	27	2833	27	2801	27
Tijuana	2082	47	2082	47	2072	47	2601	13	2595	13	2577	13	1397	26	1395	26	1376	26
Toluca Urban	2712	21	2712	21	2702	21	2650	6	2642	6	2643	6	6162	27	6122	27	6072	27
Toluca Rural	2975	17	2976	17	2974	17	3122	16	3114	16	3091	16	7587	33	7583	33	7470	33
Chihuahua	1969	33	1969	33	1962	33	2180	7	2103	7	2161	7	0	0	0	0	0	0
Ciudad Juárez	2117	39	2118	39	2114	39	2443	16	2439	16	2426	16	2610	37	2598	37	2601	37
Michoácan	2166	39	2166	39	2156	39	2504	14	2502	14	2503	14	2232	39	2232	39	2206	39
Xalapa	3716	83	3717	83	3712	83	3339	21	3335	21	3327	21	0	0	0	0	0	0
Còrdoba	2746	60	2746	60	2738	60	2991	25	2980	25	2989	25	2839	35	2832	35	2829	35
Puerto Vallarta	2241	46	2241	46	2238	46	2439	15	2439	15	2428	15	0	0	0	0	0	0
Aguascalientes	3175	19	3176	19	3165	19	3336	19	3334	19	3331	19	2907	33	2898	33	2861	33
Matamoros	806	24	806	24	799	24	2892	12	2882	12	2865	12	1315	24	1306	24	1298	24
Managua	3162	59	3162	59	3127	59	3131	50	3126	50	2973	50	0	0	0	0	0	0
Prishtina	0	0	0	0	0	0	1054	14	1056	14	1052	14	2006	14	2006	14	1977	14
Gjakova	0	0	0	0	0	0	676	5	676	5	676	5	1352	5	1352	5	1350	5
Prizren	0	0	0	0	0	0	1427	10	1427	10	1427	10	2712	10	0	0	2699	10
Gjilan	0	0	0	0	0	0	1200	6	1200	6	1200	6	1835	6	1835	6	1834	6
Ferizaj	0	0	0	0	0	0	890	9	890	9	885	9	1371	9	1372	9	1328	9
Katowice	1462	36	1462	36	1460	36	3185	29	3184	29	3180	29	2220	35	2219	35	2201	35
Auckland	1538	22	1538	22	1538	22	1885	7	1885	7	1860	7	3002	29	2994	29	2986	29
Athens	0	0	0	0	0	0	1934	20	1934	20	1934	20	1897	20	1897	20	1897	20
Cartagena	3509	61	3509	61	3496	61	3436	26	3430	26	3428	26	6961	60	6956	60	6832	60
Salamanca	2388	51	2388	51	2387	51	3485	31	3484	31	3481	31	0	0	0	0	0	0
Cantabria	2841	75	2841	75	2836	75	4381	47	4372	47	4374	47	0	0	0	0	0	0
A Coruña	3407	48	3407	48	3407	48	3462	26	3461	26	3455	26	0	0	0	0	0	0
All centres	91802	1506	91197	1467	91365	1506	132748	1260	131777	1218	131179	1260	177622	1685	173452	1600	174367	1684

			GAN Ph	ase l		ISAA	C Phase II		ISAAC Phase I			
		Survey	R	esponse	(%)	Survey	Respo	nse (%)	Survey	Respo	nse (%)	
Country	Centre name	years	6-7	13-14	Adult*	years	6-7	13-14	years	6-7	13-14	
Cameroon	Yaounde	2018-19	53.8	99.9	34.6 ^a							
Nigeria	Ibadan	2018	-	85.0	79.5 ^c	2001-02		99.7	1995		76.4	
South Africa	Cape Town	2017	-	84.4	d	2002		83.4	1995		82.8	
Taiwan	Taipei	2016-17	76.3	93.0	84.5 ^a	2001-02	96.8	95.9	1995	92.2	93.2	
Thailand	Bangkok	2017-18	86.3	97.9	86.1 ª	2001	72.8	93.8	1995-96	90.8	74.8	
Iran	Yazd	2020	-	71.3	d							
Iran	Karaj	2019-20	72.0	71.9	88.6 ^a							
Syrian Arab Republic	Lattakia	2019	93.0	99.6	d	2001-03	99.1	99.8				
Syrian Arab Republic	Damascus	2018	-	91.7	d							
India	Kottayam	2017-18	68.4	85.3	97.5 ^ª	2001-03	96.4	98.5	1994-95	78.1	90.7	
India	New Delhi	2017-18	80.9	100.0	85.7ª	2001-02	82.4	86.7	1994-95	99.2	100	
India	Chandigarh	2017-18	100.0	100.0	95.5 ^ª	2001-02		99.4	1994-95	94.0	97.4	
India	Bikaner	2017-18	86.7	90.1	99.8ª	2001		95.4				
India	Jaipur	2017-18	75.8	98.7	84.4 ^ª	2001	75.4	87.4				
India	Lucknow	2017	91.3	94.0	99.7 ^a	2001-02	85.7	75.0				
India	Kolkata	2017-18	-	99.9	80.2 ^c							
India	Pune	2017-18	79.8	99.6	81.4ª	2001-02	90.4	70.8	1994-95	99.6	99.8	
India	Mysuru (Mysore)	2017-18	90.9	99.5	97.4 ^ª							
Sri Lanka	Peradeniya	2018	74.6	80.8	d							
Sri Lanka	Anuradhapura	2018	72.7	85.4	d							
Brazil	Uruguaiana	2016-18	-	88.2	76.7 ^c							
Costa Rica	Costa Rica	2017-18	64.5	66.9	e	2001-02	80.9	69.6	1994-95	84.1	91.4	
Guatemala	Guatemala City	2018	32.2	40.6	e							
Honduras	Tegucigalpa	2017-18	76.5	98.0	e							
Mexico	Mexico City North	2015-16	86.7	93.8	55.9ª	2002-03	91.6	99.8				
Mexico	Guadalajara	2016	83.3	90.0	12.1 ^b							

Table 3Response rates for 6-7 & 13-14 year age groups to the written symptom questionnaires in GAN Phase I, ISAAC Phases I and III, by study
centre and age-group. (The adult response rate was estimated on a "per child" basis.*)

Mexico	Mexicali	2015-16	77.0	83.7	32.7ª	2002-03	74.3	93.6			
Mexico	Ciudad Victoria	2015-16	81.5	82.3	78.6ª	2003	73.1	79.5			
Mexico	San Luis Potosí	2015-16	99.4	97.3	36.7ª						
Mexico	Tijuana	2015-16	83.3	86.7	41.4 ^b						
Mexico	Toluca Urban	2015-16	95.7	98.1	65.5ª						
Mexico	Toluca Rural	2015-16	93.0	94.6	69.1ª	2002	89.5	86.1			
Mexico	Chihuahua	2015-16	87.5	87.2	d			0012			
Mexico	Ciudad Juárez	2016-17	84.7	88.8	36.7ª						
Mexico	Michoacán	2016	90.3	92.7	75.8 ^b						
Mexico	Xalapa	2016-17	92.9	90.2	d						
Mexico	Còrdoba	2016	91.5	93.5	30.2ª						
Mexico	Puerto Vallarta	2015-17	93.4	90.3	d						
Mexico	Aguascalientes	2015-16	90.7	95.3	44.0ª						
Mexico	Matamoros	2015-17	80.6	93.3	93.7 ^b						
Nicaragua	Managua	2019 17	87.9	90.5	d	2002	96.0	94.5			
Kosovo	Prishtina	2010	-	99.9	99.9°	2002	50.0	54.5			
Kosovo	Gjakova	2017	-	90.1	100.0 ^c						
Kosovo	Prizren	2018	-	89.0	99.7°						
Kosovo	Gjilan	2017	-	80.0	81.5°						
Kosovo	Ferizaj	2017	-	99.9	81.5 85.1°						
Poland	Katowice	2017-18	36.8	79.1	85.6 ^b						
New Zealand	Auckland	2017-18	63.7	85.5	51.3ª	2001	84.6	92.3	1992-93	90.2	94.6
Greece	Athens	2018-19		85.5 75.5	99.9°	2001	04.0	92.5	1992-95	90.2	94.0 87.0
			- 65 0	73.8		2001 02	72.2	70 C		C 9 F	
Spain	Cartagena	2015-16	65.9		61.5 ^a	2001-02	72.3	79.6	1993	68.5	95.1
Spain	Salamanca	2017-18	73.7	95.0	d						
Spain	Cantabria	2017-18	56.2	77.4	d	2002	72.0	00.0			
Spain	A Coruña	2018-19	71.0	92.1	u	2003	73.8	93.6			

* Adult response rate per child, derived as the percentage of schoolchildren that had one or more adult questionnaires returned, combined across age groups when both age groups were studied:

a) both age groups; b) 6-7-year-olds only; c) 13-14-year-olds only; d) neither age group;

e) adult responses not linked to child identifiers, so no response rate for adults can be derived.

Figure 1 Global Asthma Network Centres

Centres registered with GAN identifying those that completed data collection before end of May 2020 (red); registered centres expected to complete GAN Phase I later (green); centres collaborating with GAN but not expected to contribute Phase I data (yellow).

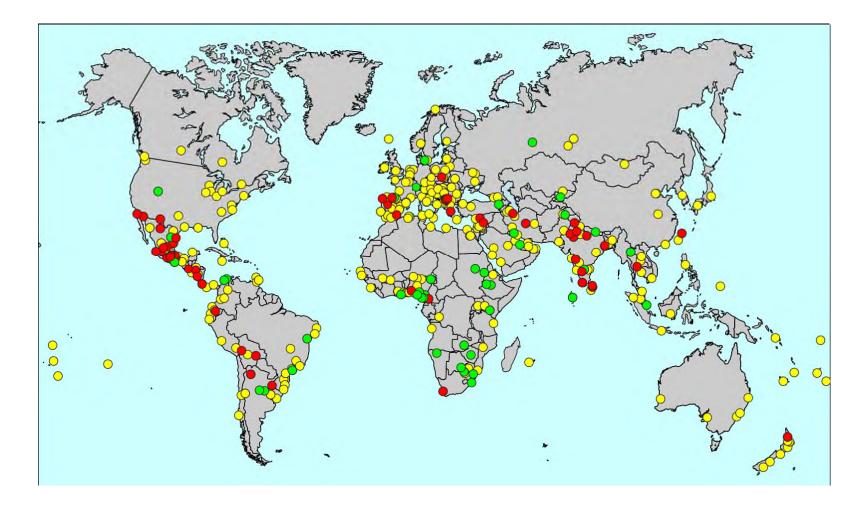


Figure 2 Overlap of GAN Phase I and ISAAC Centres

Centres that completed GAN Phase I checks before 31 May 2020 (red); GAN Phase I centres included in ISAAC Phase III but not ISAAC Phase I (blue); GAN Phase I centres included in ISAAC Phase I and ISAAC Phase III (black*); ISAAC Phase III only centres (white).

* Athens, Greece contributed data to GAN and ISAAC Phase I, but not ISAAC Phase III.

