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☐ Initial submission ☐ Revised version ☒ Final submission

Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form is intended for publication with all accepted life science papers and provides structure for consistency and transparency in reporting. Every life science submission will use this form; some list items might not apply to an individual manuscript, but all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Experimental design

1. Sample size

Describe how sample size was determined.

This study is a meta-analysis of asthma genome-wide association studies (GWAS) that was conducted in the framework of the Trans-National Asthma Genetic Consortium (TAGC). This consortium brought together worldwide groups of investigators with genome-wide data available in a total of 142,486 individuals (23,948 cases, 118,538 controls) of diverse ancestries, thus providing enough power to discover new asthma loci, based on results from GWAS of similar size for other complex diseases. The sample sizes were reported by the groups forming the consortium.

2. Data exclusions

Describe any data exclusions.

The meta-analysis included a total of 66 GWAS based on HapMap2 imputed SNPs. Imputation, quality control (QC) and analysis was done by each group independently. Data (summary statistics for association between each SNP and asthma and QC criteria for each SNP) on a predefined set of 3,952,683 autosomal SNPs was shared. From this SNP panel, we excluded 620,238 ambiguous SNPs (for which the DNA strand cannot be determined) and 501,370 SNPs that did not pass the QC criteria for all 66 studies, thus making a total of 2,831,075 SNPs for the meta-analysis. To minimize the false-positive findings and to obtain robust results, we examined the combined results for 2 million SNPs for which at least two-thirds of the studies contributed to the meta-analysis (ie SNPs passed QC in at least two-thirds of the studies).

3. Replication

Describe whether the experimental findings were reliably reproduced.

Because the meta-analysis included almost all asthma GWAS that had been conducted worldwide when TAGC was formed, no reasonable replication could be performed. This meta-analysis combined summary statistics from various populations and, thus, took into account different sample sizes, SNP effect sizes, variances and allele frequencies from each of the populations under investigation. We assesed whether the effect sizes of newly discovered variants in this analysis were not statistically different across studies by testing for heterogeneity between them.

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.

Randomization does not apply to our meta-analysis of summary statistics of asthma GWAS shared by the TAGC consortium. This is an observational study.

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

The meta-analysis was done by combining summary statistics and applying QC criteria (based on mathematical grounds) in a systematic manner for all studies. This is an observational study where no blinding was applied.

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒ A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☒	☐ A statement indicating how many times each experiment was replicated
☐	☒ The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
☐	☒ A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒ The test results (e.g. *P* values) given as exact values whenever possible and with confidence intervals noted
☐	☒ A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☒	☐ Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.

The meta-analysis was done using Stata version 14.1 (STATA Corp., College Station, Texas, USA). All sofwtare are indicated in the URL section.
Approximate conditional analysis was done using the Genome-wide Complex Trait Analysis (GCTA) software (see URLs)
The analysis of co-localization of asthma risk variants with epigenetic marks was done using the Uncovering Enrichment through Simulation pipeline (see URLs)
Connectivity between asthma-associated loci was investigated using the GRAIL software (see URLs)
The statistical analysis of pleiotropy was done using the statistical software R

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.

The summary statistics of the meta-analysis that support the findings of this study are available through a link from the GWAS Catalog entry for the TAGC study on the EMBL-EBI (European Bioinformatics Institute) web site (https://www.ebi.ac.uk/gwas/ downloads/summary-statistics).

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).

NA

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.

NA

b. Describe the method of cell line authentication used.

NA

c. Report whether the cell lines were tested for mycoplasma contamination.

NA

d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.

NA

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.	NA

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.	The study involved combining summary statistics from individual analyses of association of SNPs with asthma performed by each participating group. An overview of all studies included in the meta-analysis is presented in Supplementary Table 1. Methods used for the individual analyses are shown in Supplementary Table 2. A brief description of the participants in each study is presented in the Supplementary Note. As stated in the Online Methods, all subjects provided informed consent to participate in genetic studies and local ethics committees for each of the individual studies approved the study protocol.